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PRESIDENT'S MALARIA INITIATIVE

INTEGRATED VECTOR MANAGEMENT PROGRAMS FOR MALARIA VECTOR CONTROL (2012 UPDATE)

PROGRAMMATIC ENVIRONMENTAL ASSESSMENT

VOLUME 2 OF 2: ANNEXES

September 2011/Revised September 2012

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DISCLAIMER

Until and unless this document is approved by USAID as a 22 CFR 216 Programmatic Environmental Assessment, the findings and analysis presented herein do not necessarily reflect the views of the United States Agency for International Development or the United States Government.

ANNEX A: USAID ENVIRONMENTAL PROCEDURES[1] (22 CFR 216)

Text of Title 22, Code of Federal Regulations, Part 216

These procedures have been revised based on experience with previous ones agreed to in settlement of a law suit brought against the Agency in 1975. The Procedures are Federal Regulations and therefore, it is imperative that they be followed in the development of Agency programs.

In preparing these Regulations, some interpretations and definitions have been drawn from Executive Order No. 12114 of 4 January 1979, on the application of the National Environmental Policy Act (NEPA) to extraterritorial situations. Some elements of the revised regulations on NEPA issued by the President's Council on Environmental Quality have also been adopted. Examples are: The definition of significant impact, the concept of scoping of issues to be examined in a formal analysis, and the elimination of certain USAID activities from the requirement for environmental review.

In addition, these procedures: 1) provide advance notice that certain types of projects will automatically require detailed environmental analysis thus eliminating one step in the former process and permitting early planning for this activity; 2) permit the use of specially prepared project design considerations or guidance to be substituted for environmental analysis in selected situations; 3) advocate the use of indigenous specialists to examine pre-defined issues during the project design stage; 4) clarify the role of the Bureau's Environmental Officer in the review and approval process, and 5) permit in certain circumstances, projects to go forward prior to completion of environmental analysis. Note that only minimal clarification changes have been made in those sections dealing with the evaluation and selection of pesticides to be supported by USAID in projects or of a non-project assistance activity.

Sec. Topic

216. 1 Introduction

216. 2 Applicability of procedures

[1] Title 22 of the Code of Federal Regulations, Part 216, with preamble, is presented here in its entirety. Spelling errors have been corrected from the original to facilitate word searching. This version represents the most recent revisions, as of October 9, 1980.

216. 3 Procedures

216. 4 Private applicants

216. 5 Endangered species

216. 6 Environmental assessments

216. 7 Environmental impact statements

216. 8 Public hearings

216. 9 Bilateral and multi-lateral studies and concise reviews of environmental issues

216.10 Records and reports

Authority: 42 U.S.C. 4332; 22 U.S.C. 2381.

Source: 41 FR 26913, June 30, 1976, unless otherwise noted.

§216.1 INTRODUCTION

(a) Purpose

In accordance with sections 118(b) and 621 of the Foreign Assistance Act of 1961, as amended, (the FAA) the following general procedures shall be used by A.I.D. to ensure that environmental factors and values are integrated into the A.I.D. decision-making process. These procedures also assign responsibility within the Agency for assessing the environmental effects of A.I.D.'s actions. These procedures are consistent with Executive Order 12114, issued January 4, 1979, entitled Environmental Effects Abroad of Major Federal Actions, and the purposes of the National Environmental Policy Act of 1970, as amended (42 U.S.C. 4371 et seq.) (NEPA). They are intended to implement the requirements of NEPA as they affect the A.I.D. program.

(b) Environmental Policy

In the conduct of its mandate to help upgrade the quality of life of the poor in developing countries, A.I.D. conducts a broad range of activities. These activities address such basic problems as hunger, malnutrition, overpopulation, disease, disaster, deterioration of the environment and the natural resource base, illiteracy as well as the lack of adequate housing and transportation. Pursuant to the FAA, A.I.D. provides development assistance in the form of technical advisory services, research, training, construction and commodity support. In addition, A.I.D. conducts programs under the Agricultural Trade Development and Assistance Act of 1954 (Pub. L. 480) that are designed to combat hunger, malnutrition and to facilitate economic development. Assistance programs are carried out under the foreign policy guidance of the Secretary of State and in cooperation with the governments of sovereign states. Within this framework, it is A.I.D. policy to:

(1) Ensure that the environmental consequences of A.I.D.-financed activities are identified and considered by A.I.D. and the host country prior to a final decision to proceed and that appropriate environmental safeguards are adopted;

(2) Assist developing countries to strengthen their capabilities to appreciate and effectively evaluate the potential environmental effects of proposed development strategies and projects, and to select, implement and manage effective environmental programs;

(3) Identify impacts resulting from A.I.D.'s actions upon the environment, including those aspects of the biosphere which are the common and cultural heritage of all mankind; and

(4) Define environmental limiting factors that constrain development and identify and carry out activities that assist in restoring the renewable resource base on which sustained development depends.

(c) Definitions

(1) CEQ Regulations. Regulations promulgated by the President's Council on Environmental Quality (CEQ) (Federal Register, Volume 43, Number 230, November 29, 1978) under the authority of NEPA and Executive Order 11514, entitled Protection and Enhancement of Environmental Quality (March 5, 1970) as amended by Executive Order 11991 (May 24, 1977).

(2) Initial Environmental Examination. An Initial Environmental Examination is the first review of the reasonably foreseeable effects of a proposed action on the environment. Its function is to provide a brief statement of the factual basis for a Threshold Decision as to whether an Environmental Assessment or an Environmental Impact Statement will be required.

(3) Threshold Decision. A formal Agency decision which determines, based on an Initial Environmental Examination, whether a proposed Agency action is a major action significantly affecting the environment.

(4) Environmental Assessment. A detailed study of the reasonably foreseeable significant effects, both beneficial and adverse, of a proposed action on the environment of a foreign country or countries.

(5) Environmental Impact Statement. A detailed study of the reasonably foreseeable environmental impacts, both positive and negative, of a proposed A.I.D. action and its reasonable alternatives on the United States, the global environment or areas outside the jurisdiction of any nation as described in §216.7 of these procedures. It is a specific document having a definite format and content, as provided in NEPA and the CEQ Regulations. The required

form and content of an Environmental Impact Statement is further described in §216.7 infra

(6) Project Identification Document (PID). An internal A.I.D. document which initially identifies and describes a proposed project.

(7) Program Assistance Initial Proposal (PAIP). An internal A.I.D. document used to initiate and identify proposed non-project assistance, including commodity import programs. It is analogous to the PID.

(8) Project Paper (PP). An internal A.I.D. document which provides a definitive description and appraisal of the project and particularly the plan or implementation.

(9) Program Assistance Approval Document (PAAD). An internal A.I.D. document approving non-project assistance. It is analogous to the PP.

(10) Environment. The term environment, as used in these procedures with respect to effects occurring outside the United States, means the natural and physical environment. With respect to effects occurring within the United States see §216.7(b).

(11) Significant Effect. With respect to effects on the environment outside the United States, a proposed action has a significant effect on the environment if it does significant harm to the environment.

(12) Minor Donor. For purposes of these procedures, A.I.D. is a minor donor to a multidonor project when A.I.D. does not control the planning or design of the multidonor project and either (i) A.I.D.'s total contribution to the project is both less than $1,000,000 and less than 25 percent of the estimated project cost, or (ii) A.I.D.'s total contribution is more than $1,000,000 but less than 25 percent of the estimated project cost and the environmental procedures of the donor in control of the planning of design of the project are followed, but only if the A.I.D. Environmental Coordinator determines that such procedures are adequate.

[45 FR 70244, Oct. 23, 1980]

§216.2 APPLICABILITY OF PROCEDURES

(a) Scope

Except as provided in §216.2(b), these procedures apply to all new projects, programs or activities authorized or approved by A.I.D. and to substantive amendments or extensions of ongoing projects, programs, or activities.

(b) Exemptions

(1) Projects, programs or activities involving the following are exempt from these procedures:

(i) International disaster assistance;

(ii) Other emergency circumstances; and

(iii) Circumstances involving exceptional foreign policy sensitivities.

(2) A formal written determination, including a statement of the justification therefore, is required for each project, program or activity for which an exemption is made under paragraphs (b)(l) (ii) and (iii) of this section, but is not required for projects, programs or activities under paragraph (b)(l)(i) of this section. The determination shall be made either by the Assistant Administrator having responsibility for the program, project or activity, or by the Administrator, where authority to approve financing has been reserved by the Administrator. The determination shall be made after consultation with CEQ regarding the environmental consequences of the proposed program, project or activity.

(c) Categorical Exclusions

(1) The following criteria have been applied in determining the classes of actions included in §216.2(c)(2) for which and Initial Environmental Examination, Environmental Assessment and Environmental Impact Statement generally are not required:

(i) The action does not have an effect on the natural or physical environment;

(ii) A.I.D. does not have knowledge of or control over, and the objective of A.I.D. in furnishing assistance does not require, either prior to approval of financing or prior to implementation of specific activities, knowledge of or control over, the details of the specific activities that have an effect on the physical and natural environment for which financing is provided by A.I.D.;

(iii) Research activities which may have an effect on the physical and natural environment but will not have a significant effect as a result of limited scope, carefully controlled nature and effective monitoring

(2) The following classes of actions are not subject to the procedures set forth in §216.3, except to the extent provided herein:

(i) Education, technical assistance, or training programs except to the extent such programs include activities directly affecting the environment (such as construction of facilities, etc.);

(ii) Controlled experimentation exclusively for the purpose of research and field evaluation which are confined to small areas and carefully monitored;

(iii) Analyses, studies, academic or research workshops and meetings;

(iv) Projects in which A.I.D. is a minor donor to a multidonor project and there is no potential significant effects upon the environment of the United States, areas outside any nation's jurisdiction or endangered or threatened species or their critical habitat;

(v) Document and information transfers;

(vi) Contributions to international, regional or national organizations by the United States which are not for the purpose of carrying out a specifically identifiable project or projects;

(vii) Institution building grants to research and educational institutions in the United States such as those provided for under section 122(d) and Title XII of Chapter 2 of Part I of the FAA (22 USCA §§2151 p. (b) 2220a. (1979));

(viii) Programs involving nutrition, health care or population and family planning services except to the extent designed to include activities directly affecting the environment (such as construction of facilities, water supply systems, waste water treatment, etc.)

(ix) Assistance provided under a Commodity Import Program when, prior to approval, A.I.D. does not have knowledge of the specific commodities to be financed and when the objective in furnishing such assistance requires neither knowledge, at the time the assistance is authorized, nor control, during implementation, of the commodities or their use in the host country.

(x) Support for intermediate credit institutions when the objective is to assist in the capitalization of the institution or part thereof and when such support does not involve reservation of the right to review and approve individual loans made by the institution;

(xi) Programs of maternal or child feeding conducted under Title II of Pub. L. 480;

(xii) Food for development programs conducted by food recipient countries under Title III of Pub. L. 480, when achieving A.I.D.'s objectives in such programs does not require knowledge of or control over the details of the specific activities conducted by the foreign country under such program;

(xiii) Matching, general support and institutional support grants provided to private voluntary organizations (PVOs) to assist in financing programs where A.I.D.'s objective in providing such financing does not require knowledge of or control over the details of the specific activities conducted by the PVO;

(xiv) Studies, projects or programs intended to develop the capability of recipient countries to engage in development planning, except to the extent designed to result in activities directly affecting the environment (such as construction of facilities, etc.); and

(xv) Activities which involve the application of design criteria or standards developed and approved by A.I.D.

(3) The originator of a project. program or activity shall determine the extent to which it is within the classes of actions described in paragraph (c)(2) of this section. This determination shall be made in writing and be submitted with the PID, PAIP or comparable document. This determination, which must include a brief statement supporting application of the exclusion shall be reviewed by the Bureau Environmental Officer in the same manner as a Threshold Decision under §216.3(a)(2) of these procedures.

Notwithstanding paragraph (c)(2) of this section, the procedures set forth in §216.3 shall apply to any project, program or activity included in the classes of actions listed in paragraph (c)(2) of this section, or any aspect or component thereof, if at any time in the design, review or approval of the activity it is determined that the project, program or activity, or aspect or component thereof, is subject to the control of A.I.D. and may have a significant effect on the environment.

(d) Classes of Actions Normally Having a Significant Effect on the Environment

(1) The following classes of actions have been determined generally to have a significant effect on the environment and an Environmental Assessment or Environmental Impact Statement, as appropriate, will be required:

(i) Programs of river basin development;

(ii) Irrigation or water management projects, including dams and impoundments;

(iii) Agricultural land leveling;

(iv) Drainage projects;

(v) Large scale agricultural mechanization;

(vi) New lands development;

(vii) Resettlement projects;

(viii) Penetration road building or road improvement projects;

(ix) Power plants;

(x) Industrial plants;

(xi) Potable water and sewerage projects other than those that are small-scale.

(2) An Initial Environmental Examination normally will not be necessary for activities within the classes described in §216.2(d), except when the originator of the project believes that the project will not have a significant effect on the environment. In such cases, the activity may be subjected to the procedures set forth in §216.3

(e) Pesticides

The exemptions of §216.2(b)(l) and the categorical exclusions of §216.2(c)(2) are not applicable to assistance for the procurement or use of pesticides.

[45 FR 70244, Oct. 23, 1980]

§216.3 PROCEDURES

(a) General Procedures

(1) Preparation of the Initial Environmental Examination.

Except as otherwise provided, an Initial Environmental Examination is not required for activities identified in §216.2(b)(1), (c)(2), and (d). For all other A.I.D. activities described in §216.2(a) an Initial Environmental Examination will be prepared by the originator of an action. Except as indicated in this section, it should be prepared with the PID or PAIP. For projects including the procurement or use of pesticides, the procedures set forth in §216.3(b) will be followed, in addition to the procedures in this paragraph. Activities which cannot be identified in sufficient detail to permit the completion of an Initial Environmental Examination with the PID or PAIP, shall be described by including with the PID or PAIP: (i) An explanation indicating why the Initial Environmental Examination cannot be completed; (ii) an estimate of the amount of time required to complete the Initial Environmental Examination; and (iii) a recommendation that a Threshold Decision be deferred until the Initial Environmental Examination is completed. The responsible Assistant Administrator will act on the request for deferral concurrently with action on the PID or PAIP and will designate a time for completion of the Initial Environmental Examination. In all instances, except as provided in §216.3

(a)(7), this completion date will be in sufficient time to allow for the completion of an Environmental Assessment or Environmental Impact Statement, if required, before a final decision is made to provide A.I.D. funding for the action.

(2) Threshold Decision. (i) The Initial Environmental Examination will include a Threshold Decision made by the officer in the originating office who signs the PID or PAIP. If the Initial Environmental Examination is completed prior to or at the same time as the PID or PAIP, the Threshold Decision will be reviewed by the Bureau Environmental Officer concurrently with approval of the PID or PAIP. The Bureau Environmental Officer will either concur in the Threshold Decision or request reconsideration by the officer who made the Threshold Decision, stating the reasons for the request. Differences of opinion between these officers shall be submitted for resolution to the Assistant Administrator at the same time that the PID is submitted for approval.

(ii) An Initial Environmental Examination, completed subsequent to approval of the PID or PAIP, will be forwarded immediately together with the Threshold Determination to the Bureau Environmental Officer for action as described in this section.

(iii) A Positive Threshold Decision shall result from a finding that the proposed action will have a significant effect on the environment. An Environmental Impact Statement shall be prepared if required pursuant to §216.7. If an impact statement is not required, an Environmental Assessment will be prepared in accordance with §216.6. The cognizant Bureau or Office will record a Negative Determination if the proposed action will not have a significant effect on the environment.

(3) Negative Declaration. The Assistant Administrator, or the Administrator in actions for which the approval of the Administrator is required for the authorization of financing, may make a Negative Declaration, in writing, that the Agency will not develop an Environmental Assessment or an Environmental Impact Statement regarding an action found to have a significant effect on the environment when

(i) a substantial number of Environmental Assessments or Environmental Impact Statements relating to similar activities have been prepared in the past, if relevant to the proposed action, (ii) the Agency has previously prepared a programmatic Statement or Assessment covering the activity in question which has been considered in the development of such activity, or (iii) the Agency has developed design criteria for such an action which, if applied in the design of the action, will avoid a significant effect on the environment.

(4) Scope of Environmental Assessment or Impact Statement

(i) Procedure and Content. After a Positive Threshold Decision has been made, or a determination is made under the pesticide procedures set forth in §216.3(b) that an Environmental Assessment or Environmental Impact Statement is required, the originator of the action shall commence the process of identifying the significant issues relating to the proposed action and of determining the scope of the issues to be addressed in the Environmental Assessment or Environmental Impact Statement. The originator of an action within the classes of actions described in §216.2(d) shall commence this scoping process as soon as practicable. Persons having expertise relevant to the environmental aspects of the proposed action shall also participate in this scoping process. (Participants may include but are not limited to representatives of host governments, public and private institutions, the A.I.D. Mission staff and contractors.)

This process shall result in a written statement which shall include the following matters:

(a) A determination of the scope and significance of issues to be analyzed in the Environmental Assessment or Impact Statement, including direct and indirect effects of the project on the environment.

(b) Identification and elimination from detailed study of the issues that are not significant or have been covered by earlier environmental review, or approved design considerations, narrowing the discussion of these issues to a brief presentation of why they will not have a significant effect on the environment.

(c) A description of (1) the timing of the preparation of environmental analyses, including phasing if appropriate, (2) variations required in the format of the Environmental Assessment, and (3) the tentative planning and decision-making schedule; and

(d) A description of how the analysis will be conducted and the disciplines that will participate in the analysis.

(ii) These written statements shall be reviewed and approved by the Bureau Environmental Officer.

(iii) Circulation of Scoping Statement. To assist in the preparation of an Environmental Assessment, the Bureau Environmental Officer may circulate copies of the written statement, together with a request for written comments, within thirty days, to selected federal agencies if that Officer believes comments by such federal agencies will be useful

in the preparation of an Environmental Assessment. Comments received from reviewing federal agencies will be considered in the preparation of the Environmental Assessment and in the formulation of the design and implementation of the project, and will, together with the scoping statement, be included in the project file.

(iv) Change in Threshold Decision. If it becomes evident that the action will not have a significant effect on the environment (i.e., will not cause significant harm to the environment), the Positive Threshold Decision may be withdrawn with the concurrence of the Bureau Environmental Officer. In the case of an action included in §216.2(d)(2), the request for withdrawal shall be made to the Bureau Environmental Officer.

(5) Preparation of Environmental Assessments and Environmental Impact Statement. If the PID or PAIP is approved, and the Threshold Decision is positive, or the action is included in §216.2(d), the originator of the action will be responsible for the preparation of an Environmental Assessment or Environmental Impact Statement as required. Draft Environmental Impact Statements will be circulated for review and comment as part of the review of Project Papers and as outlined further in §216.7 of those procedures. Except as provided in §216.3(a)(7), final approval of the PP or PAAD and the method of implementation will include consideration of the Environmental Assessment or final Environmental Impact Statement.

(6) Processing and Review Within A.I.D.

(i) Initial Environmental Examinations, Environmental Assessments, and final Environmental Impact Statements will be processed pursuant to standard A.I.D. procedures for project approval documents. Except as provided in §216.3(a)(7), Environmental Assessments and final Environmental Impact Statements will be reviewed as an integral part of the Project Paper or equivalent document. In addition to these procedures, Environmental Assessments will be reviewed and cleared by the Bureau Environmental Officer. They may also be reviewed by the Agency's Environmental Coordinator who will monitor the Environmental Assessment process.

(ii) When project approval authority is delegated to field posts, Environmental Assessments shall be reviewed and cleared by the Bureau Environmental Officer prior to the approval of such actions.

(iii) Draft and final Environmental Impact Statements will be reviewed and cleared by the Environmental Coordinator and the Office of the General Counsel.

(7) Environmental Review After Authorization of Financing.

(i) Environmental review may be performed after authorization of a project, program or activity only with respect to subprojects or significant aspects of the project, program or activity that are unidentified at the time of authorization. Environmental review shall be completed prior to authorization for all subprojects and aspects of a project, program or activity that are identified.

(ii) Environmental review should occur at the earliest time in design or implementation at which a meaningful review can be undertaken, but in no event later than when previously unidentified subprojects or aspects of projects, programs or activities are identified and planned. To the extent possible, adequate information to undertake deferred environmental review should be obtained before funds are obligated for unidentified subprojects or aspects of projects, programs or activities. (Funds may be obligated for the other aspects for which environmental review has been completed.) To avoid an irreversible commitment of resources prior to the conclusion of environmental review, the obligation of funds can be made incrementally as subprojects or aspects of projects, programs or activities are identified; or if necessary while planning continues, including environmental review, the agreement or other document obligating funds may contain appropriate covenants or conditions precedent to disbursement for unidentified subprojects or aspects of projects, programs or activities.

(iii) When environmental review must be deferred beyond the time some of the funds are to be disbursed (e.g., long lead times for the delivery of goods or services), the project agreement or other document obligating funds shall contain a covenant or covenants requiring environmental review, including an Environmental Assessment or Environmental Impact Statement, when appropriate, to be completed and taken into account prior to implementation of those subprojects or aspects of the project, program or activity for which environmental review is deferred. Such covenants shall ensure that implementation plans will be modified in accordance with environmental review if the parties decide that modifications are necessary.

(iv) When environmental review will not be completed for an entire project, program or activity prior to authorization, the Initial Environmental Examination and Threshold Decision required under §216.3(a)(l) and (2) shall identify those aspects of the project, program or activity for which environmental review will be completed prior to the time financing is authorized. It shall also include those subprojects or aspects for which environmental review will be deferred, stating the reasons for deferral and the time when environmental review will be

completed. Further, it shall state how an irreversible commitment of funds will be avoided until environmental review is completed. The A.I.D. officer responsible for making environmental decisions for such projects, programs or activities shall also be identified (the same officer who has decision-making authority for the other aspects of implementation). This deferral shall be reviewed and approved by the officer making the Threshold Decision and the officer who authorizes the project, program or activity. Such approval may be made only after consultation with the Office of General Counsel for the purpose of establishing the manner in which conditions precedent to disbursement or covenants in project and other agreements will avoid an irreversible commitment of resources before environmental review is completed.

(8) Monitoring. To the extent feasible and relevant, projects and programs for which Environmental Impact Statements or Environmental Assessments have been prepared should be designed to include measurement of any changes in environmental quality, positive or negative, during their implementation. This will require recording of baseline data at the start. To the extent that available data permit, originating offices of A.I.D. will formulate systems in collaboration with recipient nations, to monitor such impacts during the life of A.I.D.'s involvement. Monitoring implementation of projects, programs and activities shall take into account environmental impacts to the same extent as other aspects of such projects, programs and activities. If during implementation of any project, program or activity, whether or not an Environmental Assessment or Environmental Impact Statement was originally required, it appears to the Mission Director, or officer responsible for the project, program or activity, that it is having or will have a significant effect on the environment that was not previously studied in an Environmental Assessment or Environmental Impact Statement, the procedures contained in this part shall be followed including, as appropriate, a Threshold Decision, Scoping and an Environmental Assessment or Environmental Impact Statement.

(9) Revisions. If, after a Threshold Decision is made resulting in a Negative Determination, a project is revised or new information becomes available which indicates that a proposed action might be "major" and its effects "significant", the Negative Determination will be reviewed and revised by the cognizant Bureau and an Environmental Assessment or Environmental Impact Statement will be prepared, if appropriate. Environmental Assessments and Environmental Impact Statements will be amended and processed appropriately if there are major changes in the project or program, or if significant new information becomes available which relates to the impact of the project, program or activity on the environment that was not considered at

the time the Environmental Assessment or Environmental Impact Statement was approved.

When ongoing programs are revised to incorporate a change in scope or nature, a determination will be made as to whether such change may have an environmental impact not previously assessed. If so, the procedures outlined in this part will be followed.

(10) Other Approval Documents. These procedures refer to certain A.I.D. documents such as PIDs, PAIPs, PPs and PAADs as the A.I.D. internal instruments for approval of projects, programs or activities. From time to time, certain special procedures, such as those in §216.4, may not require the use of the aforementioned documents. In these situations, these environmental procedures shall apply to those special approval procedures, unless otherwise exempt, at approval times and levels comparable to projects, programs and activities in which the aforementioned documents are used.

(b) Pesticide Procedures

(1) Project Assistance. Except as provided in §216.3 (b)(2), all proposed projects involving assistance for the procurement or use, or both, of pesticides shall be subject to the procedures prescribed in §216.3(b)(l)(i) through (v). These procedures shall also apply, to the extent permitted by agreements entered into by A.I.D. before the effective date of these pesticide procedures, to such projects that have been authorized but for which pesticides have not been procured as of the effective date of these pesticide procedures.

(i) When a project includes assistance for procurement or use, or both, of pesticides registered for the same or similar uses by USEPA without restriction, the Initial Environmental Examination for the project shall include a separate section evaluating the economic, social and environmental risks and benefits of the planned pesticide use to determine whether the use may result in significant environmental impact. Factors to be considered in such an evaluation shall include, but not be limited to the following:

(a) The USEPA registration status of the requested pesticide;

(b) The basis for selection of the requested pesticide;

(c) The extent to which the proposed pesticide use is part of an integrated pest management program;

(d) The proposed method or methods of application, including availability of appropriate application and safety equipment;

(e) Any acute and long-term toxicological hazards, either human or environmental, associated with the proposed use and measures available to minimize such hazards;

(f) The effectiveness of the requested pesticide for the proposed use;

(g) Compatibility of the proposed pesticide with target and non-target ecosystems;

(h) The conditions under which the pesticide is to be used, including climate, flora, fauna, geography, hydrology, and soils;

(i) The availability and effectiveness of other pesticides or non-chemical control methods;

(j) The requesting country's ability to regulate or control the distribution, storage, use and disposal of the requested pesticide;

(k) The provisions made for training of users and applicators; and

(l) The provisions made for monitoring the use and effectiveness of the pesticide.

In those cases where the evaluation of the proposed pesticide use in the Initial Environmental Examination indicates that the use will significantly affect the human environment, the Threshold Decision will include a recommendation for the preparation of an Environmental Assessment or Environmental Impact Statement, as appropriate. In the event a decision is made to approve the planned pesticide use, the Project Paper shall include to the extent practicable, provisions designed to mitigate potential adverse effects of the pesticide. When the pesticide evaluation section of the Initial Environmental Examination does not indicate a potentially unreasonable risk arising from the pesticide use, an Environmental Assessment or Environmental Impact Statement shall nevertheless be prepared if the environmental effects of the project otherwise require further assessment.

(ii) When a project includes assistance for the procurement or use, or both, of any pesticide registered for the same or similar uses in the United States but the proposed use is restricted by the USEPA on the basis of user hazard, the procedures set forth in §216.3(b)(1)(i) above will be followed. In addition, the Initial Environmental Examination will include an evaluation of the user hazards associated with the proposed

USEPA restricted uses to ensure that the implementation plan which is contained in the Project Paper incorporates provisions for making the recipient government aware of these risks and providing, if necessary, such technical assistance as may be required to mitigate these risks. If the proposed pesticide use is also restricted on a basis other than user hazard, the procedures in §216.3(b)(l)(iii) shall be followed in lieu of the procedures in this section.

(iii) If the project includes assistance for the procurement or use, or both of:

(a) Any pesticide other than one registered for the same or similar uses by USEPA without restriction or for restricted use on the basis of user hazard; or

(b) Any pesticide for which a notice of rebuttable presumption against re-registration, notice of intent to cancel, or notice of intent to suspend has been issued by USEPA, The Threshold Decision will provide for the preparation of an Environmental Assessment or Environmental Impact Statement, as appropriate (§216.6(a)). The EA or EIS shall include, but not be limited to, an analysis of the factors identified in §216.3(b)(l)(i) above.

(iv) Notwithstanding the provisions of §216.3(b)(l)(i) through (iii) above, if the project includes assistance for the procurement or use, or both, of a pesticide against which USEPA has initiated a regulatory action for cause, or for which it has issued a notice of rebuttable presumption against re-registration, the nature of the action or notice, including the relevant technical and scientific factors will be discussed with the requesting government and considered in the IEE and, if prepared, in the EA or EIS. If USEPA initiates any of the regulatory actions above against a pesticide subsequent to its evaluation in an IEE, EA or EIS, the nature of the action will be discussed with the recipient government and considered in an amended IEE or amended EA or EIS, as appropriate.

(v) If the project includes assistance for the procurement or use, or both of pesticides but the specific pesticides to be procured or used cannot be identified at the time the IEE is prepared, the procedures outlined in §216.3(b)(i) through (iv) will be followed when the specific pesticides are identified and before procurement or use is authorized. Where identification of the pesticides to be procured or used does not occur until after Project Paper approval, neither the procurement nor the use of the pesticides shall be undertaken unless approved, in writing, by

the Assistant Administrator (or in the case of projects authorized at the Mission level, the Mission Director) who approved the Project Paper.

(2) Exceptions to Pesticide Procedures. The procedures set forth in §216.3 (b)(l) shall not apply to the following projects including assistance for the procurement or use, or both, of pesticides.

(i) Projects under emergency conditions. Emergency conditions shall be deemed to exist when it is determined by the Administrator, A.I.D.. in writing that:

(a) A pest outbreak has occurred or is imminent; and

(b) Significant health problems (either human or animal) or significant economic problems will occur without the prompt use of the proposed pesticide; and

(c) Insufficient time is available before the pesticide must be used to evaluate the proposed use in accordance with the provisions of this regulation.

(ii) Projects where A.I.D. is a minor donor, as defined in §216.1(c)(12) above, to a multi-donor project.

(iii) Projects including assistance for procurement or use, or both, of pesticides for research or limited field evaluation purposes by or under the supervision of project personnel. In such instances, however, A.I.D. will ensure that the manufacturers of the pesticides provide toxicological and environmental data necessary to safeguard the health of research personnel and the quality of the local environment in which the pesticides will be used. Furthermore, treated crops will not be used for human or animal consumption unless appropriate tolerances have been established by USEPA or recommended by UNFAO/WHO, and the rates and frequency of application, together with the prescribed preharvest intervals, do not result in residues exceeding such tolerances. This prohibition does not apply to the feeding of such crops to animals for research purposes.

(3) Non-Project Assistance. In a very few limited number of circumstances A.I.D. may provide non-project assistance for the procurement and use of pesticides. Assistance in such cases shall be provided if the A.I.D. Administrator determines in writing that:

(i) emergency conditions, as defined in §216.3(b)(2)(i) above exist; or

(ii) that compelling circumstances exist such that failure to provide the proposed assistance would seriously impede the attainment of U.S. foreign policy objectives or the objectives of the foreign assistance

program. In the latter case, a decision to provide the assistance will be based to the maximum extent practicable, upon a consideration of the factors set forth in §216.3(b)(l)(i) and, to the extent available, the history of efficacy and safety covering the past use of the pesticide the in recipient country.

[43 FR 20491, May 12, 1978, as amended at 45 FR 70245, Oct. 23, 1980]

§216.4 PRIVATE APPLICANTS

Programs, projects or activities for which financing from A.I.D. is sought by private applicants, such as PVOs and educational and research institutions, are subject to these procedures. Except as provided in §216.2(b), (c) or (d), preliminary proposals for financing submitted by private applicants shall be accompanied by an Initial Environmental Examination or adequate information to permit preparation of an Initial Environmental Examination. The Threshold Decision shall be made by the Mission Director for the country to which the proposal relates, if the preliminary proposal is submitted to the A.I.D. Mission, or shall be made by the officer in A.I.D. who approves the preliminary proposal. In either case, the concurrence of the Bureau Environmental Officer is required in the same manner as in §216.3(a)(2), except for PVO projects approved in A.I.D. Missions with total life of project costs less than $500,000. Thereafter, the same procedures set forth in §216.3 including as appropriate scoping and Environmental Assessments or Environmental Impact Statements, shall be applicable to programs, projects or activities submitted by private applicants. The final proposal submitted for financing shall be treated, for purposes of these procedures, as a Project Paper. The Bureau Environmental Officer shall advise private applicants of studies or other information foreseeably required for action by A.I.D.

[45 FR 70247, Oct. 23, 1980]

§216.5 ENDANGERED SPECIES

It is A.I.D. policy to conduct its assistance programs in a manner that is sensitive to the protection of endangered or threatened species and their critical habitats. The Initial Environmental Examination for each project, program or activity having an effect on the environment shall specifically determine whether the project, program or activity will have an effect on an endangered or threatened species, or critical habitat. If the proposed project, program or activity will have the effect of jeopardizing an endangered or threatened species or of adversely modifying its critical habitat, the Threshold Decision shall be a Positive Determination and an Environmental Assessment or Environmental Impact Statement completed as appropriate, which shall discuss alternatives or modifications to avoid or mitigate such impact on the species or its habitat.

[45 FR 70247, Oct. 23, 1980]

§216.6 ENVIRONMENTAL ASSESSMENTS

(a) General Purpose

The purpose of the Environmental Assessment is to provide Agency and host country decision-makers with a full discussion of significant environmental effects of a proposed action. It includes alternatives which would avoid or minimize adverse effects or enhance the quality of the environment so that the expected benefits of development objectives can be weighed against any adverse impacts upon the human environment or any irreversible or irretrievable commitment of resources.

(b) Collaboration with Affected Nation on Preparation

Collaboration in obtaining data, conducting analyses and considering alternatives will help build an awareness of development associated environmental problems in less developed countries as well as assist in building an indigenous institutional capability to deal nationally with such problems. Missions, Bureaus and Offices will collaborate with affected countries to the maximum extent possible, in the development of any Environmental Assessments and consideration of environmental consequences as set forth therein.

(c) Content and Form

The Environmental Assessment shall be based upon the scoping statement and shall address the following elements, as appropriate:

(1) Summary. The summary shall stress the major conclusions, areas of controversy, if any, and the issues to be resolved.

(2) Purpose. The Environmental Assessment shall briefly specify the underlying purpose and need to which the Agency is responding in proposing the alternatives including the proposed action

(3) Alternatives Including the Proposed Action. This section should present the environmental impacts of the proposal and its alternatives in comparative form, thereby sharpening the issues and providing a clear basis for choice among options by the decision-maker. This section should explore and evaluate reasonable alternatives and briefly discuss the reasons for eliminating those alternatives which were not included in the detailed study; devote substantial treatment to each alternative considered in detail including the proposed action so that reviewers may evaluate their comparative merits; include the alternative of no action; identify the Agency's preferred alternative or alternatives, if one or more exists; include appropriate mitigation measures not already included in the proposed action or alternatives.

(4) Affected Environment. The Environmental Assessment shall succinctly describe the environment of the area(s) to be affected or created by the alternatives under consideration. The descriptions shall be no longer than is necessary to understand the effects of the alternatives. Data and analyses in the Environmental Assessment shall be commensurate with the significance of the impact with less important material summarized, consolidated or simply referenced.

(5) Environmental Consequences. This section forms the analytic basis for the comparisons under paragraph (c)(3) of this section. It will include the environmental impacts of the alternatives including the proposed action; any adverse effects that cannot be avoided should the proposed action be implemented; the relationship between short-term uses of the environment and the maintenance and enhancement of long-term productivity; and any irreversible or irretrievable commitments of resources which would be involved in the proposal should it be implemented. It should not duplicate discussions in paragraph (c)(3) of this section. This section of the Environmental Assessment should include discussions of direct effects and their significance; indirect effects and their significance; possible conflicts between the proposed action and land use plans, policies and controls for the areas concerned; energy requirements and conservation potential of various alternatives and mitigation measures; natural or depletable resource requirements and conservation potential of various requirements and mitigation measures; urban quality; historic and cultural resources and the design of the built environment, including the reuse and conservation potential of various alternatives and mitigation measures; and means to mitigate adverse environmental impacts.

(6) List of Preparers. The Environmental Assessment shall list the names and qualifications (expertise, experience, professional discipline) of the persons primarily responsible for preparing the Environmental Assessment or significant background papers.

(7) Appendix. An appendix may be prepared.

(d) Program Assessment

Program Assessments may be appropriate in order to assess the environmental effects of a number of individual actions and their cumulative environmental impact in a given country or geographic area, or the environmental impacts that are generic or common to a class of agency actions, or other activities which are not country-specific. In these cases, a single, programmatic assessment will be prepared in A.I.D./Washington and circulated to appropriate overseas Missions, host governments, and to interested parties within the United States. To the extent practicable, the form and content of the programmatic Environmental Assessment will be the same as for project Assessments. Subsequent

Environmental Assessments on major individual actions will only be necessary where such follow-on or subsequent activities may have significant environmental impacts on specific countries where such impacts have not been adequately evaluated in the programmatic Environmental Assessment. Other programmatic evaluations of class of actions may be conducted in an effort to establish additional categorical exclusions or design standards or criteria for such classes that will eliminate or minimize adverse effects of such actions, enhance the environmental effect of such actions or reduce the amount of paperwork or time involved in these procedures. Programmatic evaluations conducted for the purpose of establishing additional categorical exclusions under §216.2(c) or design considerations that will eliminate significant effects for classes of actions shall be made available for public comment before the categorical exclusions or design standards or criteria are adopted by A.I.D. Notice of the availability of such documents shall be published in the Federal Register. Additional categorical exclusions shall be adopted by A.I.D. upon the approval of the Administrator, and design consideration in accordance with usual agency procedures.

(e) Consultation and Review

(1) When Environmental Assessments are prepared on activities carried out within or focused on specific developing countries, consultation will be held between A.I.D. staff and the host government both in the early stages of preparation and on the results and significance of the completed Assessment before the project is authorized.

(2) Missions will encourage the host government to make the Environmental Assessment available to the general public of the recipient country. If Environmental Assessments are prepared on activities which are not country specific, the Assessment will be circulated by the Environmental Coordinator to A.I.D.'s Overseas Missions and interested governments for information, guidance and comment and will be made available in the U.S. to interested parties.

(f) Effect in Other Countries

In a situation where an analysis indicates that potential effects may extend beyond the national boundaries of a recipient country and adjacent foreign nations may be affected, A.I.D. will urge the recipient country to consult with such countries in advance of project approval and to negotiate mutually acceptable accommodations.

(g) Classified Material

Environmental Assessments will not normally include classified or administratively controlled material. However, there may be situations where environmental aspects cannot be adequately discussed without the inclusion of such material. The handling and

disclosure of classified or administratively controlled material shall be governed by 22 CFR Part 9. Those portions of an Environmental Assessment which are not classified or administratively controlled will be made available to persons outside the Agency as provided for in 22 CFR Part 212.

[45 FR 70247, Oct. 23, 1980]

§216.7 ENVIRONMENTAL IMPACT STATEMENTS

(a) Applicability

An Environmental Impact Statement shall be prepared when agency actions significantly affect:

(1) The global environment or areas outside the jurisdiction of any nation (e.g., the oceans);

(2) The environment of the United States; or

(3) Other aspects of the environment at the discretion of the Administrator.

(b) Effects on the United States: Content and Form

An Environmental Impact Statement relating to paragraph (a)(2) of this section shall comply with the CEQ Regulations. With respect to effects on the United States, the terms environment and significant effect wherever used in these procedures have the same meaning as in the CEQ Regulations rather than as defined in §216.l(c)(12) and (13) of these procedures.

(c) Other Effects: Content and Form

An Environmental Impact Statement relating to paragraphs (a)(l) and (a)(3) of this section will generally follow the CEQ Regulations, but will take into account the special considerations and concerns of A.I.D. Circulation of such Environmental Impact

Statements in draft form will precede approval of a Project Paper or equivalent and comments from such circulation will be considered before final project authorization as outlined in §216.3 of these procedures. The draft Environmental Impact Statement will also be circulated by the Missions to affected foreign governments for information and comment. Draft Environmental Impact Statements generally will be made available for comment to Federal agencies with jurisdiction by law or special expertise with respect to any environmental impact involved, and to public and private organizations and individuals for not less than forty-five (45) days. Notice of availability of the draft Environmental Impact Statements will be published in the FEDERAL REGISTER. Cognizant Bureaus and Offices will submit these drafts for circulation through the Environmental Coordinator who will have the responsibility for coordinating all such

communications with persons outside A.I.D. Any comments received by the Environmental Coordinator will be forwarded to the originating Bureau or Office for consideration in final policy decisions and the preparation of a final Environmental Impact Statement. All such comments will be attached to the final Statement, and those relevant comments not adequately discussed in the draft Environmental Impact Statement will be appropriately dealt with in the final Environmental Impact Statement. Copies of the final Environmental Impact Statement, with comments attached, will be sent by the Environmental Coordinator to CEQ and to all other Federal, state, and local agencies and private organizations that made substantive comments on the draft, including affected foreign governments. Where emergency circumstances or considerations of foreign policy make it necessary to take an action without observing the provisions of

§1506.10 of the CEQ Regulations, or when there are overriding considerations of expense to the United States or foreign governments, the originating Office will advise the Environmental Coordinator who will consult with Department of State and CEQ concerning appropriate modification of review procedures.

[45 FR 70249, Oct. 23, 1980]

§216.8 PUBLIC HEARINGS

(1) In most instances AID will be able to gain the benefit of public participation in the impact statement process through circulation of draft statements and notice of public availability in CEQ publications. However, in some cases the Administrator may wish to hold public hearings on draft Environmental Impact Statements. In deciding whether or not a public hearing is appropriate, Bureaus in conjunction with the Environmental Coordinator should consider:

(i) The magnitude of the proposal in terms of economic costs, the geographic area involved, and the uniqueness or size of commitment of the resources involved;

(ii) The degree of interest in the proposal as evidenced by requests from the public and from Federal, state and local authorities, and private organizations and individuals, that a hearing be held;

(iii) The complexity of the issue and likelihood that information will be presented at the hearing which will be of assistance to the Agency; and

(iv) The extent to which public involvement already has been achieved through other means, such as earlier public hearings, meetings with citizen representatives, and/or written comments on the proposed action.

(2) If public hearings are held, draft Environmental Impact Statements to be discussed should be made available to the public at least fifteen (15) days prior to the time of the public hearings, and a notice will be placed in the

FEDERAL REGISTER giving the subject, time and place of the proposed hearings.

[41 FR 26913, June 30, 1976. Redesignated at 45 FR 70249, Oct. 23, 1980]

§216.9 BILATERAL AND MULTILATERAL STUDIES AND CONCISE REVIEWS OF ENVIRONMENTAL ISSUES

Notwithstanding anything to the contrary in these procedures, the Administrator may approve the use of either of the following documents as a substitute for an Environmental Assessment (but not a substitute for an Environmental Impact Statement) required under these procedures:

(1) Bilateral or multilateral environmental studies, relevant or related to the proposed action, prepared by the United States and one or more foreign countries or by an international body or organization in which the United States is a member or participant; or,

(2) Concise reviews of the environmental issues involved including summary environmental analyses or other appropriate documents.

[45 FR 70249, Oct. 23, 1980]

§216.10 RECORDS AND REPORTS

Each Agency Bureau will maintain a current list of activities for which Environmental Assessments and Environmental Impact Statements are being prepared and for which Negative Determinations and Declarations have been made. Copies of final Initial Environmental Examinations, scoping statements, Assessments and Impact Statements will be available to interested Federal agencies upon request. The cognizant Bureau will maintain a permanent file (which may be part of its normal project files) of Environmental Impact Statements, Environmental Assessments, final Initial Environmental Examinations, scoping statements, Determinations and Declarations which will be available to the public under the Freedom of Information Act. Interested persons can obtain information or status reports regarding Environmental Assessments and Environmental Impact Statements through the A.I.D. Environmental Coordinator.

[45 FR 70249, Oct. 23, 1980]

(22 U.S.C. 2381; 42 U.S.C. 4332)

Dated October 9, 1980

Joseph C. Wheeler

Acting Administrator

ANNEX B: PEA SCOPING REPORT

Programmatic Environmental Assessment

Update

1st Revised Draft Report

Integrated Vector Management Programs for Malaria Vector Control

Contract No. EPP-I-13-00013-00, Task Order 12

April 25, 2011

Prepared for
Bureau for Global Health
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LIST OF ACRONYMS

ADD	average daily dose
ATSDR	Agency for Toxic Substances and Disease Registry
BEO	Bureau Environmental Officer
Bti	*Bacillus thuringiensis* israelensis
CAS	Chemical Abstracts Service
CFR	U.S. Code of Federal Regulations
CGIAR	Consultative Group on International Agricultural Research
CSF	cancer slope factor
DAF	dilution and attenuation factor
DDT	dichloro-diphenyl-trichloroethane
EA	environmental assessment
EC	emulsifiable concentrate
EC50	median effective concentration
EIR	entomological inoculation rate
EPA	U.S. Environmental Protection Agency
EXTOXNET	EXtension TOXicology NETwork
GDP	gross domestic product
GEF	Global Environment Fund
GFATM	Global Fund for AIDS, Malaria and Tuberculosis
GIS	geographic information systems
GUP	general use pesticide
HEAST	health effects assessment summary tables
HI	hazard index
HQ	hazard quotient
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
ICIPE	The International Center for Insect Physiology and Ecology
IEC	Information, Education, and Communication

IEE	Initial Environmental Examination
IPCS	International Program on Chemical Safety
IPM	integrated pest management
IRIS	integrated risk information system
IRS	indoor residual spraying
ITM	insecticide-treated material
ITN	insecticide-treated net
IUCN	The World Conservation Union
IVM	integrated vector management
KAP	knowledge, attitudes, and practices
LADD	lifetime average daily dose
LC50	median lethal concentration
LD50	lethal dose, 50 percent of the test population
LLIN	long-lasting insecticidal net
LOAEL	lowest observed adverse effect level
MEO	Mission Environmental Officer
MHO	Mission Health Officer
MOA	Ministry of Agriculture
MOE	margin of exposure
MOH	Ministry of Health
MOS	Margin of Safety
MPW	Ministry of Public Works
MRL	minimal risk level
MRLs	maximum residue limits
NC	noncancer
NGO	nongovernmental organization
NOAEL	no observed adverse effect level
NOEL	no observed effect level
OFDA	Office of Foreign Disaster Assistance
PAN	Pesticide Action Network
PEA	Programmatic Environmental Assessment

PERSUAP	Pesticide Evaluation Report and Safer Use Action Plan
POPs	persistent organic pollutants
PPE	personal protective equipment
PSCs	pyrethrum spray catches
PVO	private voluntary organization
RAGS	Risk Assessment Guidance for Superfund
RBM	Roll Back Malaria
RED	reregistration eligibility decision
REO	regional environmental officer
RfD	reference dose
RUP	restricted use pesticide
SEA	Supplemental Environmental Assessment
SF	safety factor
SIMA	System Wide Initiative On Malaria And Agriculture
SOP	standard operating procedure
UF	uncertainty factor
ULV	ultra-low volume
UNDP	United Nations Development Program
UNEP	United Nations Environment Program
UNFAO	United Nations Food and Agriculture Organization
UNICEF	United Nations Children's Fund
USAID	U.S. Agency for International Development
USDA/FAS	U.S. Department of Agriculture/Foreign Agricultural Service
WHO	World Health Organization
WHOPES	WHO Pesticide Evaluation Scheme
WP	wettable powder

EXECUTIVE SUMMARY

The purpose and content of this Scoping Report is to define the extent of the Programmatic Environmental Assessment and identify the full range of issues and potential impacts from the planned Vector Control Interventions funded under the USG Malaria Control Program. The scoping exercise is the first step in preparing a full assessment study and is in compliance with the requirements of USAID Environmental Procedures 22 CFR 216.

President's Malaria Initiative (PMI) was announced in 2005, with support for malaria control beginning in 2006 in Angola, Tanzania and Uganda, and with rapid scale up underway in 15 countries by 2008 (Angola, Tanzania, Uganda, Malawi, Mozambique, Rwanda, Senegal, Benin, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Mali and Zambia). The 2008 Lantos-Hyde Act authorized an expanded PMI program for 2009-2013 and in 2011, consistent with the United State Government (USG) Malaria Strategy, Nigeria and the Democratic Republic of the Congo (DRC) were added. This Scoping Report sets out to update the initial Programmatic Environmental Assessment (PEA) that was prepared for the PMI program in 2007, by identifying new innovations, changes to and lessons learned during the implementation of the program over the past five years, addressing issues that were not addressed in the 2007 PEA, and by assessing the full range of possible environmental issues and impacts that could arise from the planned activities funded under the USAID Integrated Vector Management for Malaria Program. The request to update the PEA is in response to the change in available pesticides and other mosquito control products, management approaches and the ecology of the malaria vectors, and provides an opportunity to review and revise the IVM program.

The Malaria Vector Control program uses an Integrated Vector Management (IVM) approach which is a rational decision-making process for the optimal use of resources in the management of vector populations, in order to reduce or interrupt transmission of vector-borne diseases. The approach seeks to improve the efficacy, cost-effectiveness, ecological soundness and sustainability of disease-vector control. The vector control interventions and management techniques include insecticide treated materials (ITM) Long Lasting Insecticide Treated Nets (LLINs) and wall lining, indoor residual spraying (IRS), larviciding and environmental management methods for controlling the mosquitoes that carry malaria. This Scoping Report examines these interventions for significant environmental impacts, and updates and expands on the findings from previous PEAs. In addition to these interventions, this report also looks at the issue of resistance, climate change and cumulative impacts. The subsequent PEA will provide guidance for the implementation of the program and will be part of the IVM decision making process.

Scoping was held in March, 2011, and was based in Washington DC. The first scoping effort involved a review of the 2002 PEA that addressed the ITM, and also the 2007 PEA that addressed IRS, ITN, larviciding and environmental methods for the IVM malaria program. This was followed by a scoping meeting that included relevant stakeholders from organizations, agencies, countries, consultants and companies who have vested interest in malaria control activities and are affected by the Malaria Vector Control Program.

The scoping process focused on the following areas to identify the relevant issues for updating the IVM PEA.

- Issues not addressed in past PEAs – LLINs and personal protection repellants

- Issues identified in past PEAs that should be further assessed – high risk pesticides
- Issues identified during past 5 years of project implementation – exposure scenarios, waste management and resistance issues
- New technologies or pesticides – two new IRS pesticides, two new larvicides and a new vector management intervention: wall lining
- IRS Best Management Practices contribution to minimizing impacts

The majority of the IVM interventions involve the use of pesticides, therefore, the economic and environmental risks and benefits of these interventions will be evaluated for their significant environmental impacts as per USAID environmental procedures.

1. INTRODUCTION

The U.S. Agency for International Development (USAID) estimates 300 to 500 million worldwide cases of malaria occur every year, resulting in up to 2.5 million deaths— mostly among young children. Since the start of USAID's Infectious Disease Initiative in 1998, the Agency has significantly increased its programs and funding to fight malaria, particularly in Africa, where 90 percent of malaria deaths occur. USAID's malaria programs focus on assisting countries to develop the capacity to effectively prevent and treat malaria through an integrated approach—Integrated Vector Management (IVM) — that uses a range of interventions designed to eliminate or greatly reduce malaria transmission.

On June 30, 2005, President Bush pledged to increase funding for malaria prevention and treatment by more than $1.2 billion over 5 years, specifically in sub- Saharan Africa. To launch the President's Malaria Initiative, the United States significantly expanded resources for malaria prevention and treatment in Angola, Tanzania, and Uganda starting in 2006; expand to four more highly endemic African countries in 2007; and eight more in 2008. This effort is expected to cover more than 175 million people in 15 or more of the most affected African countries.

In 2008, the Lantos-Hyde Act authorized an expanded PMI program for 2009-2013 by authorizing up to $5 billion in USG funding for malaria prevention and control globally. PMI is a key component of the U.S. Government's (USG) Global Health Initiative (GHI), which was announced by President Obama in May 2009. As a result, the PMI strategy was revised to achieve Africa-wide impact by halving the burden of malaria in 70 percent of at-risk population in sub-Sahara Africa, or approximately 450 million people.

The USG Malaria Strategy program includes the use of pesticides. As such, all projects involving assistance for the procurement or use, or both, of pesticides shall be subject to the procedures set out in Regulation 216 section 216.3 (b). Based on the nature of the proposed activities and geographic coverage, a Programmatic Environment Assessment (PEA) approach is warranted for meeting Regulation 216 requirements and developing a process that assures the environmental soundness of project implementation. The PEA will also serve as a reference document for preparing Supplemental Environmental Assessments (SEAs) that will be prepared for each country program.

This PEA will result in identifying the Human Health and Environmental Risks associated with the vector interventions used in the effort to reduce malaria mortality and morbidity in high-burden sub-Saharan Africa.

1.1 OBJECTIVES

The primary objective of the scoping process is to identify potentially significant environmental issues related to the proposed integrated Vector interventions for malaria programs in order to determine the scope of issues to be addressed in the PEA. The scoping process will also specifically and methodically identify issues that are not significant and which will not be addressed in the PEA. With these in mind, the PEA Team focused on the following:

- Identify the Integrated Vector Interventions that will be addressed in the PEA.
- Identify the environmental issues or concerns of these interventions (Human and Ecological health).

- Identify the significant issues that have emerged during implementation of the program over the past five years.
- Identify sources of information and available data relevant to the proposed program interventions.

The Scoping Report serves as the scope of work for the PEA, providing the issues, approach and methodology, schedule, and technical disciplines required for completing of the PEA. This scoping report builds on the 2007 scoping report and reviews all actions described in the report as a tool for determining the analysis associated with the upcoming 2011 PEA.

1.2 APPROACH AND METHODOLOGY

USAID's environmental procedures require completion of a scoping process. In order to accomplish this task, interested stakeholders were solicited to provide comments on the issues. The scope of the Malaria IVM program is quite large, and involves a diverse group of stakeholders, including international organizations (WHOPES), US government agencies (EPA, DOD, CDC, USAID), USAID Missions, pesticide manufacturers (BASF, Vestergaard Frandsen, Clarke, Syngenta, Bestnet, Sumitomo), implementing partners (RTI, Abt and Chemonics), host governments, and public and private institutions. Many of these stakeholders have offices in Washington DC, where the scoping meeting was held. To accommodate other stakeholders located in Africa and other locations throughout the world, the following two methods were used to involve as many stakeholders as possible.

- A Scoping Meeting was conducted on March 2. All identified stakeholders were invited to attend. Interested parties who could not travel to the meeting were invited to participate via webinar or conference call.
- The notes from the meeting were then sent to all stakeholders and additional comments and recommendations were requested. A two week period was allowed for providing additional comments.

All comments received have been included in this scoping report.

1.3 PROPOSED PROGRAM INTERVENTIONS AND GEOGRAPHIC AREA

The PMI IVM Malaria program will continue to focus on countrywide scale-up of a combination of four proven and highly effective interventions in each of the target countries:

- Long lasting insecticide-treated nets (LLINSs)
- Indoor residual spraying (IRS) with insecticides;
- Intermittent preventive treatment of pregnant women (IPTp,) and
- Treatment with artemisinin-based combination of therapies (ACTs).

The intent of the PEA will be to identify the significant issues associated with the integrated vector management program actions targeting Malaria and decide on the appropriate level of study. The two treatment programs, IPTp and ACTs, do not target the vector but instead target the disease; therefore the PEA will not be addressing these interventions.

In addition to LLINs and IRS, the PEA should address other specific IVM interventions that contribute to the reduction of malaria-related deaths. These include the following:

- Wall linings
- Larviciding
- Environmental Management methods
- Personal Protective Topical Repellants

The IVM Malaria program will focus on high malaria burden countries in sub-Saharan Africa and will include Angola, Tanzania, Uganda, Malawi, Mozambique, Rwanda, Senegal, Benin, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Mali, Zambia, Nigeria and Democratic Republic of the Congo (DRC), and up to seven additional endemic countries. All efforts will focus on at-risk populations in these high-burden countries.

1.4 ADMINISTRATIVE AND LEGAL FRAMEWORK

1.4.1 USAID ENVIRONMENTAL PROCEDURES

USAID environmental procedures (22 CFR 216) require that an environmental assessment (EA) be prepared and approved before proceeding with the implementation of any program that may have potential impact on the environment. This Scoping Report is part of the EA development process, and as such it describes the timing of the preparation of the environmental analyses; variations required in the format of the EA; the tentative planning and decision-making schedule; and a description of how the analysis will be conducted and the disciplines that will anticipate in the analysis.

According to section 216.6 (c) of USAID environmental procedures, programs which are financed by USAID are required to submit an Environmental Assessment. The EA is a detailed study of the reasonably foreseeable environmental impacts, both positive and negative, of the proposed USAID action and reasonable alternatives. In cases where the program objectives, along with political and institutional realities require that the program has the flexibility to determine specific interventions and specific location for these interventions on an ongoing basis, then a programmatic environmental assessment (PEA) approach is employed. The interventions identified for the IVM for Malaria control program to be employed in various geographic regions fit the criteria for a PEA, and will serve as a reference document for Supplemental Environmental Assessment (SEAs).

Programs involving assistance for the procurement or use, or both, of pesticides shall be subject to section 216.3 (b) of USAID environmental procedures. The 12 factors to be considered in such an evaluation shall include: a) USEPA registration status of the pesticides; b) basis for selection of the pesticides; c) extent to which the proposed pesticides use is part of an integrated pest management program; d) proposed method or methods of application, including availability of appropriate application and safety equipment; e) acute and long-term toxicological hazards; f) effectiveness of the pesticide for the proposed use; g) compatibility of the proposed pesticide with target and non-target ecosystems; h) conditions under which the pesticide is to be used; i) availability and effectiveness of other pesticides or non-chemical control methods; j) host-country's ability to regulate or control the distribution, storage, use and disposal of the requested pesticide; k) provisions made for training of users and applicators; l) and provision made for monitoring the use and effectiveness of the pesticide.

1.4.2 NATIONAL FRAMEWORK

The overall regulatory framework for conducting an environmental assessment for the USAID Malaria IVM Program is Regulation 216, however, host-country environmental policies, laws and regulations must also be consulted and considered. For scoping purposes, we have included a list of illustrative host-country institutions that have malaria control mandates or related functions.

- Ministry of Health/ National Malaria Control Programme (NMCP) – malaria control responsibilities, principle program partner
- Ministry of Environment/ Department of Environmental Affairs – country environmental regulations and monitoring requirements
- Ministry of Agriculture – pesticide registration
- Ministry of Public Works – often coordinate efforts with MOH
- Regional and local governments – often provide supervisors for program implementation

There are three major international treaties that govern the transport and use of pesticides, which need to be considered when preparing the PEA.

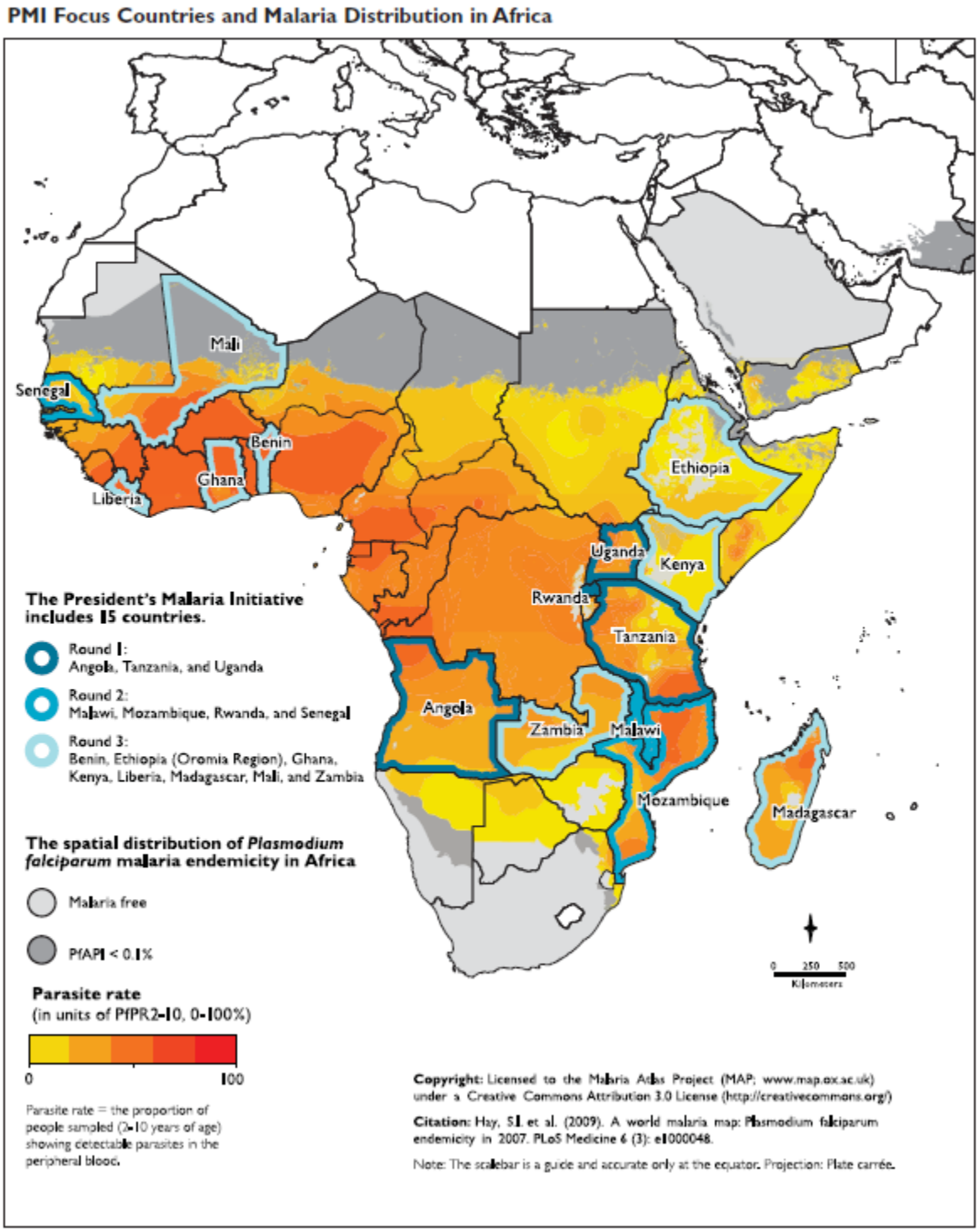
- The Basel Convention – Control of Trans-boundary Movement of Hazardous Wastes and their Disposal
- The Rotterdam Convention – Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade
- The Stockholm Convention – Persistent Organic Pollutants

There are several international institutions that also fund and implement anti-malaria initiatives. Coordination and collaboration is essential to avoid a duplication of efforts. These institutions also provide a valuable resource for information and guidelines.

- World Health Organization (WHO)
- United Nations Environment Program (UNEP)
- WHO Pesticide Evaluation Scheme (WHOPES)
- Global Fund
- United Nations Food and Agriculture Organization (FAO)

1.5 ENVIRONMENTAL SETTING

The Malaria Vector Control Program is broad by nature, and, as such, an adequate description of the diverse environments where USAID will support malaria control interventions would be difficult to provide. It is required that the Supplemental Environmental Assessments (SEAs) that fall under the PEA should address the affected environment on a country-by-country basis.



From USAID PMI Sustaining Momentum against Malaria: Saving lives in Africa, Fourth Annual Report, April 2010

2. 2011 SCOPING ACTIVITIES

As previously mentioned, USAID's environmental procedures require completion of a scoping process when undertaking a PEA. The scoping process is carried out to facilitate a more efficient preparation process and to define the issues and alternatives that will be examined in detail in the environmental assessment. In order to accomplish this task, two levels of scoping were conducted to identify the issues for updating the IVM for Malaria Vector Control PEA. The first level consisted of reviewing the existing 2007 Scoping Statement, the 2002 PEA which addresses the use of insecticide treated mosquito nets (ITNs) to control of malaria; and the 2007 PEA, which addresses indoor residual spraying, human risks with ITN, larviciding and environmental management techniques to control malaria. The findings from this review help identify issues that have been adequately addressed and do not need to be revisited in the updating of the PEA, as well as issues that were not addressed and should be included in the updated PEA. The second level consisted of soliciting relevant stakeholders to identify issues that have transpired since the start of the program or new issues that should be addressed in the PEA. This scoping exercise also provided an opportunity for the stakeholders to air their views and contribute to the development of the PEA.

2.1 PEA REVIEWS

2.1.1 2002 PEA

Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa, January 2002

Overview of the 2002 PEA

The purpose of the PEA was to assess potential environmental impacts resulting from USAID program activities involving insecticide-treated materials, and provide guidance on how to prepare activity-level assessments and action plans. The PEA addressed the health and environmental risks from potential exposure during distribution, storage, use and disposal of re-treatment pesticides, and exposure of persons using ITMs to pesticide vapors. Overall the pesticide products were classified as moderately toxic to humans and with safety precautions risks are slight, but all the products are highly toxic to aquatic organisms.

Pesticide Products

The PEA reviewed the five pyrethroid and "near" pyrethroid pesticides recommended by WHO, which include alpha-cypermethrin, cyfluthin, deltamethrin, etofenprox, lambda-cyhalothrin and permethrin. The following are issues that the PEA addressed:

- Loss of pesticide effectiveness from washing nets, based on insecticide properties, net material, number of washes and the resultant percent reduction in concentration. Most nets were found to be washed once a month, therefore net efficacy was 2-3 months. LLINs could last 20 washings (6 months to 1.5 years).
- Greater risk of mosquito resistance development with the use of only pyrethroids; there is a need to identify non-pyrethroid insecticides for treating materials.

- Selection of which insecticide to use depends on price, availability, and efficacy in the region, as well as environmental concerns.
- Mitigating environmental risks include using LLINs when possible, and avoid using permethrin EC formulations.

Overall Risks from use and treatment of ITNs:

The PEA assessed the Risks to Humans from exposure to ITN pesticides during pesticide storage and transport, net treatment and use (vapors or dermal or oral contact); and identified the acute toxicity (LD50 values), chronic toxicity (NOAEL and ADI values), and formulation impacts (water based and emulsifiable concentrate).

Risks to humans

The PEA identified the potential human exposure and insecticide toxicity based on the following exposure risks to humans:

- Occupational – handling of insecticides
- Accidental – ingestion of insecticide packet
- During use of ITMs – inhalation, skin contact, oral exposure (hand to mouth and net in mouth)

Even with extensive studies, uncertainties remain about whether all effects are fully understood. The following are the uncertainties the PEA addressed:

- Endocrine disruption
- Developmental neurotoxicity
- Special sensitivity of children to pesticides

Environmental Risks

The PEA identified the environmental risks to aquatic ecosystems from washing nets and the improper disposal of remaining net treatment solutions. Generally, the report rated each pesticide highly toxic, though it felt more studies were needed to verify this. The following are the authors' conclusions:

- Washing and improper disposal of solution would have a short term impact.
- Aquatic effects are unlikely from washing a small number of nets.
- Large number of nets washed together might impact aquatic organisms.

The assessment made use of Briggs literature review and Calamari computer modeling to identify impacts. The following are their findings:

- Different amounts of chemical required to treat a net with one chemical versus another have substantial impacts on the relative risk posed by different chemicals.
- Amount of insecticide lost in washing (Briggs) depends on the type of material, washing action, water temperature, type of detergent (50% loss first wash – 2-20% subsequent washes).
- The Calamari model estimates the concentration of pyrethroids from washing of nets.

Exposure toxicity ratio (ETR) is the risk threshold/exposure level at which adverse effects might be expected. There is a high degree of uncertainty due to lack of data, or data gaps: how many nets will be washed at once in any one body of water; just how toxic are the ITM products to aquatic organisms over the relevant timeframe; exposure estimates are subject to local water quality conditions and the release rate of chemical from bednets.

Alternatives the ITMs for vector control

Alternatives to ITMs are mentioned and include personal protection, treated curtains, eave strips, etc., avoidance, insect-proofing houses, insecticide spraying (IRS, space spraying), and breeding prevention.

Risk management

To minimize the risk of human poisoning and environmental contamination, the PEA advocated the following recommendations and mitigation measures:

- LLINs better solution over ITN
- Safer active ingredients – lower toxicity the better, avoid using Permethrin EC formulation
- Safer formulations – water based formulations, low concentration
- Single dose packaging, not large volume containers
- Pesticide safety education
- Safe and sound workplace for net treatment facilities
- Solution disposal - dumped into a latrine or garbage pit
- Disposal of pesticide containers
- Poisoning response
- Pesticide quality control
- Monitor for unsafe practices
- Managing storage, transport and disposal of pesticides
- Create local capacity

The PEA also recommended monitoring for human pesticide poisonings and environmental contamination, and provided guidelines for preparing PERSUAPS for local-level risk mitigation actions.

2.1.2. 2007 SCOPING STATEMENT

(The following was taken directly from Annex A of the 2007 PEA)

Scope and significance of key issues

Scope and significance of key issues to be analyzed in detail in this assessment, and additional issues to be analyzed in country-specific assessments, such as SEAs and PERSUAPs, that follow from this PEA are listed below.

Risks to humans from use of no IVM actions

- Mortality
- Morbidity
- Social disruption
- Impact of economic losses
- Shift in focus away from prevention to reaction
- Human risks, in sum
- Uncertainties
- Mitigation opportunities

Potential risks to humans from use of IVM pesticides

- Overall issues
  - Relatively small quantities of pesticides used with IVM
  - Chemical group and formulations available
  - Human risks, in sum
  - Uncertainties
  - Mitigation opportunities
  - Toxicity of IVM chemicals to humans, acute and chronic
  - Potential human exposure (oral, dermal, and inhalation)
  - Externalities associated with pesticide use and exposure
  - Regulatory and legal issues related to pesticides and health
  - Enforcement issues related to pesticides and health
- Logistical issues
  - Choice, selection, and availability of least-toxic pesticide
  - Labeling toxicity categories by hazard indicator
  - Quality of pesticide and pesticide supplier
  - Proper pesticide labels and training materials in local languages
  - Pesticide distribution from labeled containers to unlabeled containers
  - Pesticide pilferage for unauthorized use or sale
  - Improper pesticide storage
  - Improper pesticide container transport
  - Improper pesticide handling, formulation and use

  - Prohibited empty pesticide container re-use
  - Proper disposal of empty pesticide containers
  - Proper disposal of leftover unusable pesticides
  - Proper use of safety equipment
- Training issues
  - Training on proper use of safety equipment
  - Training on proper calibration of sprayers
  - Presence of pesticide antidotes
  - Proper first aid for pesticide overexposure
  - Use of botanical compounds for mosquito treatment
- New technology issues
  - Use of bacteriological agents for mosquito management
  - Use of mosquito repellents
  - Use of mosquito traps containing pesticides
  - Use of experimental vaccines
- Procedural issue
  - Co-mingling of USAID resources with Ministry of Health/other donor pesticides

Potential environmental risks from use of IVM pesticides, introduction of exotic fish, and water management strategies

- Overall issues
  - Toxicity of pesticides to non-target organisms (other than mosquitoes), acute and chronic
  - Invasive species issues with introduction of non-native fish
  - Environmental consequences issues of environmental modification of waterways
  - Environmental risks, in sum
  - Uncertainties
  - Mitigation opportunities
- Specific issues
  - Toxicity to economically important insects like crop pollinators
  - Ecosystem disruption through water management strategies
  - Ecosystem disruption through fish introduction

  - Potential soil exposure to pesticides
  - Potential surface and ground water exposure to pesticides
  - Potential protected area and forest resource exposure to pesticides
  - Reduction in biodiversity related to pesticide exposure
  - Potential fisheries losses related to pesticide exposure
  - Potential bird losses related to pesticide exposure
  - Pesticide drift from spraying
  - Pesticide bioaccumulation (especially related to DDT)
  - Pesticide wash entering waterways and water resources
  - Disruption of natural predator and pathogen mosquito controls
  - Mosquito resistance to insecticides
  - Resurgence of mosquito populations after predator poisoning
  - Environmental externalities related to pesticide exposure
- New technology issues
  - Environmental effects of mosquito traps and repellents
  - Environmental effects of mosquito pheromones

Alternatives to recommended IVM options for malaria control—a comparison of environmental and health risks and human benefits

- Overall issue
  - Chemical control methods available other than those recommended in this PEA, and risks associated with each
- Specific issues
  - Single tactic approach with use of chemical control methods
  - Single tactic approach without use of chemical control methods (e.g., ITN use alone)
  - Efficacy of alternatives in comparison with IVM recommendations
  - No action
  - Cost comparison of alternative malaria control approaches
- Risk mitigation
  - What mechanisms are available for reducing adverse effects from IVM pesticide and non-pesticide methods?
  - How effective are they?

– How reliable?

Decision making: What criteria should USAID use to decide on whether, when and how to use various IVM options?

- Utilization of WHO guidelines and recommended pesticides. Comparison of WHO guidelines with USEPA regulations.
- Selection of appropriate pesticides and application methods for use in IVM programs. What criteria to use? Risks, costs, efficacy? At discretion of program manager?
- Availability of effective mitigation? Is this important, or are the benefits overwhelming in all cases?
- How adequate are local pesticide regulations, infrastructure, and the institutional settings?
- Monitoring: how much is required? For how long?
- What is a "significant" effect? How to compare risks with benefits?
- What would happen in the absence of USAID support for IVM options?
- What are the local MOH and larger international (WHO) contexts and frameworks in which programs will operate?

Monitoring mechanisms

- For adverse effects from ITN use and treatment
- What mechanisms are available?
- How effective are they?
- How reliable?

Components of a PERSUAP

- What information, analysis, and mitigation measures are needed for a project using IVM options?

Identification and elimination from <u>detailed</u> study of issues expected NOT to be significant, or outside of the scope of this assessment

- ITNs that require re-treatment with pesticides have already been covered in detail in an earlier environmental review (ITM PEA) and will not be repeated in such detail, except where long-lasting nets are involved
- Mosquito control pesticide options reviewed and approved by WHO, but not covered in this PEA. Why were certain pesticides chosen for recommendation in the PEA, and others not?
- Future scientific findings regarding pesticide safety. For example, pyrethroid insecticides, which comprise the majority of those recommended for mosquito control, may cause human endocrine disruption. This is a poorly understood issue, and in the face of little scientific consensus, how much attention should be given to such open scientific questions? What type of monitoring is required, and can this function be adequately covered by WHOPES and/or EPA?

- Community small-scale water management (elimination of mosquito breeding sites) enforcement through use of fines, and/or incentives

2.1.3 2007 PEA

Integrated Vector Management Programs for Malaria Vector Control Programmatic Environmental Assessment, January 2007

Overview of 2007 PEA

The 2007 PEA was developed to serve as an umbrella evaluation of the environmental and human health issues related to malaria vector control and to assist with the preparation of country and activity specific SEA and PERSUAP for malaria vector control programs. It provided USAID project managers with the policy, procedural and technical guideline to choose appropriate interventions and insecticides and develop and implement mitigation and monitoring and evaluation activities. The PEA discussed the proposed action and alternative, including indoor residual spraying (IRS), insecticide treated nets (ITN), environmental management and larviciding, as well as alternatives that are not recommended, including "no action". The PEA conducted a screening risk assessment for the purpose of identifying the human health risks of using pesticides in IRS, ITNs and larvicides. The document also provided recommendations for mitigation, monitoring and evaluation as part of the program implementation. An overview of the regulatory, policy and institutional capacity issues to consider during the preparation of the SEAs is also included. The PEA recommended training and institutional capacity building for to ensure program quality and sustainability. Three cross-cutting issues were addressed, including interaction with the agricultural sector, hazardous waste management and prevention versus treatment interventions.

Proposed Actions and Alternatives

The following are the malaria control methods assessed in this document:

- **No action to control malaria**. The impacts of taking the "no action" alternative
- **Indoor residual spraying (IRS)** uses 12 pesticides recommended by WHO:
  - Bendiocarb, Propoxur, DDT, Fenitrothion, Malathion, Pirimiphos-methyl, Alpha-cypermethrin, Bifenthrin, Cyfluthrin, Delamethrin, Etofenprox, Lambda-cyhalothrin
- **Human health consequences of Insecticide-treated nets** (ITNs)
- **Environmental management methods for Larvae control** for small-scale readily identifiable areas and areas with high human population density, including:
  - Environmental Modification – permanent, high cost changes such as filling breeding sites, lining water sources and canals, physical drainage of wetlands (surface, subsoil and coastal swamp) biological wetland drainage (tree planting), impoundments
  - Environmental manipulation – recurrent, moderate cost activities such as deepening and narrowing of old drains, vegetation manipulation, synchronized cropping and intermittent irrigation, larvivorous fish introduction, salt water flooding
    - Environmental consequences of using the above methods
- **Larvicidal agents** for standing water, shallow ponds, swamps and marshes
  - Bacterial larvicides, methoprene, temephos, monomolecular films, monomolecular oils

Activities not addressed in the PEA

Only the risks posed to human through the ITN net-retreatment process were addressed, otherwise, ITNs and LLINs were not addressed in this PEA. Also developing technologies such as neem oil, nightshade extract, natural pyrethrum, copepods, flatworms, nematodes, fungi, diatom/brown algae, microsporidia/protozoans, mosquito viruses, predatory vertebrates/bugs/mosquitoes ,were not addressed as they were not considered feasible, economically viable and commercially available.

Activities not recommended for analysis in the 2007 PEA

- Spraying open spaces around villages or spraying room spaces inside houses
- Pyrethroid –based larvicides as they are highly toxic to aquatic life, or motor oil as a larvicide
- Emergency approaches during floods or refugee camps such as ultra low volume (ULV) sprayers, LLIN, tarps and tents.

Affected Environment

The authors felt the PEA was too broad to provide adequate descriptions of the diverse environments of all the regions where the IVM program would be implemented, and recommended that the SEAs and PERSUAP address the affected environment on a country-by-country basis.

Human Health Consequences

The PEA included pesticide toxicity profiles and screening assessments for pesticides for IVM pesticides. It also assessed the exposure pathways for IRS, ITNs re-treatment and larviciding, and established baseline information on the acute, intermediate and chronic effects on workers and general population. The following risk assessment process was used to determine the human health consequences of the Malaria Vector Control Interventions:

1) Problem formulation or hazard characterization, described the IVM practices and pesticides, presented conceptual models developed to frame the exposure assessment, and summarized pesticide characteristics relevant to environmental behavior and health effects and includes the following:

- WHO and EPA class and status, registration status for each pesticide.
- Physical properties and health effects for each pesticide.
- Possible exposure pathways using conceptual models for the following:
  - Mixing/preparation for IRS, ITNs
  - Spraying, contact with sprayed surfaces, spills and ingestion of sprayed food for IRS
  - Treating nets, nets used for fishing
  - Grinding of insecticide granules, spraying, contact with treated water and spills from larviciding
  - Disposal of pesticide residuals, expired pesticides; pesticide packaging and PPE
  - Reuse of pesticide containers for drinking water of food
  - Storage – mishandling, spills or damaged containers; "daughter" products (chemical breakdown)

2) Analysis , identified the exposure scenarios and provides a concise description of the methodology developed for the screening risk assessment

- Exposure scenarios, including the following:
  - Mixing/preparation for IRS, ITNs
  - Spraying for IRS – inhalation during spraying, contact of sprayed surfaces, sprayed food,
  - Treating nets
  - Disposal of pesticide residuals, expired pesticides -contaminated groundwater (ingestion and bathing)
  - Reuse of pesticide containers for drinking water of food
  - Storage –spills or damaged containers

    Methodology – based on algorithms developed by EPA and refer to standard operation procedures (SOP), modified for the developing world

    Does not include environmental fate and transport modeling
- Human health benchmarks for cancer risks (lifetime average daily dose) and non-cancer hazards (average daily dose)
  Methodology- calculation of hazard quotient (HQ) using reference dose (RfD) specific to the duration of the exposure, derived from NOAEL and LOAEL (benchmark dose); and cancer risks using cancer slope factor (CSF); health benchmarks were identified from EPA RED documents, EPA IRIS, EPA HEAS, and ATSDR toxicological profiles

3) Risk characterization, discussed and interpreted the results.

Results that are a concern are pesticides that 'failed' the non-cancer results include DDT, Fenitrothion and Pirimiphos-methyl; all pesticides except DDT 'failed' the groundwater contamination and food/drink contamination. For Cancer results, DDT 'failed'; Etofenprox, Permethrin and Propoxur 'failed' groundwater contamination.

In conclusion, the report compared the pesticides and rated each as either low, moderate or high risk for each exposure scenario for cancer risk or non-cancer hazard. (IRS occupational and residential, ITN retreatment, container reuse and groundwater contamination)

Environmental Consequences

The PEA reviewed environmental consequences for each IRS WHO pesticide and larvicidal agent and their effects on non-target organisms such as birds, aquatic organisms, and other animals. The PEA briefly reviews the potential negative environmental impacts and ranks each intervention as either little or no impact, low impact, medium impact or high impact; though it concluded that environmental impacts associated with environmental management are location specific.

Mitigation, monitoring and evaluation

The PEA addressed the issues to consider when selecting appropriate location, intervention and timing for Malaria control interventions, (gathering malaria data, entomological monitoring, choosing location appropriate interventions, and sustainability). It also included guidelines for selecting the appropriate pesticide (vector resistance, effectiveness, costs, and types of indoor surfaces) and integrating human health and environment considerations (SEA/PERSUAP). The PEA recommended monitoring activities

for mitigation, environmental, livestock and human health impacts, entomological and malaria cases. It also identified the potential negative activities/impacts and the recommended mitigation actions for IRS, larviciding and environmental management IVM interventions.

Regulatory, legal, and institutional settings

The PEA confirmed that Regulation 216 is the regulatory framework for USAID funded projects, but requires that, host-country environmental policies, laws and regulations must be consulted and considered when preparing the SEA/PERSUAP. It also provided information on international treaties, which govern international transport and use of pesticides. The report surmised that all efforts should be coordinated with international institutions that also fund and implement antimalaria initiatives.

Training and institutional capacity building

The PEA recommended training to assist in developing a sustainable malaria vector control program, ranging from in-field training of implementers to ministry decision making.

Cross-cutting issues

The PEA looked at two cross-cutting issues.

- Malaria control and the agricultural sector
  - A major problem is the diversion of public health pesticides for use in agriculture.
  - Use of public health pesticides in the agricultural sector may increase the risk of crop exports exceeding Maximum Residue Limits (MRLs).
  - In areas where large quantities of pesticides are used for agricultural crops, mosquito resistance may develop much faster.
- Malaria control and hazardous waste management
  - Safe disposal of pesticide-contaminated waste products should be addressed through either exportation to the pesticide manufacturer or incineration at an internationally recognized facility.
  - Efforts should be made to prevent obsolete pesticide stocks.
  - The PEA identifies the actions to take when handling of obsolete pesticides.

2.2 2011 SCOPING MEETING

2.2.1 STAKEHOLDER IDENTIFICATION

The scope of the Malaria IVM program is quite large, and therefore required consulting a diverse group of relevant stakeholders. USAID identified the stakeholders based on experience from managing the IVM program over the past five years and included organizations, agencies, countries, consultants and companies who have vested interest in malaria control activities and are affected by the IMV program, such as:

- international organizations (WHOPES),
- US government agencies (EPA, DOD, USDA, CDC, USAID),
- USAID Missions,

- pesticide manufacturers (BASF, Vestergaard Frandsen, Clarke, Syngenta, Bestnet, Sumitomo),
- implementing partners (RTI, Abt and Chemonics), and
- host-country governments, and public and private institutions.

Please see Annex A for a list of the scoping meeting attendees.

2.2.2 SCOPING METHODOLOGY

Two methods were used in the scoping exercise to try to involve as many stakeholders as possible.

- A Scoping Meeting was held on March 2, 2011, in Washington DC. All identified stakeholders were invited to attend. Interested parties who could not travel to the meeting were invited to participate via webinar or conference call.
- The notes from the meeting were then sent to all stakeholders including attendees, Mission Environmental Officers and other invitees, and additional comments and recommendations were requested. A two week period was allowed for providing additional comments.

2.2.3 SCOPING MEETING PROCESS

An "informational packet" was sent to the invitees prior to the meeting in order for the participants to have an understanding of the program beforehand and enable them to make an informed contribution during the scoping process. The informational packet contained a scoping meeting agenda, background information, explanation of the purpose and need of the PEA, IVM decision making factors, status of the existing program, and issues to be discussed. It also included a summary of the *Integrated Vector Management Program for Malaria Vector Control PEA,* January 2007 and the *PEA for Insecticide-Treated materials in USAID Activities in Sub-Saharan Africa,* January 2002.

To engage the stakeholders that were not able to personally attend, the meeting was also relayed on *webinar*, which allowed live video and audio access. These participants could also provide comments via a live chat box. For those that did not have broadband access, a conference call number was provided for people to call in and participate. The meeting was facilitated by the PEA team and consisted of presentations and interactive discussions. This meeting generated valuable information about the stakeholder's concerns and expectations for the IVM program and the broader implications.

Following the scoping meeting, a transcript of comments was sent to participants and stakeholders that were not able to participate, and additional comments were solicited.

Feedback and input received were incorporated into this scoping report. This consultative process will continue throughout the PEA development process.

3. SIGNIFANCT ISSUES TO BE ADDRESSED IN THE 2011 PEA

3.1 SUMMARY OF STAKEHOLDER COMMENTS AND ISSUES

The following are the comments, opinions and issues that the stakeholders provided during the scoping meeting, grouped by topic. All written comments received following the meeting have also been included.

General Issues

- Identify lessons learned from the implementation of the program over the past five years
- PMI doesn't compare the effectiveness of one intervention versus another, but does consider the limitations of each (costs, labor intensive, geographic adaptation) when selecting the appropriate intervention - therefore the PEA should not compare the effectiveness of the interventions
- PMIs main focus is ITN, IRS and ACTs
- The lessoned learned from stakeholders (implementing partners) should be captured
- Include the IVCC (innovative vector control consortium) in discussions
- The PEA should be synchronized with WHOPES, WHO and Global Fund
- Draw on best practices to date
- Build host governments environmental compliance capacity
- Include the BMP manual and its effectiveness in the PEA
- Consider climate change and how it impacts malaria
- Include governance issues: pilferage, insecticide resistance, waste management
- Include the three key PEA principles of sustainability; economic viability, social responsibility and environmental soundness

Pesticides

- Encourage low impact packaging; minimize waste
- Need to emphasize manufacturer credibility and formulations when procuring
- Include pesticide registration and EPA and WHOPES status
- Consider additional pesticides other than ones recommended by EPA and WHOPES
- Consider new pesticide formulations

- PEA should address how to deal with new technologies; include regulatory flexibility
- Consider entomopathogenic fungi and other new technologies
- Consider pesticide intoxications/poisonings (and appropriate medical treatments/first aid)
- Include information on pesticide efficacy and duration in a given environment
- Thoroughly evaluate DDT use and its impacts
- Include agricultural use of the same pesticide used in the IVM program; and this contribution to resistance
- Include hazardous wastes disposal options
- Include country registration of pesticides
- New pesticides: chlorfenapyr for IRS, primiphos-methyl as CS formulation, Spinosad larvicide
- Predict the residential chronic risk

LLINs – consider the following:

- Efficacy of nets after 20 washings
- Resistance issues and mosquito net effectiveness
- Number of nets distributed and the impacts to the environment
- Proper disposal of the nets after they are no longer viable
- Reuse and recycling of nets -including behavior change
- How do we make good vector control tools out of expired nets (house screening, repair/retreat strategies)
- Biodegradable packaging for nets
- Waste management
- Qualitatively predict the risk of washing and fishing on aquatic organisms
- Predict the residential chronic exposure

Larviciding

- Larviciding is effective, however, dealing with all water bodies is not feasible, but the PMI program will support targeted and justified use
- Evaluate the effects of larviciding on the ecosystem
- Evaluate the basis for use of larviciding

Environmental Management

- Consider larvivorous fish and the impact to indigenous species; invasive issues

- Consider filling in wetlands, treating standing water, larviciding

New techniques – consider the following:

- Wall lining
- Plastic sheeting
- Personal protection material treated with permethrin, topical repellents, and spatial repellents with metofluthrin
- Space spraying for emergency situations
- Insect repelling blanket

Program implementation

- Ensure the SEA is more effective in aiding decision making when selecting appropriate interventions
- Provide small scale methodologies based on geographical differences
- Make SEA more effective at country level
- Include adaptive management
- Include IVM decision making process

Efficacy and resistance issues

- Insecticide resistance data and entomological capacity building has been positive result of PMI vector interventions
- Address resistance management, develop resistance management plans
- Address environmental pathways and growing pesticide resistance
- Consider evolution proof insecticides
- Discuss how vector resistance to pesticides affects decision making

3.2 SIGNIFICANT ISSUES

The PEA team assessed the results from reviewing the 2002 and 2007 PEA and screened the stakeholder comments to identify the major issues and determine their significance in the context of the IVM for Malaria control program. The PEA Team also considered the issues that were encountered during PMI program environmental evaluation visits and during discussions with various USAID Country Missions and implementing partners. The PEA Team focused on identifying the following issues which are relevant for updating the IVM PEA.

- Issues not addressed in past PEAs
- Issues identified in past PEAs that should be further assessed
- Issues identified during past 5 years of program implementation

- New technologies or pesticides
- IRS Best Management Practices contribution to minimizing impacts

Issues not addressed in past PEAs

The previous PEA's are very comprehensive and thorough in their assessment of the malaria control interventions and their potential significant impacts to human health and the environment. As such, the updating of the PEA sought to not duplicate these efforts, but to address issues that were not addressed in this document. Though the past PEAs assessed the risk of ITNs, the PMI program is actually distributing Long Lasting Insecticide Treated Nets (LLINs), which will require different assessment parameters than the ITNs that require retreatment every three months.

USAID has identified the need to address personal protection repellants for workers in Malaria prone areas. The 2011 PEA will assess the human and environmental impacts from the waste and exposure issues from the use of such repellants.

There are reports that state temperatures are rising due to climate change which lead to the spread of malaria. The effects of climate on malaria will be investigated as part of the effort to provide recommendations for an effective IVM program.

Issues identified in past PEAs that should be further assessed

The 2007 PEA conducted a screening of Human Health consequences which included problem formulation, analysis, and risk characterization. This study identified three pesticides that are high risk and will require further assessment to identify if they remain a viable option for use in the IVM program. During the review of all pesticides during the preparation of the 2011 PEA, any additional pesticides deemed to be at high risk will also be included in this evaluation. The pesticides from the 2007 report include:

- DDT
- Fenitrothion
- Pirimiphos methyl
- Malathion

Issues identified during past 5 years of program implementation

Since the start of USAID malaria program, in particular the scale up of the PMI, several issues have come to light that should be addressed in the update PEA. These issues may have been addressed in past PEAs, but their persistence and complexity were not foreseen and are more significant than initially perceived. These include:

- Waste Management (solid and effluent)
- Incineration of pesticides/plastics packaging materials
- Expired pesticides
- Resistance issues
- Pilferage for other use

- Excessive pesticide packaging
- Net Reuse
- Net Recycling
- Net Misuse-fishing nets
- Net efficacy after 20 washings
- Spraying under eaves
- Acute exposure from contact with residue on walls (children and adults touching sprayed walls)
- Residential chronic exposure and risks from IRS pesticides and LLINs

Resistance and its impacts were identified in the previous PEA, but have become a challenge for the PMI program. The 2011 PEA will attempt to identify the resistance issues and update the management options, and will also look at the combined impacts from IRS, LLIN, wall linings and agriculture pesticide use (cumulative impacts).

New pesticides or technologies

Over the past five years, new technologies or pesticides have been introduced to control malaria carrying mosquitoes. As per Regulation 216 section 216.3 (b) requirements, they will need to undergo an environmental assessment in order to identify the human and environmental risks. They include:

- Chlorfenapyr (pyrroles class) IRS
- Primiphos-methyl CS (new, long lasting formulation) IRS
- Spinosad (larvicide) actimonycete soil bacterium
- Pyriproxyfen (larvicide) juvenile hormone mimic
- Wall Linings - laminated polyethylene incorporated with pyrethroids

IRS Best Management Practices contribution to minimizing impacts

The 2007 PEA recommended Mitigation Actions to avoid or minimize the risk associated with IRS activities. These actions were then developed into Standard Operation Procedures (SOP) by partners who are implementing the IRS program. The SOPs were then developed further into Best Management Practices that provide standard guidelines for a safe and low risk implementation of the IRS program. Many of these practices are recommended by WHO and FAO. As part of the human health exposure scenarios and environmental risk assessment, these BMPs will be evaluated for their effectiveness in avoiding or minimizing the risks associated with the IRS program.

Table 1. Significant Issues

IVM Technique		Issues	Significant impacts	Comments	Actions
IRS					
12 WHO approved pesticides	• alpha-cypermethrin • bendiocarb • bifenthrin • cyfluthrin • DDT • deltamenthrin • etofenprox • fenitrothion • lambda-cyhalothrin • malathion • pirimiphosmethyl • propoxur			2007 PEA conducted a thorough deterministic screening evaluation of these pesticides	Update risk characterization for each pesticide
high risk pesticides	• DDT • Fenitrothion • Pirimiphosmethyl • Malathion • Other pesticides identified during the updating process and high risk	Identified as high risk in the 2007 PEA	• Mixing inhalation and dermal • Spraying inhalation • Contact on walls dermal • Sprayed food ingestion • Groundwater contamination ingestion and dermal • Chronic residential exposure	For DDT follow Stockholm guidelines	Human Health and Ecological Risk Assessment
New Pesticides	• Chlorfenapyr (Pyrroles) • Primophos-methyl CS (OP)	• Storage • Mixing • Spraying • Waste disposal • Spillage	• Human dermal, oral and inhalation exposure • Water contamination • Non-target bird, bee and mammal impacts, aquatic organisms		Deterministic screening and Human Health and Ecological Risk Assessment;

	Real-life impacts based on 5 years of program implementation	• Waste Management • Expired pesticides • Resistance • Pilferage for other uses • Packaging	• Air quality • Human exposure • Solid waste		Risk Characterization
	Review exposure scenarios based on 5 years of program implementation	Exposure scenarios using PPE and other BMPs	• Human dermal, oral and inhalation exposure • Ground water contamination		• Risk Characterization • BMP effectiveness
		• Spraying under eaves • Mixing pesticides • Leaking spray pumps • Contact with residue on walls	• Human dermal, oral and inhalation exposure • Air quality • Non-target bee and bird impacts • Ground water contamination • Livestock exposure		• Risk Characterization • Exposure Assessment
Late-life acting insecticides (LLA)	Low dose conventional insecticides and biopesticides				Will be discussed under Resistance Management
ITM					
LLIN					
WHO recommended nets	• Duranet® Alpha-cypermethrin • incorporated into polyethylene • Interim • Interceptor® Alpha-cypermethrin • coated on polyester Interim • Netprotect® Deltamethrin • incorporated into polyethylene • Interim • Olyset® Permethrin incorporated • into polyethylene Full • PermaNet® 2.0 Deltamethrin				• Risk characterization

	• coated on polyester Full • PermaNet® 2.5 Deltamethrin • coated on polyester with • strengthened border Interim • PermaNet® 3.0 Combination of • deltamethrin coated on polyester • with strengthened border				
	Real-life impacts based on 5 years of program implementation	• Solid waste management • Packaging • Reuse • Recycling • Misuse-fishing nets • Resistance issues • Net efficacy after 20 washings	• Human dermal, oral and inhalation exposure • Water contamination • Non-target aquatic organism impacts • Human behavior • Solid waste		• Quantitative and qualitative studies of pesticides in water bodies after washing • Risk characterization • Address impacts to resistance
Wall lining					
	Laminated polyethylene incorporated with pyrethroids or pemethrin treated plastic sheeting	• Waste management • Storage • Exposure scenarios • Resistance issues	• Human dermal, oral and inhalation exposure • Solid waste		• Deterministic screening • Risk Characterization
Larviciding					
WHO approved methods	• methoprene • temephos • microbial / bacterial • monomolecular flims • monomolecular oils		• Water contamination • Non-target aquatic organisms, bird and bee impacts • Impacts to food chain • Efficacy	2007 PEA conducted a thorough deterministic screening evaluation of this technique	Update risk characterization
New pesticides	• Spinosad • Pyriproxyfen				Deterministic screening

Environmental Management					
	• Deepening/ narrowing existing drains • cropping/irrigation strategies • filling-in /removing larval breeding sites • lining waterways • saltwater flooding • larvivorous fish • impoundment construction • biological drainage • vegetation manipulation • physical drainage		• Impacts to Indigenous fish/Invasive species • Aquatic organism impacts • Water quality and quantity • Flood control • Biodiversity impacts	2007 PEA conducted a thorough deterministic screening evaluation of this technique	Update risk characterization
Personal Protective topical repellants					
	citronella, DEET, p-menthane-3.8-did, IR3535, picaridin, 2-undecanone, oil of lemon/eucalyptus, catnip oil	Human and ecological toxicity	• Human dermal, oral and inhalation exposure • Non-target insects	Workers	Screening Risk Assessment

3.3 ISSUES ELIMINATED FOR FURTHER CONSIDERATION

The PEA Team screened out issues raised by stakeholders during the scoping process as that were not deemed appropriate for assessment in this PEA. Elimination justification was based on three issues: 1) lack of relevance to the IVM program, 2) new technology not ready for mainstream use and insufficient information available to be able to conduct a thorough environmental assessment on these technologies, and 3) issues previously addressed in other PEAs.

Table 2. Issues that will not be addressed in the 2011 PEA

IVM Technique		Significant impacts	Comments
	Flexibility to include new pesticides as they become available		New technology, Insufficient information available to be able to conduct an environmental assessment at this time, New pesticides can be addressed in a PEA addendum
IRS			
	• Entomopathogenic fungi • Transgenic fungi	Genetic engineering (precedes Reg. 216 and requires approval from USAID Biosafety officer)	New technology, not ready for mainstream use in the field, limited information available to be able to conduct an environmental assessment,
Personal protection treated materials			
Treated blankets and apparel products			Could be used in an emergency situation, not included in the general IVM program
Topical and Spatial Repellents			
Impregnated plastic strip	metofluthrin		New technology, not ready for mainstream use in the field, limited information available to be able to conduct an environmental assessment
Space Spraying			
Fogging	Pyrethoids or OP		Emergency response
Issues addressed in 2002/2007 PEA			
IRS	12 WHO recommended pesticides	Exposure scenarios: mixing of pesticides, inhalation of vapors during spraying, contact with sprayed surfaces, ingestion of sprayed foods, exposure from leaky equipment and spills, disposal of pesticides contaminate water, reuse of pesticide containers, storage spills	Deterministic screening of Human health impacts in 2007 PEA (problem formulation, analysis, and risk characterization) Note: The 2011 PEA will address new issues relating to IRS
		Toxicity of pesticides to birds, Aquatic organism and other animal (Non-target species)	Describes the toxicity of each pesticide

ITN	Retreatment of nets	Exposure scenarios: mixing of pesticides, ingestion from children touching nets, nets used for fishing, disposal of pesticides contaminate water, reuse of pesticide containers, storage spills	Deterministic screening of in 2002 PEA; Deterministic screening of Human health impacts in 2007 PEA (problem formulation, analysis, and risk characterization) **Note**: The 2011 PEA will address issues relating to LLIN; ITNs will be included by referencing and including text from the 2002 ITN PEA
Larviciding	Bacterial larvicides, Methoprene, Temephos, Monomolecular films, monomolecular oils	Exposure scenarios: spraying, spills, grinding of pesticides, contact of ingestion of treated water, disposal of pesticides contaminate water, reuse of pesticide containers, storage spills	Deterministic screening of human health impacts in 2007 PEA (problem formulation, analysis, and risk characterization) **Note**: The 2011 PEA will address new issues relating to Larviciding
		Toxicity of pesticides/other methods to non-target organisms	Describes the appropriate use of each larvicide method
Environmental Management Methods	filling breeding sites, lining water sources and canals, physical wetland drainage (surface, subsoil and coastal swamp) biological wetland drainage (tree planting), Impoundments deepening and narrowing of old drains, vegetation manipulation, synchronized cropping and intermittent irrigation, Larvivorous fish introduction, salt water flooding	Impact to food web	Environmental impacts addressed in 2007 PEA Discusses the environmental impacts from the methods used to reduce mosquito habitats and larvivorous fish **s**: The 2011 PEA will address new issues relating to these Environmental methods

4. 2011 PROPOSED APPROACH TO ADDRESS SIGNIFICANT ISSUES

The analysis completed in this Scoping Report provides the framework that will guide the completion of the PEA.

The assessment will rely on an abundance of reliable information already available in journals and publications by environmental and public health organizations, such as WHO and EPA, as well as the existing 2002 and 2007 PEAs. Additional information will be compiled from field reports and from discussions with implementing experts in the field. Analyses will be conducted by a pesticide specialist, human health and ecological risk assessors, and general environmental specialists. Each PEA team member will assist in the analysis of issues relevant to his/her discipline, with the team leader managing the analysis within the context of the PEA objectives.

EPA Standard health risk assessment procedures will be followed, including:

- Hazard identification: what health effects can be caused by the pesticide?
- Exposure assessment: How much of the pesticide are people exposed to through food, drinking water, and various nonagricultural uses?
- Dose-response assessment: What are the health effects at different exposure levels?
- Risk characterization: What is the extra risk of health problems likely to result from a pesticide in the exposed population?

The completed PEA will provide an environmental review for the USAID malaria vector control activities that have been identified at this time, and will help guide IVM program decision makers.

5. 2011 SCHEDULE AND CONTENT FOR THE PEA PREPARATION

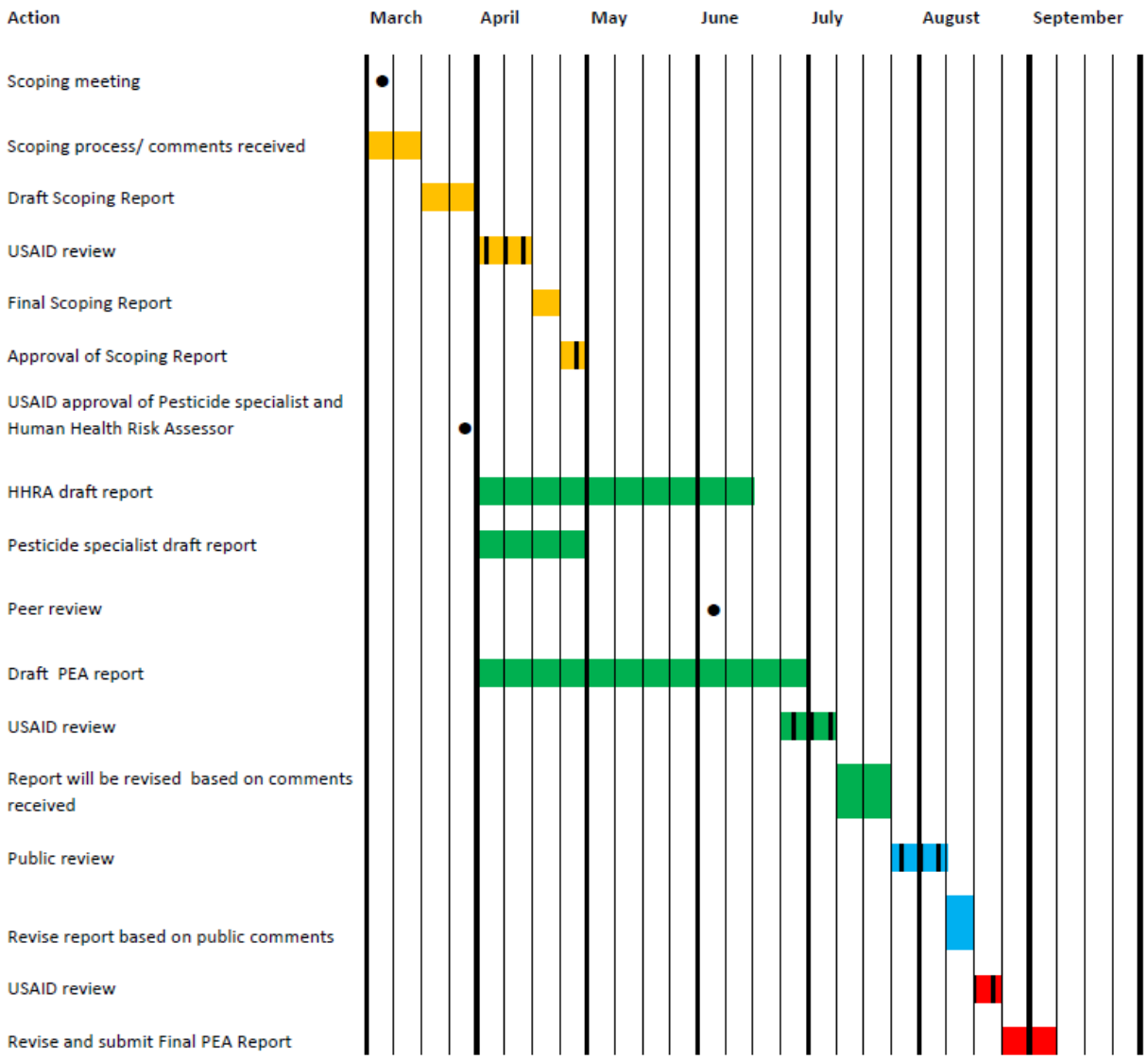
The development of the PEA will take place over a six month period, and will be completed by the end of the 2011 fiscal year. The PEA Team intends to prepare the draft report by the end of June. The document will be available for Public review by mid-July.

Table 3. IVM PEA Schedule

Action	Timeline	LOE	Responsible party	Deliverables
Scoping meeting	March 2		IRG/USAID	Scoping notes
Scoping process/ comments received	March 18	2 weeks	USAID/Interested stakeholders	
Prepare Draft Scoping Report		2 weeks	IRG	Draft Scoping Report
Submit Draft Scoping Report to USAID for review	April 1	2 weeks	USAID/Interested stakeholders	
USAID/stakeholder comments received	April 15			
Final Scoping Report	April 22	1 week	IRG	Final Scoping Report
Approval of Scoping Report	April 29	1 week	USAID	
USAID approval of Pesticide specialist and Human Risk Assessor	March 30 tentative date		USAID COTR and CO	
Pesticide specialist draft report	April 15	4 weeks (20 days)	James Litsinger	Pesticide toxicology/updates draft report
Peer review	May 25	3 days	EnDyna (and others)	
HHRA draft report	June 10	8 weeks (40 days)	Neptune and Company	HHRA draft report
Draft PEA report	June 24	10 weeks from Draft scoping report	IRG	PEA Draft report

Action	Timeline	LOE	Responsible party	Deliverables
Submit Draft PEA to USAID for review	June 24	2 weeks	USAID/various stakeholders	
USAID comments received	July 8			
Report will be revised based on comments	July 22	2 weeks	IRG/Pesticide specialist/HHRA	Revised draft report
Public review	July 22	2 weeks	USAID/IRG	Notification in Federal Register
Public comments received	August 5		IRG	Public response report
Prepare Final draft report		1 week	IRG	Draft final report
Final draft PEA report submitted to USAID for review	August 19	1 week	USAID	
Receive USAID comments	August 26		IRG	
Submit Final PEA Report	September 9	2 weeks	IRG	Final PEA Report submitted to USAID - 508 compliant

PEA Schedule Timeline



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ANNEX A. LIST OF SCOPING STAKEHOLDERS

Name	Agency	Attended scoping meeting		Provided additional comments
Susan Anderson	IRG		yes	yes
Jeanne Chabrier	IRG		yes	yes
Teresa Bernhard	USAID		yes	yes
Elissa Jensen	USAID	no		
Laura Harley	USAID – Senior Malaria Advisor	no		
Julie Wallace	USAID		yes	
Mike MacDonald	USAID	no		yes
Victor Bullen	USAID – LAC BEO	no		
Brian Hirsch	USAID - AFR ISEO		yes	
Barbara Britton	USAID – Europe BEO	no		
William Gibson	USAID – Europe BEO		yes	
Erika Clesceri	USAID – DCHA BEO		yes	
Joyce Jatko	USAID - EGAT BEO	no		
James Hester	USAID		yes	
Anila Jacob	USAID – toxins on people	no		
Emilie Stander	USAID - water	no		yes
Walter Knausenberer	USAID-African bureau		yes	yes
John Milliner	USAID		yes	
Eco San Martini	DOS	no		
Melanie Biscoe	EPA – office of Pesticides		Yes	
Susan Jennings	EPA – Office of Pesticides		webinar	yes
Kevin Sweeney	EPA – registration division	no		
Stanton Cope	DOD AFPMB (Armed Forces Pest Management Board)	no		
CAPT Mark Beavers	DOD AFPMB		yes	
LTC William Sames	Armed Forces Pest Management Board		yes	
Gerhard Hesse	Croplife	no		
Egon Weinmueller	Croplife	no		
Ms. Jessica Rockwood (BASF)	Croplife – Chair		Yes	

Name	Agency	Attended scoping meeting		Provided additional comments
Mr. John Thomas (Vestergaard Frandsen)	Croplife		Yes	
Mr. William Jany (Clarke)	Croplife		webinar	yes
Ms. Therese St Peter (Syngenta)	Croplife DFI/BASF		Yes	yes
Ms. Doreen Weatherby (Bestnet)	Croplife		Yes	yes
Ms. Lisa Goldman (Sumitomo)	Croplife		yes	yes
Michaela Pfeiffer	WHO		webinar	
Morteza Zaim	WHO	no		
Matt Lynch	Executive Director at JH University	no		
Jacob Williams	RTI	no		
David Macguire	Abt	no		
Peter Chandonait	Abt		yes	
Alan Schroeder	Abt	no		
Steve Hawkings	Chemonics		Yes	
Hoang Kim Vu	Chemonics		yes	
Karl Malamud-Roam	Public Health Pesticides Program Manager, Rutgers University		Conference call	
Gastao Lukangu	Luanda, Angola		webinar	
Kitty Andang		no		
Tiana Razafimahatratra	Antananarivo, Madagascar		webinar	
Yitayew Abebe	Addis Ababa, Ethiopia	no		
David Kinyua	Nairobi, Kenya	no		
Robert Buzzard	Accra, Ghana	no		
Madalitso Chisale	Lilongwe, Malawi	no		
Robert Layng	Maputo, Mozambique	no		
Timothy Karera	Kigali, Rwanda	no		
Aminata Niane Badianem	Dakar, Senegal	no		
Camilien Saint-Cyr	Pretoria, South Africa	no		yes
Tito Kodiaga	RTI, Nairobi		webinar	
Mark Hoppé	Lead of the Public Health IRAC group, Lawn and Garden Research Biology	no		yes

ANNEX C: GUIDANCE FOR DEVELOPING SEAS FOR MALARIA VECTOR CONTROL PROGRAMS

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NOTE

This *Guidance for Developing SEAs for Malaria Vector Control Programs* is a stand-alone document that has also been included as an annex to *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (the PEA). As a result, it refers to the PEA as a separate document, even though it is here an annex to the PEA.

INTRODUCTION

Before Reading this Document

If you are a prospective preparer of Supplemental Environmental Assessments (SEAs) for malaria vector control programs, it is **essential** that you read the following resources prior to reading this document:

- USAID (Agency for International Development). 2005a. *Environmental Compliance Procedures, Title 22 Code of Federal Regulations (CFR), Part 216*. Available at http://www.usaid.gov/our_work/environment/compliance/ reg216.pdf.
- USAID (Agency for International Development). 2005b. *USAID Environmental Procedures Training Manual.* Available at http://www.encapafrica.org/ EPTM.htm.
- USAID (Agency for International Development). 2006. *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment.*
- USAID (Agency for International Development). 2002. *Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa.*

These documents provide in-depth information about environmental compliance procedures in the U.S. Agency for International Development (USAID) and context for this guidance document.

The SEA: Part of USAID Environmental Compliance

Under the U.S. Code of Federal Regulations (22 CFR §216), malaria vector control activities supported or planned by USAID must undergo environmental examination. To assist USAID missions in planning malaria vector control interventions, USAID recently drafted a Programmatic Environmental Assessment (PEA), *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (USAID, 2006), that provides a broad view of the human health and environmental impacts that could result from implementation of malaria vector control interventions. However, the PEA cannot account for intercountry and interregional variation regarding issues such as the capacity to manage pesticides used for vector control and the environment likely to be impacted. For this reason, SEAs must be developed to describe in-country impacts of interventions and describe country-specific activities to minimize those impacts. This process of using the PEA as the basis on which the country-specific SEA is developed is called "tiering." Tiering off from the PEA saves substantial time and money by not having to repeat environmental review that applies generically to all activities within a program. Tiering also ensures basic consistency and quality across all of the program's activities, no matter where they are undertaken.

Whenever an in-country malaria vector control activity involves "assistance for the procurement or use, or both, of pesticides," SEAs supplementing the PEA must address the pesticide procedures found in 22 CFR 216.3(b). The pesticide procedures list 12 factors to address in SEAs and are described in the following chapters.

In sum, the SEA should be looked upon as the overall picture within the country. The SEA should address the human health and environmental impacts that may occur as a result of USAID support of malaria vector control activities.

The purpose of a malaria program is to save lives and reduce illness and suffering. The purpose of the SEA is to optimize these goals by ensuring malaria control programs use only safe and efficacious pesticides and use them in the way that will minimize inadvertent poisonings and intoxications; by ensuring the natural resources on which people depend for their daily food production and nutrition are not damaged; by ensuring that long term development is promoted by avoiding disruption of agricultural exports by avoiding misuse of malaria pesticides on agricultural crops; and, by participating in international environmental agreements such as the Stockholm Convention on Persistent Organic Pollutants, among others.

When to Prepare an SEA

Since there are minor variations in the way USAID bureaus approach 22 CFR 216 in order to address special circumstances in their regions, *it is important to consult with the Bureau Environmental Officer (BEO) about his or her expectations prior to development of the environmental assessment*. Because the majority of USAID-supported malaria interventions occur in Africa, this section will discuss the types of environmental assessments that need to be conducted for various types of malaria vector control interventions.

Within the Africa Bureau, the level of analysis in the SEA for a country-specific malaria project will depend on which pesticides are proposed to be used. In all cases the SEA will address the 12 factors required by the pesticide procedures in 22 CFR 216.3(b). The level of analysis in the these twelve factors can be more streamlined in cases where all pesticides being proposed for a malaria project are registered by the U.S. Environmental Protection Agency (EPA) for same or similar use without restriction. If one or more pesticides are registered for same or similar use but with restrictions (restricted use pesticides), then the level of analysis will be greater. Should one or more pesticides not be registered for same or similar use or be cancelled-use pesticides, then the level of analysis in the pesticide procedures portion of the SEA would be greatest in order to justify their selection and use.

In all cases public participation is required since each SEA is an amendment to the PEA. The level of public participation will track the degree of analysis in the pesticide procedures that is driven by the type of pesticides proposed. It will also be affected by other aspects of the SEA. The degree and method of public participation is decided by the USAID Mission undertaking the SEA in consultation with their BEO.

A SEA is prepared for a 5 year program and covers all potential geographic locations and types of pesticides potentially considered over that five year period. On an annual basis, and for programs that are continuing to use pyrethroids or carbamates, an annual letter report will be submitted to the BEO (regional and pillar). It must contain information regarding program changes (such as mortality rates etc.), entomological/resistance monitoring results and data, and program response to those results. It should also contain the results of the environmental monitoring results and how the program will improve areas of deficiency. The letter report will be filed with the SEA.

Should the program propose the use of an Organophosphate or Organochlorine an amended SEA must be submitted to the Regional and Pillar Bureau BEO's via the MEO, REA and mission director. The Amended SEA must be submitted prior to the procurement of pesticides.

Who Prepares an SEA

SEAs should be prepared during the initial planning stages of one or more interventions in-country before an intervention or pesticide has been chosen and before funding has been

committed. The SEA will guide the decision-making process in designing the overall approach to fighting malaria in the country an must be completed prior to making descisons regarding pesticide selection, application and geographic location. The SEA is also a living document used for adaptive management of the malaria program throughout the life of the project. It is a day-to-day management tool, and amendments to the SEA are likely as new information or new directions emerge. The individuals preparing the SEA may be employees of the contractor who will implement the intervention or an independent contractor. Quality control is provided by the host mission staff with the final decision for sufficiency being made by the BEO in the approval process.

Individuals preparing an SEA should be well acquainted with the possible human health and environmental impacts of the intervention and best practices to mitigate those impacts. These individuals also need sufficient experience with interpretation and implementation of USAID environmental procedures, parallel procedures of the host country, and the environmental impact assessment and review process. SEA preparers will be aided substantially by guidance provided in the *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (USAID, 2006).

The SEA preparers should conduct their work in conjunction with specialists in the various interventions considered, host-country malaria control program staff, any regional or local health program staff, and any other stakeholders affected by the interventions considered including local communities and nongovernmental organizations. Specialists should furnish details about the design and implementation of their respective interventions. It is especially important for SEA preparers to work closely with USAID Mission staff so monitoring, mitigation, and evaluation activities can be incorporated into overall project planning.

The USAID Mission health team and the USAID Mission Environmental Officer (MEO) should be actively involved in the preparation of the SEA. This can be achieved by accompanying the SEA preparers on site visits and participating in discussions, or simply posing questions or making comments or suggestions when the SEA is initially drafted. Once the SEA has been drafted, it must be signed by the preparers, cleared by the activity manager or SO team leader, the MEO, and the Regional Environmental Advisor (REA). It is then signed by the mission director prior to submitting it to the BEO who shall make the decision whether to approve/disapprove the SEA and sign. Communication with the BEO throughout the process is useful to avoid having the draft SEA returned for revisions.

COMPONENTS OF AN SEA AND LETTER REPORT

22 CFR 216.6 (c) describes the content and form that should be used for all USAID environmental assessments, including SEAs. The following sections examine each component of the SEA in detail. The text boxes in each section contain the CFR text. These are followed by discussion of what the section should contain to comply with CFR text and address malaria-specific issues. When relevant, the section will provide additional guidance for on-the-ground research.

Acronyms

Provide a list of all acronyms and abbreviations used in the SEA.

Table of Contents

A table of contents at the beginning of the document will enable readers to find relevant information quickly.

Summary

The summary shall stress the major conclusions, areas of controversy, if any, and the issues to be resolved.

Along with these aspects, the summary may include discussion of the intervention in the context of the timeframe of USAID support, other USAID actions, Ministry of Health (MOH) initiatives, and the activities of other donors. If pesticides are to be procured or used, the ones for which approval is requested shall be listed in this summary. Mitigative measures required by the SEA will also be listed with page number references to where they are more fully described in the text of the SEA.

Background and Purpose

The Environmental Assessment shall briefly specify the underlying purpose and need to which the Agency is responding in proposing the alternatives, including the proposed action and no action alternative.

To explain the purpose and need for the proposed action, this section should describe the background of malaria and malaria control in the country and the intervention target area. To the extent possible, this section should include information on the following:

- Malaria in the country and intervention target area

– Malaria parasite species

– Malaria endemic and epidemic risk areas

– Start, end, and duration of highest malaria transmission

– Malaria incidence

– Malaria prevalence

– Malaria vector species

- History of malaria control in the country and intervention target area

– Historical use of insecticides

– Previous house spraying campaigns, including the nuber of house sprayed and the change in Malaria cases of the course of successive spray seasons.

– Insecticide-treated net (ITN) distribution targets and mechanisms

– Previous environmental management campaigns

– Previous use of larviciding

- Current malaria control policies

– Interventions supported by the MOH

– Rationale for interventions selected

– Status of intervention implementation or success

– Pesticide use policies

– Current capacity of clinics and hospitals and their workers to diagnose and treat pesticide intoxications

– Baseline data for pre-existing presence of the pesticides being proposed to be used by the project, both in the target populations of communities to be treated and in the natural environment and agricultural crops in the area to be able to monitor and measure safe and correct use

- Administration of malaria control activities

– Role of national malaria control program

– Existence and role of separate department of vector borne diseases

– Authority of the MOH versus local or regional malaria control programs

- Other donor activities

Additionally, this section should describe the effectiveness of the malaria interventions already in place and provide some indication of whether they need strengthening through training, better planning, more efficient management, or other processes.

Much of this information can be obtained by talking to national malaria control program staff and reviewing existing relevant documents, such as a national strategic plan for malaria control. Local or regional malaria control program staff may also provide valuable information on the history of malaria and malaria control in the target area and the status of intervention implementation and success. In some instances the SEA team may need to develop this information.

Alternatives Including the Proposed Action, and no action alternative

This section should present the environmental impacts of the proposal and its alternatives in comparative form, thereby sharpening the issues and providing a clear basis for choice among options by the decision maker. This section should explore and evaluate reasonable alternatives and briefly discuss the reasons for eliminating those alternatives that were not included in the detailed study; devote substantial treatment to each alternative considered in detail including the proposed action so that reviewers may evaluate their comparative merits and risks; include the alternative of no action; identify the Agency's preferred alternative or alternatives, if one or more exists; and include appropriate mitigation measures not already included in the proposed action or alternatives.

Affected Environment

This section overlaps with section h of the Pesticide Procedures section, which is addressed in Environmental Consequences. When preparing an SEA for an intervention supporting pesticide

use, put the information that would be included in this section in the Pesticide Procedures section (see below). When preparing an SEA for environmental management, where pesticides are not used, this section should include the conditions under which the environmental management intervention will take place, including climate, flora, fauna, geography, hydrology, and soils.

The affected environment also includes the human environment. Include information on the administrative divisions in the target area so that when administrative entities are referenced in subsequent sections, they will be familiar to the reader. In addition, include the populations that will be affected by the intervention. The national malaria control program and the local or regional malaria control program can usually provide this information.

Environmental Consequences

This section forms the analytic basis for the comparisons under [Alternatives Including the Proposed Action]. It will include the environmental impacts of the alternatives including the proposed action; any adverse impacts that cannot be avoided should the proposed action be implemented; the relationship between short-term uses of the environment and the maintenance and enhancement of long-term productivity; and any irreversible or irretrievable commitments of resources which would be involved in the proposal should it be implemented. It should not duplicate discussions in [Alternatives Including the Proposed Action]. This section of the Environmental Assessment should include discussions of direct effects and their significance; indirect effects and their significance; possible conflicts between the proposed action and land use plans, policies and controls for the areas concerned; energy requirements and conservation potential of various alternatives and mitigation measures; natural or depletable resource requirements and conservation potential of various requirements and mitigation measures; urban quality; historic and cultural resources and the design of the built environment, including the reuse and conservation potential of various alternatives and mitigation measures; and means to mitigate adverse environmental impacts.

Not every aspect listed here is relevant for malaria vector control interventions. Thus, only the points described below need to be considered.

Any adverse effects than cannot be avoided. For alternatives involving pesticide use, unavoidable adverse effects include human and environmental exposure from emergencies, such as spills or fires, and possible effects from residential or occupational exposure that **cannot** be mitigated. For alternatives involving environmental management, unavoidable impacts on water resources used by humans and other organisms, destruction of flora and fauna, reduction of biodiversity, etc. (see Table 11 in the integrated vector management [IVM] PEA), should be described here.

Any irreversible or irretrievable commitments of resources. For alternatives involving pesticide use, the MOH often acquires new insecticides or larvicides, storage facilities, vehicles, application equipment, and protective wear and accoutrements that could be used in future interventions with chemicals that have not undergone environmental review or pilfered and used for activities not related to malaria control, potentially harming human health and the environment.

Discussion of direct and indirect effects and their significance. Direct effects can be characterized as negative and positive. The negative impacts of the intervention are discussed in depth in other parts of the SEA and need only very brief mention here. The positive effects of the intervention,

such as providing protection against malaria to a target area population; reduced incidence of adult morbidity, miscarriages, low birth-weight, and adverse effects on malaria-induced fetal neurodevelopment; and reduced incidence of malaria-related childhood anemia, complications, organ failure, and death can be described briefly here.

Indirect effects can be considered equivalent to "irreversible commitments of resources," in that support of malaria vector control interventions may result in procurement of pesticides, equipment, storage facilities, vehicles, or other commodities that can be used for purposes other than those intended or that adhere to best practices.

Conflicts with other policies, plans, or controls for the areas under consideration. It is crucial that malaria vector control interventions supported by USAID do not contradict U.S. or host-country laws, regulations, and policies or international treaties (Stockholm, Basel, Rotterdam) to which the United States or the host country are party. It is also important to identify whether the proposed action contradicts the goals of other host-country or donor activities in the target area.

Provide an overview of the local environmental and public health regulations as they apply to malaria vector control. This would include any information on

- Pertinent national legislation
- International treaties (Stockholm, Basel, Rotterdam, or other applicable treaties)
- National environmental assessment procedures
- Systems for registration of chemicals
- Guidelines for control operations.

Consult with the Ministries of Health, Environment, and Agriculture and donor projects to ensure that all aspects of the intervention are legal or complementary to current activities in the target area.

To the extent a country may need advice or assistance in complying with the requirements of international treaties, especially the Stockholm Convention on Persistent Organic Pollutants, the SEA will need to identify how the USAID malaria activity will provide the needed training and/or support.

Environmental impacts of the alternatives, including the proposed action. The environmental impacts of alternatives involving pesticide use will be addressed in the Pesticide Procedures (see below). Thus, for alternatives involving pesticide use, simply highlight in this section the primary human health and/or environmental risks of the interventions considered. For alternatives involving environmental management, however, the environmental impacts should be described in depth here. This section must include a discussion on the cumulative impacts of pesticide use on human health and the environment, including a discussion of the impacts of agricultural use combined with IRS/ITN use.

Pesticide procedures. 22 CFR 216.3(b) requires that when "a project includes assistance for procurement or use, or both, of pesticides," that the Initial Environmental Examination or subsequent Environmental Assessment address the following 12 factors:

a) EPA registration status of the requested pesticide

b) The basis for selection of the requested pesticide

c) The extent to which the proposed pesticide use is part of an IVM program

d) The proposed method or methods of application, including availability of appropriate application and safety equipment

e) Any acute and long-term toxicological hazards, either human or environmental, associated with the proposed use and measures available to minimize such hazards

f) The effectiveness of the requested pesticide for the proposed use

g) Compatibility of the proposed pesticide with target and nontarget ecosystems

h) The conditions under which the pesticide is to be used, including climate, flora, fauna, geography, hydrology, and soils

i) The availability and effectiveness of other pesticides or nonchemical control methods

j) The requesting country's ability to regulate or control the distribution, storage, use and disposal of the requested pesticide

k) The provisions made for training of users and applicators

l) The provisions made for monitoring the use and effectiveness of the pesticide.

Guidance on addressing these factors appears in the following:

Pesticide Procedures

As previously described, 22 CFR §216.3(b) mandates the consideration of 12 factors when a project includes "assistance for procurement or use, or both, of pesticides." In this chapter, each factor is discussed in sequence. For each factor, a text box highlights the relevant guidance from USAID's Pest Management Guidelines (USAID, 1991), and two subsections provide guidance specific to malaria vector control on what to write and how to obtain information required to consider the factor (for some factors, these are presented in a tabular format instead of two subsections, where there is a relationship between what to write and how to obtain information).

(a) EPA Registration Status of the Requested Pesticide

What to Write

This section should include the following essential information:

- Host-country registration status
- EPA registration status as
  - General Use Pesticide (GUP)
  - Restricted Use Pesticide (RUP)
  - Cancelled (state reasons for cancellation—e.g., health concerns, no market incentive)
  - Not Registered
  - Pesticide formulation and percent of active ingredient
  - Registration of any same or similar uses. (Note: Larvicides should have same or similar uses in the United States; however, the closest "same or similar use" for

insecticides is indoor pest control, because insecticides are not used for Indoor Residual Spraying (IRS) or ITN programs in the United States.)

The section may also include the following optional information:

- Chemical Abstracts Service number (CAS number)
- Trade name
- Manufacturer

Sources of Information

For Host-Country Registration

Each country should have a pesticide registration office. This registration office, typically in the Ministry of Agriculture (MOA), may or may not handle the registration of pesticides for public health use—sometimes these pesticides are registered by the MOH. The national malaria control program is likely to know which institution registers public health pesticides.

For EPA Registration

The PEA for malaria vector control interventions and the PEA for ITMs contain information on EPA registration of World Health Organization (WHO)–recommended pesticides; if there is a question as to the status of a pesticide, search EPA's Web site (www.epa.gov) or contact EPA's Office of Pesticides to confirm the current status since this status can and does change from time to time as new information becomes available to EPA.

(b) The Basis for Selection of the Requested Pesticide

What to Write

Describe how each of the criteria listed in Section 6.1.2 of the PEA for IVM (and listed again in this section) were considered in the host country's decision to use a particular pesticide. Four threshold criteria must be met in making decisions on pesticides used in malaria vector control:

- Pesticide registration in the host country
- Acceptability of the pesticide to the national malaria control program
- Risk to human health—pesticides must be approved by the WHO and should be preferred based on their safety as described in USAID's Programmatic Environmental Assessment for Integrated Vector Management
- Risk to environment, livestock, and/or agricultural trade.

Beyond these four threshold considerations, technical and logistical factors must be addressed in comparing and selecting insecticides for malaria vector control. The primary factor to be addressed is

- Vector resistance

Secondary factors include

- Appropriateness of surface for spraying

- Duration of effectiveness (and implications for cost)
- Cost of insecticide

Tertiary factors include

- The need for an insecticide of a different class to prevent resistance
- Major classes of insecticides used in other vector control interventions that could promote resistance
- Major classes of insecticides used in the agricultural sector that could promote resistance
- Host-country capacity to prevent pilferage

Sources of Information

The person or institution deciding which pesticide to use may include

- Minister of health
- National malaria program manager
- National malaria program vector control specialist
- A body of key technical experts and stakeholders, such as the National IRS Technical Team in Zanzibar.

Also consult individuals involved in pesticide selection to complete this section.

(c) The Extent to Which the Proposed Pesticide Use Is Part of an Integrated Pest Management Program

What to Write

Describe the extent to which the national malaria control program supports the following interventions:

- Environmental management
- Larviciding
- IRS
- ITNs

If the national malaria control program does not support a certain intervention, describe where and when that intervention may be appropriate. Discuss possibilities for combining the goals and regulations of other sectors with those of the malaria control program. For example, Uganda national law mandates that each district conduct sanitation work for public health; such activities could be adapted to reduce vector breeding sites.

Sources of Information

Typically, the national malaria control strategy details the extent to which different vector management options are considered, and target populations or geographic areas that correspond

to those options (for example, ITN distribution free of cost to pregnant women and children under 5 years old). Discuss with national and regional or local malaria control program staff the extent to which the various vector control options are supported, both ideologically and financially. Additional stakeholders, such as public works officers, may provide additional perspectives.

(d) The Proposed Method or Methods of Application, Including Availability of Appropriate Application and Safety Equipment

Examine in detail how the pesticide is to be applied and the measures that will be taken to ensure its safe use, using the guideline in the table below.

What to Write	***Sources of Information***
General introduction to the intervention; include the purpose for which pesticides are used in that intervention	PEA and other Environmental Assessments
Describe the specific method of pesticide preparation and application	In-field specialist, trainer, IRS program manager, needs assessor, and/or national, regional or local malaria vector control specialists
Describe the method, duration, and general content of training for workers and supervisors	In-field specialist, trainer, IRS program manager, needs assessor, and/or national, regional or local malaria vector control specialists
Describe methods for protecting workers and supervisors from exposure	PEAs for IVM and ITMs, WHO manuals, industry manuals (see Resources chapter)
Describe method of supervision	In-field specialist, trainer, IRS program manager, needs assessor, and/or national, regional or local malaria vector control specialists
Describe how intervention workers and supervisors are chosen	National malaria control program, local or regional malaria control program

(e) Any Acute and Long-Term Toxicological Hazards, Either Human or Environmental, Associated with the Proposed Use, and Measures Available to Minimize Such Hazards

Describe measures the program will take to reduce the potential for exposing humans or nontarget organisms to selected pesticides using the guidelines in the table below. Also describe monitoring measures that will allow the program to identify problems with users applying pesticides and with people who live in intervention areas. The level of monitoring for higher risk pesticides is expected to be proportionally higher than for ones that are registered by EPA for same or similar use without restrictions.

What to Write	*Sources of Information*
Acute and long-term toxicological hazards to humans	Include Pesticide Profile (from Annex E of the PEA for IVM) as an annex to the SEA and reference it
Steps to prevent occupational exposure	Reference Pesticide Procedures section (d)
Steps to prevent residential exposure, typically information, education, and communication (IEC) campaigns through a local subcontractor or local health office	Methods of communication from local health office or potential subcontractor, critical information content from the PEA for IVM and ITMs
Steps to mitigate pesticide poisoning, including information provided to target area health practitioners and medicines necessary for treatment	Target area hospital or health facility manager, Ministry of Health formulary office
Steps to inform or train drivers transporting pesticide (for long-distance travel and daily operations)	PEA for IVM
Steps to monitor pesticide levels in a statistically significant sample of workers implementing the intervention and/or potential beneficiaries of the intervention. (A mechanism for making corrections or reconsidering pesticide selection or how it is applied must be created, including how to Amend the SEA). Baseline data on the current situation regarding any pre-existing use of the proposed pesticides and their levels in people and the environment should be summarized in this section.	EPA, host country health and environment authorities, and private-sector specialists; see also the WHO's Field surveys of exposure to pesticides—Standard Protocol published in 1982 for guidance.

(f) The Effectiveness of the Requested Pesticide for the Proposed Use

What to Write

- Describe the vector species and its/their resistance to the chosen insecticide or larvicide in the target location, if that information is available
- Describe the impact (or potential impact) of agricultural pesticide use on vector resistance
- Describe steps to ensure quality of the pesticide imported. Some producers, especially those based in developing countries, may not manufacture pesticides to WHO specifications, which can result in pesticides with harmful contaminants and/or reduced efficacy of the product. A practical system to ensure testing of pesticides for purity and potency is needed.
- Reference Pesticide Procedures section (l) for program monitoring activities that will be conducted to determine pesticide efficacy

- For IRS, describe the insecticide's appropriateness for the wall construction material(s) used in the target location.
- For IRS, describe the extent to which the community will accept the intervention taking into account the education that will be provided to individuals through the IEC campaign. Widespread community acceptance of the activity is necessary for it to be effective.

Sources of Information

The national malaria control program and the local or regional malaria control program will have information on vector resistance. The MOA, a local or district agriculture office, or area nonprofit organizations may have information on the impact (or potential impact) of agricultural pesticide use. The MOH or the MOA should have facilities for reliably testing imported insecticides; if no facilities are available in the host country, ask where pesticides can be independently tested in the region by a laboratory not affiliated with either the producer or the broker. Local, regional, or national NGOs, local administrative officers, as well as Ministries of Agriculture, Trade, Natural Resources, or Environment will be able to provide their perspectives on the intervention's acceptability to the community

(g) Compatibility of the Proposed Pesticide with Target and Nontarget Ecosystems

What to Write

This section examines the potential effect of the pesticide on organisms other than the target pest–both wildlife and domestic (for example, the effect on the bee colonies kept in the area). Nontarget species of concern also include birds, fish, bats, dragonflies and other predator species that naturally reduce mosquito populations. Discuss the potential for negative impact on nontarget species and identify appropriate steps the program will take to mitigate potential adverse impacts. Describe key concerns based on the pesticide's toxicity to nontarget organisms and opportunities for negative impacts on nontarget organisms typically associated with noncompliance with best practices (for example, pesticide pilferage, locating a storehouse in a flood plain, improper dumping of pesticide in water bodies). Larviciding of open water (if it is part of the proposed program) and the effects of improper use of pesticides after pilferage should receive special attention in this section.

Describe the steps the program will take to monitor and mitigate these potential impacts, referencing Pesticide Procedures sections (d) and (e) when appropriate. Under 22 CFR §216.3(a), projects and programs for which Environmental Assessments are prepared must include measurement of any changes in environmental quality, positive or negative, during their implementation "to the extent feasible and relevant."

Sources of Information

The PEAs on IVM and ITMs indicate toxicity to nontarget organisms. Major concerns about how environmental contamination will occur can be discussed with in-field specialists, the program manager, the Ministry of Environment, and the national malaria control program. Typical mitigation and monitoring steps are described in the PEAs on IVM and ITMs.

(h) The Conditions under Which the Pesticide Is To Be Used, Including Climate, Flora, Fauna, Geography, Hydrology, and Soils

What to Write

Describe the environmental conditions under which the pesticide is to be used, identifying environmental factors that might accentuate (or diminish) the risk of non-target organisms' exposure to pesticides, discussing the need for any additional mitigative measures to reduce exposure risk (citing Pesticide Procedures (g) as needed). Describe aspects of the environment that may be particularly sensitive or subject to contamination as a result of the intervention, and provide a brief overview of the monitoring and mitigation efforts to prevent negative environmental impacts (citing Pesticide Procedures (g) as needed). Discuss any pertinent information on the target area and corresponding peripheral areas, such as:

- Geographic location of target area
- Land area of target location
- Ecological zone
- Climate
- Range and average temperatures
- Range and average rainfall
- Seasonal weather patterns
- Sensitive ecosystems
- Protected areas
- Forest resources
- Common flora and fauna
- Endangered fauna
- Surface water resources
- Groundwater resources (including water table depth, when available)
- Soil types.

Sources of Information

General land area maps can be found on the United Nations Web site or just by searching on the internet. One might expect the Ministry of Environment or a similar ministry to have the information listed above; however, these ministries usually do not have summary information on specific areas in the country. Sometimes the best places to get this information are local environmental nonprofit organizations, local donor projects dealing with the environment, or a search on the internet. (An institution may even have geographic information system [GIS] maps containing this information.) Surface water resources, groundwater resources, and soil types may be found through the Food and Agriculture Organization (FAO) Web site, although the MOA

may also have this information. Lists of endangered species can be acquired through the World Conservation Union (IUCN) Red List of endangered species.

(i) The Availability and Effectiveness of Other Pesticides or Nonchemical Control Methods

What to Write

Identify other WHO-recommended malaria control chemicals that could be used in the intervention, taking into account host-country pesticide laws and regulations. Describe the potential for using environmental management for malaria vector control, taking into consideration host-country sanitation laws and environmental regulations.

Sources of Information

The MOA and the MOH should know which WHO-recommended chemicals are registered in-country and could be used. The MOH should know what the sanitation laws require and how they can be leveraged to attain malaria control program goals. The Ministry of Environment will know the regulatory constraints on nonchemical approaches to malaria vector control, such as drainage projects, wetland destruction, etc.

(j) The Requesting Country's Ability to Regulate or Control the Distribution, Storage, Use, and Disposal of the Requested Pesticide

Examine in detail how the pesticide is to be distributed and stored, and how waste materials will be disposed, using the guideline in the table below.

What to Write	*Sources of Information*
General	
If there are local, regional, or national laws, regulations, or guidelines on distribution, storage, and disposal of pesticides, describe them, describe how well they are actually implemented, and the measures the program will take to follow those guidelines.	The MOA and the Ministry of Environment can provide information on national government laws, regulations, and guidelines on pesticide distribution, storage, and disposal.
Describe any capacity-building activities the program will undertake to improve the host-country distribution, storage, and disposal capacity for pesticides.	Discussions with the national malaria control program, the needs assessor, and local and regional officials can elicit suggestions for capacity building for managing distribution, storage, and disposal of pesticides.
Distribution	
Describe how the pesticide will be transported to the target area	In-field specialist, IRS program manager, needs assessor, national regional or local malaria vector control specialists
Storage	
Describe the current pesticide storage infrastructure in the target area, measures to protect and control it, and whether the	Site visit with needs assessor, and local malaria vector control specialist

What to Write	*Sources of Information*
location is sufficient to avoid flooding.	
Describe the number of storage facilities that are needed for the operation, and where they will be located.	In-field specialist, IRS program manager, needs assessor, national malaria vector control specialists
Describe any construction or renovations that must be undertaken for storage facilities to comply with standards described in UNFAO's Pesticide Storage and Stock Control Manual, including necessary emergency equipment and any need for storekeeper training.	Site visit and UNFAO's Pesticide Storage and Stock Control Manual
Describe measures taken to keep storage facilities secure, such as locating the site in a secure area, storing pesticides off the ground, on sturdy shelving, in a well organized manner and maintaining inventory controls and records, double-padlocking, and guarding. Security of storage facilities is vital to preventing pilferage. Describe process for safe disposal of pesticides that may become obsolete or unusable.	In-field specialist, IRS program manager, needs assessor, national malaria vector control specialist, and PEA recommendations
Disposal	
Describe anticipated waste materials from operations, including but not limited to the following: Insecticide containers, wrappers, and/or sachets Rinse-water from cleaning personal protective equipment (e.g., overalls, gloves, face shield or mask), sprayers, and spray operators themselves (for IRS)	Pesticide manufacturer, PEA recommendations, in-field specialist, IRS program manager, needs assessor, national malaria vector control specialist
Describe whether or not waste materials are expected to be contaminated with insecticide.	Pesticide manufacturer, in-field specialist, IRS program manager, needs assessor, national malaria vector control specialist
Describe procedures to deal with contaminated materials; it is particularly important to ensure that empty pesticide containers are not reused for domestic purposes.	Typically PEA recommendations and UNFAO guidelines; check to make sure any host-country laws and international treaties are followed

(k) The Provisions Made for Training of Users and Applicators

What to Write

Generally describe the training that will be provided to users and applicators. Reference Pesticide Procedures sections (d) and (e).

Sources of Information

Pesticide Procedures sections (d) and (e).

(l) The Provisions Made for Monitoring the Use and Effectiveness of the Pesticide

What to Write

Describe the elements of a Human Health and Environmental Evaluation Report (described in the PEA for IVM), their purpose, the activities that must be conducted to achieve that purpose, and the parties responsible for those activities, using the table below as a guide.

Environmental Reporting Elements	***Purpose***	***Activities and Responsible Parties***
Post-training evaluation of applicators and supervisors, storekeepers, and medical practitioners	Preliminary assessment of trainees' understanding of training material	Trainers responsible for developing evaluation forms, conducting evaluation, and providing report to program manager and contractor
Post-training evaluation of instructors	Determine effectiveness of training	Program manager responsible for evaluating instructor quality, reporting to contractor
Pesticide stock management reports	Track insecticide leakage/pilferage	Team leaders and supervisors responsible for recording data and submitting it to logistics coordinator or data manager for data aggregation and reporting to program manager and contractor
Mitigation monitoring reports	Identify gaps in implementation of best practices, need for corrective action	Program manager, logistics manager, and/or select supervisors will be responsible for spot-checks of operations. Data manager responsible for synthesizing data and reporting to program manager and USAID contractor
Human exposure monitoring reports	Ensure the program is improving overall health and livelihoods of people	Contractor or subcontractor responsible for collecting baseline data, intermittent data during and after spray operations, and reporting to

Environmental Reporting Elements	***Purpose***	***Activities and Responsible Parties***
		the program manager and USAID contractor
Environmental impact monitoring reports	Determine whether IRS is exposing sensitive species and ecosystems to pesticide	Contractor or subcontractor responsible for collecting baseline data, intermittent data during and after spray operations, and reporting to the program manager and USAID contractor
Entomological monitoring reports	Determine effectiveness of IRS on reducing mosquito population	Vector control division and national malaria control program of the MOH
Reports on malaria incidence and morbidity	Determine effectiveness of IRS on reducing malaria incidence and morbidity	Health center heads are responsible for collecting malaria incidence and morbidity data (baseline and subsequent) and sending it to the district vector control officer
		The USAID program data manager and regional or local health office counterpart are responsible for synthesizing data and reporting findings to the program manager and USAID contractor
Post-intervention survey, assessing knowledge, attitudes, and practices (KAP) of community regarding community roles and responsibilities	Identify information that requires more emphasis or different communication strategy before the next phase or intervention	IEC subcontractor responsible for survey design, implementation, data analysis, and reporting

The report may exclude some of these elements, depending on the nature of the intervention, the nature of USAID support, the country situation, and USAID and stakeholder concerns.

Sources of Information

The PEA for IVM should be a general guide for monitoring procedures. Details on entomological monitoring can be acquired from the in-field specialist, needs assessor, program manager, or national malaria control program. Environmental and human health monitoring procedures should be determined by a credible host-country institution or other subcontractor.

Conclusions:

A summary statement to cohesively outline the deliberative process, the criteria for decision-making and the consideration given to the decision criteria is needed. Those decision criteria include: pest susceptibility, socioeconomic impact, cost , country preference, and human and ecological impacts. Each of these criteria should be evaluated against each of the alternatives including the no action alternative. The table below presents a way to document how each of the criteria was considered weighted against the other criteria. For instance, should susceptibility be a concern the pesticide under consideration might get a negative three while it may be the country preference thereby receiving a positive three and so on for the remaining criteria. The end result should be a qualitative assessment of all the weights of the criteria. If the deliberative process was appropriately executed the table should show that the pesticide of choice in the preferred alternative has the greatest value of all pesticides considered. The same summary should be repeated for all alternatives considered such a variable geographic locations, and pesticide disposal alternatives.

Criteria	Pesticide choice	Susceptibility	Socio-economic Impact	Cost	Country preferences	Human and ecological impacts	Total
Preferred Alternative	Organophosphate						
	Carbamates						
	Pyrethroids						
No Action							

Susceptibility refers to a pesticides ability to effectively manage the vector thereby achieving the purpose and need to the action. Socioeconomic impact discusses the effect that the pesticide/alternative will have on the economics and society. For instance, the no action alternative will allow for an increased transmission rate. This leads to decreased GDP and mortality. The socioeconomic impacts of the no action alternative are therefore, negative. Cost is a consideration during the assessment. The goal of the PMI program is to reduce mortality by 80%. Cost affects the number of houses sprayed and therefore affects efficacy. Host country preference is also a deliberative consideration. The PMI program heavily considers the host country preferences but retains the decision as to which pesticide the PMI program will chose. However, the country preference is considered as part of the decision making process. Last, human and ecological impacts of the action are considered. Not all pesticides have the same effect on the environment (human and ecological). Therefore, the effect that the pesticide is considered during deliberation. This allows for the most efficacious program with the least environmental effect. The conclusion must discuss how the values displayed in the table were derived. It must summarize the evidence that lead to the weight of each criteria.

Required and recommended mitigation measures. This subsection is the most vital part of the SEA. An SEA is meaningless if the actions required and/or recommended are not implemented. This section serves to expedite planning and budgeting for monitoring, mitigation, and evaluation activities. It provides a synopsis of monitoring, mitigation, and evaluation measures that logistical needs assessors, program managers, host-country government staff, and other stakeholders can easily incorporate into project planning. This section should include the type of impact monitored, mitigated, or evaluated and which entity is responsible for the monitoring, mitigating, or evaluating action. Use the recommended mitigation measures in the PEA for IVM (USAID, 2006) and the PEA for insecticide-treated materials (ITMs) (USAID, 2002) as a guide for recommended mitigation measures in the SEA. Additionally, if pesticide stocks are identified that need to be analyzed and either repackaged or disposed, describe the location of the stocks and the procedures that must be taken to handle those stocks during the program (see the PEA for IVM for the protocol for finding potentially obsolete pesticide stocks).

An SEA is a living document and process. The SEA must include a workable plan for ongoing monitoring of environmental soundness to identify any problems that may develop and create a workable mechanism to address them through amendments to the SEA. This may include mechanisms for measuring pesticide levels in people – both sprayers and residents of sprayed houses, as well as in the surrounding environment. This is especially critical for any pesticides that are not registered by EPA for same or similar use without restrictions.

Preparation Methodology

The Environmental Assessment shall list the names and qualifications (expertise, experience, professional discipline) of the persons primarily responsible for preparing the Environmental Assessment or significant background papers.

In this section, provide a brief methodology for the SEA, including the dates of visits to the host country, names and qualifications of the SEA preparers, and credits to individuals in the host country who provided information for the SEA. If the SEA involved public comment (see Public Comment chapter), provide the date of the scoping meeting, scoping meeting participants, and dates of the host-country public comment period.

Bibliography

List the resources used in preparing the SEA, such as host-country documents and governments, journal articles, United Nations or U.S. best-practice guidelines, the IVM or ITM PEA, or other "significant background papers."

Appendices

An appendix may be prepared.

Appendices can be useful in organizing the SEA so that only the most critical information for decision making is in the body of the SEA. If the SEA involved public comment, include the scoping statement and any public comments on the SEA as appendices.

PUBLIC COMMENT PROCESS

All SEAs must have some degree of public participation. At a minimum, draft SEAs should be provided to individuals consulted during the SEA development process, and the SEA should then be revised based on their suggestions. This is often an acceptable practice for pesticides registered for general use by EPA. For pesticides that EPA has designated as restricted-use pesticides or for pesticides whose registration has been cancelled by EPA, stricter public comment guidelines may apply. The degree of public participation required should be discussed with the USAID Mission undertaking the SEA and the BEO.

If an MOH is receptive to the idea of public comment, USAID should work with the ministry to organize and implement a public comment process that conforms to host-country regulations. Most host countries will have laws or regulations that deal with environmental assessment and public participation; to the extent that there are such laws and regulations, they can be the basis for conducting public comment in a country. If no laws or regulations exist concerning public participation, the host-country government, USAID Mission, and BEO should discuss.

The only guidance for public comment provided by the CFR is in 22 CFR 216.6(e), which states that "Missions will encourage the host government to make the Environmental Assessment available to the general public of the recipient country." Thus if a MOH rejects making an SEA available to the public, the Mission should try again by educating the ministry as to why it is important, and work with it to conduct a public comment process either through the government, NGOs, or other nongovernmental channels. There may be rare cases where a mission finds that a host-country government is so averse to civil society that it is not possible to undertake any kind of public participation.

RESOURCES

This chapter provides a comprehensive list of resources that might be necessary in preparing SEAs or providing guidance to host-country governments on a variety of topics related to malaria vector control and pesticide management.

USAID Environmental Compliance

The following documents are essential references for USAID guidance on environmental compliance:

- USAID (Agency for International Development). 2005a. *Environmental Compliance Procedures, Title 22 Code of Federal Regulations, Part 216*. Available at http://www.usaid.gov/our_work/environment/compliance/ reg216.pdf.

- USAID (Agency for International Development). 2005b. *USAID Environmental Procedures Training Manual.* Available at http://www.encapafrica.org/ EPTM.htm.

- USAID (Agency for International Development). 2002. *USAID/AFR Guidance: Preparing PERSUAPs for Pesticide Programs in Africa.* Available at http://www.encapafrica.org/docs/pest-pesticide%20mgmt/PERSUAP%20 Guidance.doc.

Storage

Storage capacity and conditions are essential to minimizing exposure, emergencies, and pilferage. All pesticides used for malaria control activities should be stored according to the guidelines in the following manual:

- FAO (Food and Agriculture Organization). 1996. *Pesticide Storage and Stock Control Manual.* FAO Pesticide Disposal Series. Rome.

Additionally, storehouse managers and storekeepers should be trained to manage pesticide stores according to these best practices.

Transport

Transport of pesticides poses risk of spillage, contamination of the environment, human exposure, and contamination of other transported goods. All pesticides used for malaria control activities should be transported according to the guidelines in the following manual:

- FAO (Food and Agriculture Organization). 1996. *Pesticide Storage and Stock Control Manual.* FAO Pesticide Disposal Series. Rome.

Emergencies and Spills

Mitigation and handling of spill and fire hazards are crucial to preventing human and environmental exposure to pesticides. Of particular concern is inhalation of toxic fumes when pesticides burn in an open flame. Storage facilities should be outfitted for such emergencies, and storehouse managers should be trained in best practices of handling emergency situations according to the guidelines in the following manuals:

- FAO (Food and Agriculture Organization). 1996. *Pesticide Storage and Stock Control Manual.* FAO Pesticide Disposal Series. Rome.
- World Health Organization (WHO). 2006. *Pesticides and their application for the control of vectors and pests of public health importance.* 6th ed. Department of Control of Neglected Tropical Diseases, WHO Pesticide Evaluation Scheme.

Additionally, any fire-fighting or emergency services should be trained on handling pesticide emergencies, and notified immediately when any emergencies occur.

Poison Control

In the event that spray operators or residents experience symptoms of pesticide exposure, treatment should be available and accessible. To that end, physicians in health facilities, health centers, and hospitals should be trained in recognizing and treating poisoning symptoms. Treatment medicines should be available in health facilities, health centers, and hospitals. The following manual should be used to guide training and treatment on pesticide poisoning in malaria vector control programs:

- Reigart JR, Roberts JR. 1999. *Recognition and Management of Pesticide Poisonings. 5th Edition.* U.S. Environmental Protection Agency, Washington, DC.

Decontamination and Disposal

Proper decontamination and disposal of expired insecticides, contaminated rinse and wash water, and contaminated packaging products is necessary to mitigate human and environmental exposure to pesticides. The following guidelines should be used to choose decontamination and disposal options that suit the host-country situation:

- Thompson, R. 2004. Guidance Document: The Selection of Waste Management Options for the Disposal of Obsolete Pesticides and Contaminated Materials. Draft. Food and Agriculture Organization (FAO). Rome.
- World Health Organization (WHO). 2006. Pesticides and their application for the control of vectors and pests of public health importance. 6th ed. Department of Control of Neglected Tropical Diseases, WHO Pesticide Evaluation Scheme.

Pesticide Application Equipment

Pesticide application equipment (e.g., compression sprayers) should be manufactured according to WHO standards, and safety equipment (e.g., face shield, overalls) should be procured and worn according to WHO standards. The following documents fully describe specifications for pesticide application equipment:

- WHO (World Health Organization). 2000. *Manual for Indoor Residual Spraying—Application of Residual Sprays for Vector Control*. Geneva.
- Najera, J. and Zaim, M. 2002. *Malaria Vector Control: Decision-Making Criteria and Procedures for Judicious Use of Insecticides*. World Health Organization. Geneva.
- WHO (World Health Organization). 1990. *Equipment for Vector Control. 3rd Edition*. Geneva

Pesticide Quality Control

Pesticide procured for public health use should be tested for quality assurance. Regardless of whether the pesticide is tested in the host country or whether a sample is sent outside the host country, the following specifications should be used to determine the quality of the pesticide:

- WHO (World Health Organization). 2002. *Specifications for Public Health Pesticides*. Geneva.

Pesticide Labels

The durability, design, and information content of pesticide labels are crucial to ensuring safe use of pesticides. Pesticide manufacturers should adhere to the guidelines for pesticide labels contained in the following manual:

- FAO (Food and Agriculture Organization). 1995. *Guidelines on Good Labeling Practice*. Rome.

Resistance Monitoring

Resistance monitoring is crucial to the appropriate selection and targeted use of pesticides for malaria vector control. Resistance monitoring should be conducted according to the following guidelines:

- WHO (World Health Organization). 1998. *Techniques to Detect Insecticide Resistance Mechanisms (Field and Laboratory Manual)*. Geneva.
- WHO (World Health Organization). 1998. *Test Procedures for Insecticide Resistance Monitoring in Malaria Vectors, Bio-efficacy and Persistence of Insecticide-Treated Surfaces*. Report of the WHO Informal Consultation, Geneva, 28039, September 1998. Geneva.
- Additionally, resistance management practices should be implemented in malaria vector control programs in accordance with the following guidelines:
- WHO (World Health Organization). 2003. *The Manual for Insecticide Resistance Management in Vectors and Pests of Public Health Importance*. Geneva.

Finally, ministries of health and agriculture should work together to ensure agricultural use of pesticides will not adversely impact vector control efforts, and vice versa.

Additional Resources

In addition to the best practices guidelines referenced in the preceding sections, several manuals have been published that may provide further guidance for malaria vector control strategies involving pesticides:

Chavasse, D. and Yap, H. 1997. Chemical Methods for the Control of Vectors and Pests of Public Health Importance. Geneva.

FAO (Food and Agriculture Organization). 1988. Post-Registration Surveillance and Other Activities in the Field. Rome.

FAO (Food and Agriculture Organization). 1988. Guidelines for the Retail Distribution of Pesticides with Particular Reference to Storage and Handling at Point of Supply to Users in Developing Countries. Rome.

FAO (Food and Agriculture Organization). 1990. Personal Protection When Working with Pesticides in Tropical Climates. Rome.

FAO (Food and Agriculture Organization). 1991. Initial Introduction and Subsequent Development of a Simple National Pesticide Registration and Control Scheme. Rome.

FAO (Food and Agriculture Organization). 1994. Provisional Guidelines on Tender Procedures for the Procurement of Pesticides. Rome.

FAO (Food and Agriculture Organization). 1995. Disposal of Bulk Quantities of Obsolete Pesticides in Developing Countries. Rome. (Note: this is guidance for governments.)

FAO (Food and Agriculture Organization). 2002. International Code of Conduct on the Distribution and Use of Pesticides (Revised Version). Rome.

FAO (Food and Agriculture Organization). 2002. Manual on Development and Use of UNFAO and WHO Specifications for Pesticides. Plant Production and Protection Paper No. 173. Rome.

FAO (Food and Agriculture Organization), WHO (World Health Organization), and UNEP (United Nations Environment Program). 1999. Guidelines for the Management of Small Quantities of Unwanted and Obsolete Pesticides. FAO Pesticide Disposal Series, No. 7. Rome.

Najera, J. and Zaim, M. 2001. Malaria Vector Control: Insecticides for Indoor Residual Spraying. Geneva.

United Nations. 2002. Recommendations on the Transport of Dangerous Goods: Model Regulations. 10th revised edition. New York.

UNEP (United Nations Environment Program). 2001. Stockholm Convention on Persistent Organic Pollutants. Geneva.

WHO (World Health Organization). 1996. Report of the WHO Informal Consultation on the Evaluation and Testing of Insecticides. WHO/HQ, Geneva, 7-11 October 1996. Geneva.

WHO (World Health Organization). 1997. Guidelines for Poison Control. Geneva.

WHO (World Health Organization). 1997. Report of the First WHOPES Working Group Meeting. WHO/HQ, Geneva, 26–27 June 1997.

WHO (World Health Organization). 1998. Review of Alpha-Cypermethrin 10% SC and 5% WP and Cyfluthrin 5% EW and 10% WP. Report of the Second WHOPES Working Group Meeting: WHO/HQ, Geneva, 22–23 June 1998.

WHO (World Health Organization). 1999. Review of Deltamethrin 1% SC and 25% WT and Etofenprox 10% EC and 10% EW. Report of the Third WHOPES Working Group Meeting: WHO/HQ, Geneva, 23–24 September 1999.

WHO (World Health Organization). 1999. Safe and Effective Use of Household Insecticide Products: Guide for the Production of Educational and Training Materials. Geneva.

WHO (World Health Organization). 2000. Guidelines for the Purchase of Public Health Pesticides. Geneva.

WHO (World Health Organization). 2001. Information, Education and Communication: Lessons from the Past, Perspectives for the Future. Occasional paper. Geneva.

WHO (World Health Organization). 2001. Chemistry and Specification of Pesticides. Sixteenth Report of the WHO Expert Committee on Vector Biology and Control. WHO Technical Report Series No. 899. Geneva.

WHO (World Health Organization). 2001. Review of IR3535, KBR 3023, (RS)-Methoprene 20% EC, Pyriproxyfen 0.5% GR, and Lambda-Cyhalothrin 2.5% CS. Report of the Fourth WHOPES Working Group Meeting, WHO/HQ, Geneva, 4–5 December 2000.

WHO (World Health Organization). 2001. Review of Olyset Net and Bifenthrin 10% WP. Report of the Fifth WHOPES Working Group Meeting: WHO/HQ, Geneva, 30–31 October 2001.

WHO (World Health Organization). 2003. Spray Space Application of Insecticides for Vector and Public Health Pest Control—A Practitioners Guide. Geneva.

WHO (World Health Organization). 2003. Draft Guidelines on the Management of Public Health Pesticides. Report of the WHO Interregional Consultation, Chiang Mai, Thailand, 25–28 February 2003. Geneva.

WHO (World Health Organization). 2005. Recommended Classifications of Pesticides by Hazard: Guidelines to Classification 2004. Geneva.

ANNEX D: INPUT PARAMETER TABLES

Table D-1: Chemical/Physical Properties

Alpha Cypermethrin (67375-30-8)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			9.50E-06	HSDB, 2005	
Melting Point (K)			3.50E+02	IPCS, 2005	
Molecular Weight (g/mol)			4.16E+02	IPCS, 2005	
Octanol-water partition coefficient (log Kow)			5.16E+00	IPCS, 2005	
Half-life in air (d)			7.50E-01	HSDB, 2005	Hydroxyl radicals
Half-life in air (d)			4.90E+01	HSDB, 2005	Ozone
Half-life in soil (d)	7.00E+00	1.40E+01		HSDB, 2005	
Half-life in water (d) Photolysis			8.00E+00	HSDB, 2005	Model river
Half-life in water (d) Hydrolysis			6.50E+01	HSDB, 2005	Model lake
Solubility (mg/L)	5.00E-03	1.00E-02		IPCS, 2005	
Vapor pressure (mm Hg)			1.70E-12	IPCS, 2005	At 20 oC

Bendiocarb (22781-23-3)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			3.90E-08	HSDB, 2005	
Melting Point (K)			4.00E+02	HSDB, 2005	
Molecular Weight (g/mol)			2.23E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			1.70E+00	HSDB, 2005	
Half-life in air (d)			5.00E+00	HSDB, 2005	
Half-life in soil (d)	1.00E+00	3.50E+00		U.S. EPA 1999b	aerobic
Half-life in water (d)			3.30E-01	U.S. EPA 1999b	At pH 9
Half-life in water (d)			2.00E+00	U.S. EPA 1999b	At pH7

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Half-life in water (d)			4.65E+01	U.S. EPA 1999b	At pH 5
Solubility (mg/L)			2.60E+02	HSDB, 2005	At 25 oC
Vapor pressure (mm Hg)			6.60E-09	U.S. EPA 1999b	At 25 oC

Bifenthrin (82657-04-3)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			1.00E-06	HSDB, 2005	
Melting Point (K)			3.40+02	EXTOXNET, 2005	
Molecular Weight (g/mol)			4.23E+02	EXTOXNET, 005	
Octanol-water partition coefficient (log Kow)			6.00E+00	EXTOXNET, 2005	
Half-life in air (d)			5.42E-01	HSDB, 2005	Hydroxyl radicals
Half-life in air (d)			7.00E+00	HSDB, 2005	Ozone
Half-life in soil (d)	6.50E+01	1.25E+02		HSDB, 2005	
Half-life in water (d)			5.55E+02	HSDB, 2005	Model lake
Half-life in water (d)			5.00E=01	HSDB, 2005	Model river
Solubility (mg/L)			1.00E-01	HSDB, 2005	Temperature not specific
Vapor pressure (mm Hg)			2.40E-10	HSDB, 2005	

Chlorfenyapry (122453-73-0)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			$5.7x10^{-9}$	Toxnet	
Melting Point (oC)	100	101		Toxnet	
Molecular Weight (g/mol)			407.62	Toxnet	
Octanol-water partition coefficient (log Kow)			4.83	Toxnet	
Organic carbon partition coefficient (K_{oc}) ml/g	10,000	11,500	11,750	Toxnet	
Half-life in air (d)			1.2	Toxnet	
Half-life in soil (d)	230	250	240	Toxnet	Aerobic

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
			250		Anaerobic
Half-life in water (d) Photolysis	5	7	6	Toxnet	
Half-life in water (d) Hydrolysis			> 30	Toxnet	
Solubility (mg/L)			0.14	Toxnet	pH 7
Vapor pressure (mm Hg)			$7.36X10^{-8}$	Toxnet	

Cyfluthrin (baythroid) (68359-37-5)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			5.80E-10	HSDB, 2005	
Melting Point (K)			3.30E=02	HSDB, 2005	
Molecular Weight (g/mol)			4.34E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			5.94E+00	HSDB, 2005	
Half-life in air (d)			NF		
Half-life in soil (d)			5.95E+01	PAN, 2005	aerobic
Half-life in soil (d)			3.36E+01	PAN, 2005	anaerobic
Half-life in water (d)			NF		
Solubility (mg/L)			2.00E+00	HSDB, 2005	At 20 oC
Vapor pressure (mm Hg)			2.67E-12	HSDB, 2005	At 25 oC

DDT (50-29-3)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			8.30E-06	ATSDR, 2003a	Temperature not reported
Melting Point (K)			3.82E+02	EXTONET, 2005	
Molecular Weight (g/mol)			3.54E+02	EXTONET, 2005	
Octanol-water partition coefficient (log Kow)			6.91E+00	HSDB, 2005	
Half-life in air (d)			5.00E+00	HSDB, 2005	At 25oC
Half-life in soil (d)	7.30E+02	5.48E+03		EXTONET, 2005	
Half-life in water (d)			5.60E+01	EXTONET, 2005	Lake water

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Half-life in water (d)			2.80E+01	EXTONET, 2005	River water
Solubility (mg/L)			2.50E-02	ATSDR, 2003a	At 25 oC, pH not reported
Vapor pressure (mm Hg)			2.48E-10	EXTONET, 2005	At 25 oC

Deltamethrin (52918-63-5)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			5.00E-06	HSDB, 2005	
Melting Point (K)			3.70E+02	IPCS, 2005	
Molecular Weight (g/mol)			5.05E+02	IPCS, 2005	
Octanol-water partition coefficient (log Kow)			5.43E+02	IPCS, 2005	
Half-life in air (d)			NF		
Half-life in soil (d)	3.43E+01	4.83E-01		HSDB, 2005	
Half-life in water (d)			1.25E+00	HSDB, 2005	Model river
Half-life in water (d)			2.08E+01	HSDB, 20 IPCS, 200505	Model lake
Solubility (mg/L)		2.00E-03			At 20oC, reported as < value
Vapor pressure (mm Hg)			2.00E-11	IPCS, 2005	

Etofenprox (8-844-07-1)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			2.26E-08	Chemfinder (SRC), 2005	
Melting Point (K)			3.10E+02	Chemfinder (SRC), 2005	
Molecular Weight (g/mol)			3.77E+02	Chemfinder (SRC), 2005	
Octanol-water partition coefficient (log Kow)			7.05E+00	Chemfinder (SRC), 2005	
Half-life in air (d)			NF		

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Half-life in soil (d)	6.00E+00	9.00E+00		FAO, 1993	Lab
Half-life in soil (d)	9.00E+00	7.90E+01		FAO, 1993	Field
Half-life in water (d)			NF		
Solubility (mg/L)			1.00E-03	Chemfinder (SRC), 2005	At 25 oC
Vapor pressure (mm Hg)			8.93E-12	Chemfinder (SRC), 2005	At 25 oC

Fenitrothion (122-14-5)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			9.30E-07	HSDB, 2005	
Melting Point (K)			2.70E+02	IPCS. 2005	
Molecular Weight (g/mol)			2.77E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			3.16E+00	IPCS. 2005	
Half-life in air (d)			2.67E-01	HSDB, 2005	
Half-life in soil (d)	4.40E+00	1.54E+02		HSDB, 2005	Hydroxyl radicals
Half-life in soil (d)	3.90E+00	1.09E+01		HSDB, 2005	Aerobic
Half-life in water (d)	4.00E+00	8.00E+00		IPCS. 2005	Anaerobic
Half-life in water (d)	2.00E+02	6.30E+02		IPCS. 2005	At pH of 5-9, at 45 oC
Half-life in water (d)	1.70E+01	6.10E+01		IPCS. 2005	At pH of 5-9, at 15 oC
Solubility (mg/L)	5.00E+00	1.40E+01		U.S. EPA, 1995	Min at 20 oC; max at 30 oC
Vapor pressure (mm Hg)			2.80E-07	U.S. EPA, 1995	At 25 oC

Lambda-Cyhalothrin (91465-08-6)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			9.09E-06	HSDB.2005	At 20 oC
Melting Point (K)			3.22E+02	IPCS, 2005	
Molecular Weight (g/mol)			4.50E+02	IPCS, 2005	
Octanol-water partition coefficient (log Kow)			7.00E+00	IPCS, 2005	
Half-life in air (d)					
Half-life in soil (d)			3.00E+01	NPIC, 2005	
Half-life in water (d) Photolysis			7.00E+00	NPIC, 2005	
Solubility (mg/L)			5.00E-03	IPCS, 2005	pH not reported
Vapor pressure (mm Hg)			2.96E-08	IPCS, 2005	At 80 oC
Vapor pressure (mm Hg)			1.97E-12	IPCS, 2005	At 20 oC

Malathion (121-75-5)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			4.90E-09	ATSDR, 2003a	At 25 oC
Melting Point (K)			2.76E+02	EXTOXNET, 2005	
Molecular Weight (g/mol)			3.30E+02	EXTOXNET, 2005	
Octanol-water partition coefficient (log Kow)			2.75E+02	EXTOXNET, 2005	
Half-life in air (d)			1.50E+00	EXTOXNET, 2005	
Half-life in soil (d)	1.00E+00	2.50E+01		EXTOXNET, 2005	
Half-life in water (d)		7.00E+00		EXTOXNET, 2005	Raw river water, reported as <number
Half-life in water (d)			2.10E+01	EXTOXNET, 2005	Distilled water
Solubility (mg/L)			1.30E+02	EXTOXNET, 2005	pH not reported
Vapor pressure (mm Hg)			5.25E-08	EXTOXNET, 2005	At 30 oC

Methoprene (40596-69-8)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			6.90E-06	HSDB, 2005	
Molecular Weight (g/mol)			3.10E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			5.50E+00	HSDB, 2005	
Half-life in air (d)	3.33E-02	6.25E-02		HSDB, 2005	
Half-life in soil (d)			1.00E+01	HSDB, 2005	
Half-life in water (d)			1.30E+01	HSDB, 2005	
Solubility (mg/L)			1.40E+00	HSDB, 2005	Room temperature
Vapor pressure (mm Hg)			3.11E-08	HSDB, 2005	At 25 oc

Permethrin (52645-53-1)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			1.90E-06	HSDB, 2005	Temperature not reported
Melting Point (K)	3.07E+02	3.08E+02		HSDB, 2005	
Molecular Weight (g/mol)			3.91E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			6.50E+00	HSDB, 2005	
Half-life in air (d)			4.08E-01	HSDB, 2005	Hydroxyl radical
Half-life in air (d)			4.90E+01	HSDB, 2005	Ozone
Half-life in soil (d)			3.00E+01	HSDB, 2005	
Half-life in water (d)			3.30E+01	HSDB, 2005	
Solubility (mg/L)			6.00E-03	HSDB, 2005	At 20 oC, pH not reported
Vapor pressure (mm Hg)			2.87E-11	HSDB, 2005	At 25 oC

Piperonyl butoxide (51-03-6)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			8.9×10^{-11}	Toxnet	
Melting Point (oC)				FAO	Liquid at room temperature
Molecular Weight (g/mol)			338.43	Toxnet	
Octanol-water partition coefficient (log Kow)			4.29	Toxnet	
Organic carbon partition coefficient (K_{oc}) ml/g			4.75	Toxnet	
Half-life in air (d)			0.2	Toxnet	
Half-life in soil (d)			4	Toxnet	aerobic
			24	Glynne Jones,	anaerobic
Photolysis			8.4 h	Toxnet	
Half-life in water (d)			Stable	Toxnet	
Solubility (mg/L)			14.3	FAO	
Vapor pressure (mm Hg)			5.2×10^{-6}	Toxnet	

Pirimiphos-Methyl (29232-93-7)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			7.00E-07	HSDB, 2005	
Melting Point (K)			2.90E+02	HSDB, 2005	
Molecular Weight (g/mol)			3.05E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			4.23E=00	HSDB, 2005	
Half-life in air (d)			2.00E-01	HSDB, 2005	
Half-life in soil (d)	5.20E+00	5.90E+00		HSDB, 2005	
Half-life in water (d) Photolysis			NF	HSDB, 2005	Varies too much depending on condition
Solubility (mg/L)			8.60E+00	HSDB, 2005	At 20 oC
Vapor pressure (mm Hg)			1.97E-08	HSDB, 2005	At 20 oC

Propoxur (114-26-1)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			1.43E-09	HSDB, 2005	
Melting Point (K)			3.60E+02	WHO, 2005	
Molecular Weight (g/mol)			2.09E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			1.56E+00	WHO, 2005	At 20 oC
Half-life in air (d)			5.00E-01	HSDB, 2005	Hydroxyl radicals
Half-life in soil (d)	8.00E+01	2.10E+02		HSDB, 2005	Min is silt loam, max is sandy loam
Half-life in water (d)			>365	WHO, 2005	At pH, at 22 oC
Half-life in water (d)			1.25E+00	WHO, 2005	At pH9, at 22 oC
Half-life in water (d)			9.32E+01	WHO, 2005	At pH 7, at 22 oC
Solubility (mg/L)			1.75E+03	WHO, 2005	At 20 oC
Vapor pressure (mm Hg)			2.50E-05	WHO, 2005	At 20 oC

Pyriproxyfen (95737-68-1)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			1.16×10^{-02}	VSDB	
Melting Point (oC)	45	47		Toxnet	
Molecular Weight (g/mol)			321.37	Toxnet	
Octanol-water partition coefficient (log Kow)			2.34×10^{05}	VSDB	
Organic carbon partition coefficient (K_{oc}) ml/g			21,175	VSDB	
Half-life in air (d)			0.3	Toxnet	
Half-life in soil (d)			12.4	Sullivan	aerobic
			347	Sullivan	anaerobic
Half-life in water (d)			7.5	Toxnet, VSDB	
Half-life in water (d) photolysis	3.72	6.23		Sullivan	
Half-life in water (d) hydrolysis			Stable	VSDB	
Solubility (mg/L)			0.37g/100ml	FAO	
Vapor pressure (mm Hg)			1.33×10^{-02}	VSDB	

Spinosad = Spinosyn A (131929-60-7) (85% concentration)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			9.82×10^{-10}	Kollman	
Melting Point (oC)	84	99.5		Kollman	
Molecular Weight (g/mol)			731	Krieger	
Octanol-water partition coefficient (log Kow)			4.10	USEPA 2008	
Organic carbon partition coefficient (K_{oc}) ml/g			10,000	Thompson	
Reaction half-life in air (d)			<1 d	Kollman	Not volatile
Photolysis half-life (soil)			8.68 days	Kollman	
Half-life in soil (d) aerobic			17.3 days	Kollman	silt loam soil
Half-life in soil (d) anaerobic			161 days	Kollman	silt loam soil
Photolysis half-life aqueous (d)			0.96	Kollman	
Hydolysis half-life (d)			> 30	Kollman	25°C, pH 7
			200		25° C, pH 9
Solubility (mg/L)			235	Kollman	
Vapor pressure (mmHg)			2.4×10^{-10}	Kollman	

Spinosad = Spinosyn D (131929-63-0) (15%)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			4.87×10^{-7}	Kollman	
Melting Point (oC)	161.5	170		Kollman	
Molecular Weight (g/mol)			746	Krieger	
Octanol-water partition coefficient (log Kow) pH7			4.5	USEPA 2008	

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Organic carbon partition coefficient (K_{oc}) ml/g			32,000	Thompson	
Reaction half-life in air (d)			< 1 day	Kollman	Not volatile
Photolysis Half-life (soil)			9.44	Kollman	
Half-life in soil (d) aerobic			14.5 days	Kollman	silt loam soil
Half-life in soil (d) anaerobic			250 days	Kollman	silt loam soil
Photolysis half-life (aqueous) (d)			0.84	Kollman	
Hydrolysis half-life (d)			> 30	Kollman	25°C, pH 7
			259		25°C, pH 9
Solubility (mg/L)			0.332	Kollman	
Vapor pressure (mmHg)			1.6×10^{-10}	Kollman	

Temephos (3383-96-8)

Parameter	Min Value	Max Value	Mean Value	Reference	Comment
Henry's law constant (atm-cu m/mol)			1.96E-09	HSDB, 2005	At 25 oC
Melting Point (K)			3.04E+02	HSDB, 2005	
Molecular Weight (g/mol)			4.66E+02	HSDB, 2005	
Octanol-water partition coefficient (log Kow)			5.96E+00	HSDB, 2005	
Half-life in air (d)			1.17E-01	HSDB, 2005	
Half-life in soil (d)			3.00E+01	EXTOXNET, 2005	
Half-life in water (d)	4.00E+03			HSDB, 2005	River water, reported as > number
Solubility (mg/L)			2.70E-01	HSDB, 2005	At 20 oC, pH not reported
Vapor pressure (mm Hg)			1.13E-12	HSDB, 2005	At 25 oC

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Table D-2: Pesticide Use Data

New Pesticides Under Review

Chlorfenyapyr (122453-73-0)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Phantom 15% SC	Application (kg ai/m2)			1000	Hudson compression sprayer equipped with a flat fan nozzle.	N'Guessan et al. 2009
	SC	Application (kg ai/m2)	250mg/m2 and	500mg/m2		Killed 50% of adults equal to alpha-cypermethrin SC	Oxborough et al. 2010
			100mg/m2 and	500mg/m2		All rates equally effective	Mosha et al. 2008

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Oxborough RM, Kitau J, Matowo J, Mndeme R, Feston E, Mosha FW, Rowland MW. 2010. Evaluation of indoor residual spraying with the pyrrole insecticide chlorfenapyr against pyrethroid susceptible Anopheles arabiensis and resistant Culex quinquefasciatus mosquitoes. Trans R Soc Trop Med Hyg 104(10):639-45.

Mosha F, Lyimo IN, Oxborough RM et al. 2008. Experimental hut evaluation of the pyrrole insecticide chlorfenapyr on bed nets for the control of Anopheles arabiensis and Culex quinquefasciatus. Tropical Medicine & International Health 13:644–652.

Spinosad = Spinosyn A (131929-60-7) + Spinosyn D (131929-63-0)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
Larviciding	Conserve SC	gm ai per hectare	100	200		Lower rates not as effective	Cetin et al. 2005

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Pyriproxyfen (95737-68-1)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
Larviciding	Sumilarv 0.5 G	mg a·i/m2	12.5	100			Li-Feng 1994
		0.1 ppm					Chavasse et al. 1995
		0.1 kg ai/ha					Mulligan 1990
		0.1 ppm				Culex	Kamimura and Arakawa 1991
		0.05 ppm				Aedes	Andrighetti et al. 2008
	Sumilarv 0.5 G	0.5 kg ai/ha				Culex	**Jambulingam et al. 2008**

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Piperonyl butoxide (51-03-6)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
LLIN					1.1 g/m2 bednet (25 g/kg net)	deltamethrin at 4 g/kg (approx. 180 mg/m^2	Tungu et al. 2010.
					1.7%	1% pyrethrum	Bøgh et al. 1998
					25 g ai/kg net	4 g ai/kg deltamethrin	Corbell et al. 2010

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WHO approved Pesticides for IVM Malaria Program

Alpha-cypermethrin (67375-30-8)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)	2.00E-05	3.00E-05			Najera and Ziam, 2002
ITNs	Suspension concentrate	Application (kg ai/m2)			4.00E-05	SC 10%	WHO, 2002b
IRS	Wettable powder	Application frequency (times/year	2	4		Duration of effective action 4-6 months	Najera and Ziam, 2002

Bendiocarb (22781-23-3)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)	1.00E-04	4.00E-04			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year	2	6		Duration of effective action 2-6 months	Najera and Ziam, 2002

Bifenthrin (82657-04-3)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)	2.50E-05	5.00E-05			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002

Cyfluthrin (baythroid) (68359-37-5)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)	2.00E-05	5.00E-05			Najera and Ziam, 2002
ITNs	Emulsion	Application (kg ai/m2)			5.00e-05	SC 10%	WHO, 2002b
IRS	Wettable powder	Application frequency (times/year	2.00e+00	4.00E+00		Duration of effective action 3-6 months	Najera and Ziam, 2002

DDT (50-29-30)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)	1.00E-03	2.00E-03			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year	2.00E+00			Duration of effective action 6 months	Najera and Ziam, 2002

Deltamethrin (52918-63-5)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application frequency (times/year	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002
IRS	Wettable powder and water dispersible granules	Application (kg ai/m2)	2.00E-05	2.50E-05			Najera and Ziam, 2002
ITNs	Suspension concentrate	Application (kg ai/m2)			2.50E-05	SC 1%	WHO, 2002b
ITNs	Water dispensable tablet	Application (kg ai/m2)			2.50E-05	WT 25%	WHO, 2002b

Etofenprox (80844-07-1)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)	1.00E-04	3.00E-04			Najera and Ziam, 2002
ITNs	Emulsion	Application (kg ai/m2)			2.00E-04		WHO, 2002b
IRS	Wettable powder	Application frequency (times/year	2.00E+00	4.00E+004		Duration of effective action 3-6 months	Najera and Ziam, 2002

Fenitrothion (122-14-5)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)			2.00E-04		Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002

Lambda-Cyhalothrin (91465-08-6)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
ITNs	Capsule suspension	Application (kg ai/m2)	1.00E-05	1.50E-05			Najera and Ziam, 2002
IRS	Wettable powder	Application (kg ai/m2)	2.00E-05	3.00E-05			Najera and Ziam, 2002
ITNs	Capsule suspension	Application frequency (times/year	3.00E+00	4.00E+00		Duration of effective action 3-4 months	Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year	2.00E+00	4.00E+00		Duration of effective action 3-6 months	Najera and Ziam, 2002
ITNs	Capsule suspension	Percent ai	2.50E+00			Percent active ingredient in the insecticide formulation. For a liter.	WHO, 2002b

Malathion (121-75-5)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)			2.00E-03		Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year	4.00E+00	6.00E+00		Duration of effective action 2-3 months	Najera and Ziam, 2002
IRS	Wettable powder	Percent ai	5.00E+01			Percent active ingredient in the insecticide formulation	WHO, 2004b

Methoprene (40596-69-8)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
Growth Regulator	Emulsifiable concentrate	Application (kg ai/m2)	2.00E-06	4.00E-06			Najera and Ziam, 2002
IRS Growth Regulator	Emulsifiable concentrate	Application frequency (times/year					Najera and Ziam, 2002

Permetrhin (52625-53-1)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
ITNs	Emulsifiable	Application (kg ai/m2)	2.00E-04	5.00E-04			Najera and Ziam, 2002
ITNs	Emulsifiable	Application frequency (times/year	3.00E+00	4.00E+00		Duration of effective action 3-4 months	WHO, 2004b
ITNs	Emulsifiable	Percent ai	1.00E+01			Percent active ingredient in the insecticide formulation	WHO, 2004b

Pirimiphos-methyl (29232-93-7)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder and emulsifiable concentrate	Application (kg ai/m2)	1.00E-03	2.00E-03			Najera and Ziam, 2002
IRS		Application frequency (times/year	4.00E+00	6.00E+00		Duration of effective action 2-3 months	Najera and Ziam, 2002

Propoxur (114-26-1)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
IRS	Wettable powder	Application (kg ai/m2)	1.00E-03	2.00E-03			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002

Temephos (3383-96-8)

Vector management practice	Pesticide formulation	Parameter	Minimum Value	Maximum Value	Mean value	Comments	Reference
Larviciding	Emulsifiable concentrate, granule	Application (kg ai/m2)	5.60E-06	1.12E-05			Najera and Ziam, 2002

Table D-3. Carcinogenic and Non-Carcinogenic Toxicity Criteria

Alpha-cypermethrin						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	5.00E+00	IPCS, 1992	No new data
dermal	chronic	noncancer	all ages	5.00E+00	IPCS, 1992	No new data
dermal	intermediate	noncancer	all ages	5.00E+00	IPCS, 1992	No new data
inhalation	acute	noncancer	all ages	4.00E+00	IPCS, 1992	No new data
inhalation	chronic	noncancer	all ages	4.00E+00	IPCS, 1992	No new data
inhalation	intermediate	noncancer	all ages	4.00E+00	IPCS, 1992	No new data
oral	acute	noncancer	all ages	1.00E-01	USEPA, 2008	RED acute RfD
oral	chronic	noncancer	all ages	6.00E-02	USEPA, 2008	RED chronic RfD
oral	intermediate	noncancer	all ages	6.00E-02	USEPA, 2008	RED chronic RfD
Bendiocarb						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	5.00E-01	USEPA, 1999a	No new data
dermal	chronic	noncancer	all ages	1.30E-03	USEPA, 1999a	No new data
dermal	intermediate	noncancer	all ages	2.00E-01	USEPA, 1999a	No new data
inhalation	acute	noncancer	all ages	2.00E-03	USEPA, 1999a	No new data
inhalation	chronic	noncancer	all ages	2.00E-03	USEPA, 1999a	No new data
inhalation	intermediate	noncancer	all ages	2.00E-03	USEPA, 1999a	No new data
oral	acute	noncancer	all ages	1.30E-03	USEPA, 1999a	No new data
oral	chronic	noncancer	all ages	1.30E-03	USEPA,1999a	No new data
oral	intermediate	noncancer	all ages	1.30E-03	USEPA, 1999a	No new data
Bifenthrin						

Exposure Pathway	Duration	Endpoint	Receptor	Value	Reference	Comments
dermal	acute	noncancer	all ages	2.00E-01	USEPA, 2003	No new RfD
dermal	chronic	noncancer	all ages	2.00E-01	USEPA, 2003	No new RfD
dermal	intermediate	noncancer	all ages	2.00E-01	USEPA, 2003	No new RfD
inhalation	acute	noncancer	all ages	7.00E-03	USEPA, 2003	No new data
inhalation	chronic	noncancer	all ages	4.00E-03	USEPA, 2003	No new data
inhalation	intermediate	noncancer	all ages	7.00E-03	USEPA, 2003	No new data
oral	acute	noncancer	all ages	3.30E-01	USEPA, 2008a	acute RfD
oral	chronic	noncancer	all ages	1.30E-02	USEPA, 2008a	chronic RfD
oral	intermediate	noncancer	all ages	7.00E-03	USEPA, 2003	No new data
Chlorfenapry - pyrroles						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	4.50E-02	USEPA, 2003a	oral used as surrogate based on 2007 precedent
dermal	chronic	noncancer	all ages	3.00E-03	USEPA, 2003a	oral used as surrogate based on 2007 precedent
dermal	intermediate	noncancer	all ages	3.00E-03	USEPA, 2003a	oral used as surrogate based on 2007 precedent
inhalation	acute	noncancer	all ages	4.50E-02	USEPA, 2003a	oral used as surrogate based on 2007 precedent
inhalation	chronic	noncancer	all ages	3.00E-03	USEPA, 2003a	oral used as surrogate based on 2007 precedent
inhalation	intermediate	noncancer	all ages	3.00E-03	USEPA, 2003a	oral used as surrogate based on 2007 precedent
oral	acute	noncancer	all ages	4.50E-02	USEPA, 2003a	acute dietary (general population including infants and children), NOAEL = 45 mg/kg/d, UF = 1000, aRFD = 0.045 mg/kg/d

oral	chronic	noncancer	all ages	3.00E-03	USEPA, 2003a	chronic dietary (all populations), NOAEL = 2.6 mg/kg/d, UF = 1000, cRFD = 0.003 mg/kg/d
oral	intermediate	noncancer	all ages	3.00E-03	USEPA, 2003a	chronic used as surrogate
Cyfluthrin						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	3.00E+00	IPCS, 1997	No new data
dermal	chronic	noncancer	all ages	3.00E+00	IPCS, 1997	No new data
dermal	intermediate	noncancer	all ages	3.00E+00	IPCS,1997	No new data
inhalation	acute	noncancer	all ages	7.00E-04	USEPA, 2000c	No new data
inhalation	chronic	noncancer	all ages	2.00E-04	USEPA, 2005c	No new data
inhalation	intermediate	noncancer	all ages	2.00E-04	USEPA, 2005c	No new data
oral	acute	noncancer	all ages	2.50E-02	USEPA, 2011	chronic used as surrogate
oral	chronic	noncancer	all ages	2.50E-02	USEPA, 2011	IRIS value for baythroid (synonym of cyfluthrin)
oral	intermediate	noncancer	all ages	2.50E-02	USEPA, 2011	chronic used as surrogate
DDT						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	chronic	cancer	all ages	3.40E-01	USEPA, 2005	Oral benchmark
dermal	acute	noncancer	all ages	5.00E-04	USEPA, 2005	Oral benchmark
dermal	chronic	noncancer	all ages	5.00E-04	USEPA, 2005	Oral benchmark
dermal	intermediate	noncancer	all ages	5.00E-04	USEPA, 2005	Oral benchmark
inhalation	chronic	cancer	all ages	3.40E-01	USEPA, 2005	Oral benchmark
inhalation	acute	noncancer	all ages	5.00E-04	USEPA,2005	Oral benchmark
inhalation	chronic	noncancer	all ages	5.00E-04	USEPA,2005	Oral benchmark
inhalation	intermediate	noncancer	all ages	5.00E-04	USEPA,2005	Oral benchmark
oral	chronic	cancer	all ages	3.40E-01	USEPA,2005	No new data

oral	acute	noncancer	all ages	5.00E-04	ATSDR, 2002	No new data
oral	chronic	noncancer	all ages	5.00E-04	USEPA,2005	No new data
oral	intermediate	noncancer	all ages	5.00E-04	ATSDR, 2002	No new data
Deltamethrin						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	1.00E+01	Barlow et al., 2001	No new data
dermal	chronic	noncancer	all ages	1.00E+01	Barlow et al., 2001	No new data
dermal	intermediate	noncancer	all ages	1.00E+01	Barlow et al., 2001	No new data
inhalation	acute	noncancer	all ages	1.00E-02	USEPA 2004	No new data
inhalation	chronic	noncancer	all ages	1.00E-02	USEPA 2004	No new data
inhalation	intermediate	noncancer	all ages	1.00E-02	USEPA 2004	No new data
oral	acute	noncancer	all ages	1.00E-02	USEPA 2004	No new data
oral	chronic	noncancer	all ages	1.00E-02	USEPA 2004	No new data
oral	intermediate	noncancer	all ages	1.00E-02	USEPA 2004	No new data
Etofenprox						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	chronic	cancer	all ages	5.10E-03	NYSDEC 2005	No new data
dermal	acute	noncancer	all ages	4.00E-01	NYSDEC 2005	No new data
dermal	chronic	noncancer	all ages	3.70E-02	NYSDEC 2005	No new data
dermal	intermediate	noncancer	all ages	4.00E-01	NYSDEC 2005	No new data
inhalation	chronic	cancer	all ages	5.10E-03	NYSDEC 2005	No new data
inhalation	acute	noncancer	all ages	1.00E-01	NYSDEC 2005	No new data
inhalation	chronic	noncancer	all ages	1.00E-01	NYSDEC 2005	No new data
inhalation	intermediate	noncancer	all ages	1.00E-01	NYSDEC 2005	No new data

oral	chronic	cancer	all ages	5.10E-03	NYSDEC 2005	No new data
oral	acute	noncancer	all ages	3.70E-02	NYSDEC 2005	No new data
oral	chronic	noncancer	all ages	3.70E-02	NYSDEC 2005	No new data
oral	intermediate	noncancer	all ages	3.70E-02	NYSDEC 2005	No new data
Fenitrothion						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	1.00E-02	USEPA 1999b	No new data
dermal	chronic	noncancer	all ages	1.00E-02	USEPA 1999b	No new data
dermal	intermediate	noncancer	all ages	1.00E-02	USEPA 1999b	No new data
inhalation	acute	noncancer	all ages	4.00E-04	USEPA 1999b	No new data
inhalation	chronic	noncancer	all ages	4.00E-04	USEPA 1999b	No new data
inhalation	intermediate	noncancer	all ages	4.00E-04	USEPA 1999b	No new data
oral	acute	noncancer	all ages	1.30E-01	USEPA 1999b	No new data
oral	chronic	noncancer	all ages	1.30E-03	USEPA 1999b	No new data
oral	intermediate	noncancer	all ages	1.30E-03	USEPA 1999b	No new data
Lambda-Cyhalothrin						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	1.00E-01	USEPA 2002a	No new data
dermal	chronic	noncancer	all ages	1.00E-01	USEPA 2002a	No new data
dermal	intermediate	noncancer	all ages	1.00E-01	USEPA 2002a	No new data
inhalation	acute	noncancer	all ages	8.00E-04	USEPA 2002a	No new data
inhalation	chronic	noncancer	all ages	8.00E-04	USEPA 2002a	No new data
inhalation	intermediate	noncancer	all ages	8.00E-04	USEPA 2002a	No new data
oral	acute	noncancer	all ages	5.00E-03	USEPA 2002a	No new data

oral	chronic	noncancer	all ages	5.00E-03	USEPA, 2011a	IRIS. Synonym Cyhalothrin/Karate (68085-85-8)
oral	intermediate	noncancer	all ages	5.00E-03	USEPA, 2011a	chronic used as surrogate
Malathion						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	adult	1.27E+00	USEPA, 2009	
dermal	acute	noncancer	child	1.27E-01	USEPA, 2009	
dermal	chronic	noncancer	adult	5.00E-01	USEPA 2005a	
dermal	chronic	noncancer	child	5.00E-02	USEPA 2005a	
dermal	intermediate	noncancer	adult	1.27E+00	USEPA, 2009	
dermal	intermediate	noncancer	child	1.27E-01	USEPA, 2009	
inhalation	acute	noncancer	adult	1.00E-03	USEPA, 2009	
inhalation	acute	noncancer	child	1.00E-04	USEPA, 2009	
inhalation	chronic	noncancer		2.60E-02	USEPA 2009	
inhalation	intermediate	noncancer	adult	1.00E-03	USEPA, 2009	
inhalation	intermediate	noncancer	child	2.60E-02	USEPA 2005a	
oral	acute	noncancer	all ages	7.00E-02	USEPA, 2009	non-dietary acute and intermediate: BMDL_10 = 7.1 mg/kg-day, UF = 100.
oral	chronic	noncancer	all ages	7.00E-02	USEPA, 2009	dietary chronic: BMDL_10 = 7.1 mg/kg-day, UF = 100.
oral	intermediate	noncancer	all ages	7.00E-02	USEPA, 2009	non-dietary acute and intermediate: BMDL_10 = 7.1 mg/kg-day, UF = 100.
Methoprene						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	1.00E+00	ATSDR 2005	No new data

dermal	chronic	noncancer	all ages	1.00E+00	ATSDR 2005	No new data
dermal	intermediate	noncancer	all ages	1.00E+00	ATSDR 2005	No new data
inhalation	acute	noncancer	all ages	2.50E+01	ATSDR 2005	No new data
inhalation	chronic	noncancer	all ages	2.50E+01	ATSDR 2005	No new data
inhalation	intermediate	noncancer	all ages	2.50E+01	ATSDR 2005	No new data
oral	acute	noncancer	all ages	4.00E-01	USEPA 1991	No new data
oral	chronic	noncancer	all ages	4.00E-01	USEPA 1991	No new data
oral	intermediate	noncancer	all ages	4.00E-01	USEPA 1991	No new data
Permethrin						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	chronic	cancer	all ages	9.60E-03	USEPA 2005b	No new data
dermal	acute	noncancer	all ages	5.00E+00	USEPA 2005b	No new data
dermal	chronic	noncancer	all ages	5.00E+00	USEPA 2005b	No new data
dermal	intermediate	noncancer	all ages	5.00E+00	USEPA 2005b	No new data
inhalation	chronic	cancer	all ages	9.60E-03	USEPA 2005b	No new data
inhalation	acute	noncancer	all ages	1.10E-01	USEPA 2005b	No new data
inhalation	chronic	noncancer	all ages	1.10E-01	USEPA 2005b	No new data
inhalation	intermediate	noncancer	all ages	1.10E-01	USEPA 2005b	No new data
oral	chronic	cancer	all ages	9.60E-03	USEPA 2005b	No new data
oral	acute	noncancer	all ages	2.50E-01	USEPA 2005b	No new data
oral	chronic	noncancer	all ages	2.50E-01	USEPA 2005b	No new data
oral	intermediate	noncancer	all ages	2.50E-01	USEPA 2005b	No new data
Piperonyl butoxide						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**

oral	acute	noncancer	all ages	6.30E+00	USEPA, 2006	acute RfD
oral	chronic	noncancer	all ages	1.60E-01	USEPA, 2006	chronic RfD
oral	intermediate	noncancer	all ages	1.60E-01	USEPA, 2006	chronic used as surrogate: intermediate-term incidental oral (1-6 months) = 0.89 mg/kg/d. No RfD reported
dermal	acute	noncancer	all ages	6.30E+00	USEPA, 2006	oral used as surrogate based on 2007 precedent
dermal	chronic	noncancer	all ages	1.60E-01	USEPA, 2006	oral used as surrogate based on 2007 precedent
dermal	intermediate	noncancer	all ages	1.60E-01	USEPA, 2006	oral used as surrogate based on 2007 precedent
inhalation	acute	noncancer	all ages	6.30E+00	USEPA, 2006	acute RfD
inhalation	chronic	noncancer	all ages	3.91E-03	USEPA, 2006	chronic RfD
inhalation	intermediate	noncancer	all ages	3.91E-03	USEPA, 2006	chronic used as surrogate: intermediate-term incidental oral (1-6 months) = 0.013 mg/kg/d. No RfD reported.
Pirimiphos-methyl						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	1.50E-02	USEPA 2006a	No new data
dermal	chronic	noncancer	all ages	7.00E-04	USEPA 2006a	No new data
dermal	intermediate	noncancer	all ages	7.00E-04	USEPA 2006a	No new data
inhalation	acute	noncancer	all ages	1.50E-02	USEPA 2006a	No new data
inhalation	chronic	noncancer	all ages	7.00E-04	USEPA 2006a	No new data
inhalation	intermediate	noncancer	all ages	7.00E-04	USEPA 2006a	No new data
oral	acute	noncancer	all ages	5.00E-03	USEPA 2006a	Table 3; dietary population dose

oral	chronic	noncancer	all ages	6.70E-05	USEPA 2006a	Table 3; dietary population dose
Oral	intermediate	noncancer	all ages	6.70E-05	USEPA 2006a	chronic used as surrogate
Propoxur						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	chronic	cancer	all ages	3.70E-03	USEPA 1997a	No new data
dermal	acute	noncancer	all ages	1.00E+01	USEPA 1997a	No new data
dermal	chronic	noncancer	all ages	1.00E+01	USEPA 1997a	No new data
dermal	intermediate	noncancer	all ages	1.00E+01	USEPA 1997a	No new data
inhalation	chronic	cancer	all ages	3.70E-03	USEPA 1997a	No new data
inhalation	acute	noncancer	all ages	4.00E-03	USEPA 1997a	No new data
inhalation	chronic	noncancer	all ages	4.00E-03	USEPA 1997a	No new data
inhalation	intermediate	noncancer	all ages	4.00E-03	USEPA 1997a	No new data
oral	chronic	cancer	all ages	3.70E-03	USEPA 1997a	No new data
oral	acute	noncancer	all ages	5.00E-03	USEPA 1997a	No new data
oral	chronic	noncancer	all ages	5.00E-03	USEPA 1997a	No new data
oral	intermediate	noncancer	all ages	5.00E-03	USEPA 1997a	No new data
Pyriproxyfen						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	3.50E-01	USEPA 2003a	chronic used as surrogate
dermal	chronic	noncancer	all ages	3.50E-01	USEPA 2003a	oral used as surrogate based on 2007 precedent: Long-term dermal (6 months - lifetime), (occupational/residential): Oral NOAEL = 35.1 mg/kg/d (dermal absorption rate = 30%)with LOC for MOE = 100
dermal	intermediate	noncancer	all ages	3.50E-01	USEPA 2003a	chronic used as surrogate
inhalation	acute	noncancer	all ages	3.50E-01	USEPA 2003a	chronic used as surrogate

inhalation	chronic	noncancer	all ages	3.50E-01	USEPA 2003a	oral used as surrogate based on 2007 precedent: Oral NOAEL = 35.1 mg/kg/d (inhalation absorption rate = 100%)with LOC for MOE = 100
inhalation	intermediate	noncancer	all ages	3.50E-01	USEPA 2003a	chronic used as surrogate
oral	acute	noncancer	all ages	3.50E-01	USEPA 2003a	Short-term, incidental (1-30 days), residential: Oral maternal NOAEL = 100 mg/kg/d with LOC for MOE = 100
oral	chronic	noncancer	all ages	3.50E-01	USEPA 2003a	chronic dietary all populations: NOAEL = 35.1 mg/kg/d, UF=100, Chronic RfD = 0.35 mg/kg/d
oral	intermediate	noncancer	all ages	3.50E-01	USEPA 2003a	chronic used as surrogate: Intermediate-term, incidental (1-6 months), occupational/residential: Oral NOAEL = 35.1 mg/kg/d with LOC for MOE = 100
Spinosad						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer	all ages	4.90E-02	USEPA, 2002	oral used as surrogate based on 2007 precedent
dermal	chronic	noncancer	all ages	2.70E-02	USEPA, 2002	oral used as surrogate based on 2007 precedent
dermal	intermediate	noncancer	all ages	2.70E-02	USEPA, 2002	oral used as surrogate based on 2007 precedent
inhalation	acute	noncancer	all ages	4.90E-02	USEPA, 2002	inhalation (short-term, 1 to 30 days) (residential), oral NOAEL = 4.9 mg/kg/d (absorption = 100%), LOC for MOE = 100)
inhalation	chronic	noncancer	all ages	2.70E-02	USEPA, 2002	oral used as surrogate based on 2007 precedent: inhalation (long-term, >6 months) (residential), oral NOAEL = 2.7 mg/kg/d (absorption = 100%), LOC for MOE = 100)

inhalation	intermediate	noncancer		2.70E-02	USEPA, 2002	oral used as surrogate based on 2007 precedent: inhalation (intermediate-term, 1 to 6 months) (residential), oral NOAEL = 2.7 mg/kg/d (absorption = 100%), LOC for MOE = 100)
oral	acute	noncancer		4.90E-02	USEPA, 2002	incidental oral (short-term, 1 to 30 days) (residential), NOAEL =4.9 mg/kg/d with LOC for MOE = 100
oral	chronic	noncancer		2.70E-02	USEPA, 2002	chronic dietary all populations. NOAEL = 2.7 mg/kg/d, UF = 100. Chronic RfD = 0.027 mg/kg/d.
oral	intermediate	noncancer		2.70E-02	USEPA, 2002	chronic used as surrogate: incidental oral (intermediate-term, 1 to 6 months) (residential), NOAEL =2.7 mg/kg/d with LOC for MOE = 100
Temephos						
Exposure Pathway	**Duration**	**Endpoint**	**Receptor**	**Value**	**Reference**	**Comments**
dermal	acute	noncancer		3.00E-03	USEPA 2000	No new data
dermal	chronic	noncancer		3.00E-03	USEPA 2000	No new data
dermal	intermediate	noncancer		3.00E-03	USEPA 2000	No new data
inhalation	acute	noncancer		3.00E-03	USEPA 2000	No new data
inhalation	chronic	noncancer		3.00E-03	USEPA 2000	No new data
inhalation	intermediate	noncancer		3.00E-03	USEPA 2000	No new data
oral	acute	noncancer		2.00E-01	USEPA 1997	Subchronic HEAST (no adjustment for exposure)
oral	chronic	noncancer		2.00E-02	USEPA 1997	
oral	intermediate	noncancer		2.00E-01	USEPA 1997	

Noncancer endpoint units: mg/kg-day

Cancer endpoint units $(mg/kg\text{-}day)^{-1}$

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Glossary

Molecular Weight: The molecular weight, also called formula weight, is the sum of the atomic weights of all the atoms in a molecule (http://www.answers.com/topic/molecular-mass). The molecular weight is a chemical-specific property and is important for the determination of other properties such as the Henry's Law Constant.

Solubility: Solubility is the amount of mass of a compound that will dissolve in a unit volume of solution (http://iaspub.epa.gov/trs/trs_proc_qry.alphabet?p_term_nm=S&p_reg_auth_id=1&p_data_id=79501&p_version=1). Aqueous solubility is an extremely important chemical property because it plays a major role in assessing the migration and fate of chemicals in the environment. In general, a higher solubility is quickly distributed by the hydrologic cycle through biodegradation, where a chemical rapidly and completely dissolves in water and has a low affinity for adsorption to solids. A highly water soluble chemical tends to leach faster (i.e., be mobile in soil) and is more easily degraded by microorganisms. In contrast, chemicals with low solubility have a strong partitioning to the subsurface solids, soil, or sediment. Therefore, a chemical that is highly soluble will be easily transported along with the general flow of water and will demonstrate limited bioconcentration (http://www.crwr.utexas.edu/gis/gisenv98/class/risk/lecture/Lect4/Fate.html#solubility; http://ca.water.usgs.gov/mtbe/fs20396/; http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/830_Product_Properties_Test_Guidelines/Series/830-7560.pdf).

Henry's Law Constant: The Henry's Law Constant characterizes the equilibrium distribution of dilute concentrations of volatile, soluble chemicals between gas and liquid. (http://www.epa.gov/ATHENS/learn2model/part-two/onsite/esthenry.htm). The Henry's Law Constant can also be described as the ratio of concentration of a volatile chemical in air to concentration in an aqueous solution (at equilibrium). Henry's Law Constant is important because it can be used as a general indicator of volatility of a chemical, and to estimate amount of a volatile chemical available for inhalation during activities such as spraying of pesticide inside of a residence (http://mepas.pnl.gov/FRAMESV1/physical.html). In general, a compound with a Henry's Law Constant value of 0.05 or larger would be very volatile from water (http://ca.water.usgs.gov/mtbe/fs20396/) while a low Henry's Law Constant value indicates that volatilization from water is slow.

Vapor Pressure: Vapor pressure is the pressure exerted by a vapor in equilibrium with its solid or liquid phase (i.e., it is the pressure at which a liquid will vaporize at a given temperature) (http://www.answers.com/topic/vapor-pressure and http://www.ce.utexas.edu/prof/kinnas/319LAB/Book/fr_book.html). A chemical's vapor pressure is important with respect to the rate at which it will volatilize or evaporate (i.e., the transfer of a chemical from water, soil, or plant surfaces to air). Volatilization occurs when pesticide surface residues change from solid or liquid to a gas and each pesticide has a characteristic tendency to become a gas, which is called its vapor pressure. It is also useful in conjunction with other chemical properties (e.g., solubility in water) for estimating partition coefficients between air and water (http://www.crwr.utexas.edu/gis/gisenv98/class/risk/lecture/Lect4/Fate.html#vapor). Once a pesticide is converted to a vapor, the pesticide vapors diffuse a very short distance and then are moved away with the air current (http://extoxnet.orst.edu/faqs/pesticide/pestfate.htm). Vapor

pressure is a significant property because during the spraying of a household, a person would be exposed to the volatilized chemical and therefore be at risk of exposure.

Octanol-Water Partition Coefficient: The octanol-water partition coefficient is the ratio of the concentration of a chemical in octanol and in water at equilibrium and at a specified temperature. The octanol-water partition coefficient provides a thermodynamic measure of the tendency of the substance to prefer a nonaqueous or oily milieu rather than water (i.e., its hydrophilic/lipophilic balance) (http://www.wiley.com/WileyCDA/WileyTitle/productCd-0471973971.html). The octanol-water partition coefficient is a chemical-specific property that characterizes a chemical's affinity for water or lipids. This parameter is used to help determine the fate of chemicals in the environment (http://toxics.usgs.gov/definitions/kow.html) and it has been shown to be correlated to water solubility, soil/sediment sorption coefficient, and bioconcentration (http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/830_Product_Properties_Test_Guidelines/Series/830-7560.pdf). Specifically, a chemical with a high octanol-water partition coefficient or a compound that is more soluble in octanol (more hydrophobic and lipophilic) is expected to partition out of the water and to bind to soil, suspended particulate matter, or into lipophilic tissue.

Reaction Half-Life: The half-life of a substance is simply the time required for half of the amount originally present to react or degrade in a specified media. (http://www.psigate.ac.uk/newsite/reference/plambeck/chem2/p02143.htm). The half-life is a measure of persistence, which is the ability of a chemical to resist degradation in various media, such as air, soil, water and sediment.

Reaction Half-Life in Water: This property is significant because chemicals with long half-lives, or persistence times, in water have a high potential for accumulation in this medium and also for uptake by living organisms. This property is important for the discussion of the risk from the disposal of a pesticide because pesticides with greater half-lives in water that are disposed of improperly may end up in the surface or groundwater and may adversely impact the environment and human health.

Reaction Half-Life in Air: The reaction half-life in air is a measure of a chemical's persistence in the atmosphere and is significant because a chemical with a long half-life in the air has a greater potential to be inhaled. This property is especially important for the risk from spraying the inside of a household with insecticide.

Reaction Half-Life in Soil: The reaction half-life in soil is important because chemicals with long persistence times in soil or sediments have a high potential for accumulation in the medium and also for uptake by living organisms. In general, the longer the half-life in soil, the greater the potential for pesticide movement. A pesticide with a half-life greater than 21 days may persist long enough to leach or move with surface runoff before it degrades (http://www.agf.gov.bc.ca/pesticides/c_2.htm). This property is important when discussing the disposal of pesticides because pesticides with a greater half-life in soil will persist longer and will therefore have the ability to leach and present a highly likelihood of human exposure.

ANNEX E: PESTICIDE PROFILES

Acronym List for Toxicological Profiles

ATSDR	Agency for Toxic Substances and Disease Registry
CSF	cancer slope factor
EC_{50}	median effective concentration (concentration that is lethal to 50% of organisms)
EPA	U.S. Environmental Protection Agency
EXTOXNET	Extension TOXicology NETwork
HSDB	Hazardous Substances Data Bank
IPCS	International Program on Chemical Safety
IRIS	Integrated Risk Information System
LC_{50}	lethal concentration 50 (concentration that is lethal to 50% of organisms)
LD_{50}	lethal dose 50 (dose that is lethal to 50% of organisms)
MRL	minimal risk level
LOAEL	lowest observed adverse effect level
NOAEL	no observed adverse effects level
NOEL	no observed effect level
PAN	Pesticide Action Network
RfD	Reference Dose
SF	safety factor
UF	uncertainty factor
WHO	World Health Organization

Profile for Alpha-Cypermethrin:

CAS Registry Number 67375-30-8

Summary of Insecticide

Chemical History

Alpha-cypermethrin is a highly active synthetic pyrethroid insecticide used to control a wide variety of pests in agricultural and public health applications. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (ATSDR, 2003; IPCS, 1992). Alpha-cypermethrin is available in technical grade formulation, emulsifiable concentrate, ultra-low-volume formulation, suspension concentrate, and in mixtures with other insecticides (HSDB, 2005; IPCS, 1992). For mosquito control, it is used in bed nets and other materials that are dipped in alpha-cypermethrin to protect the user (WHO, 1997, 1998). It is considered one of the best insecticides for impregnation of traps and screens (WHO, 1997). Alpha-cypermethrin is not currently registered for use in the United States (HSDB, 2005), but cypermethrin is.

Alpha-cypermethrin is of low risk to humans when used at levels recommended for its designed purpose (ATSDR, 2003; HSDB, 2005). However, as a synthetic pyrethroid, alpha-cypermethrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels of nerve cells (ATSDR, 2003; HSDB, 2005). It has moderate acute toxicity and is a suspected endocrine disruptor but does not inhibit cholinesterase (PAN, 2005). EPA has not classified synthetic pyrethroids, including alpha-cypermethrin, as endocrine disruptors. Typical symptoms of acute exposure are irritation of skin and eyes, headaches, dizziness, nausea, vomiting, diarrhea, and excessive salivation and fatigue. Inhaled alpha-cypermethrin has been shown to cause cutaneous paraesthesia or a burning, tingling, or stinging of the skin. However, these effects are generally reversible and disappear within a day of removal from exposure (ATSDR, 2003; HSDB, 2005; PAN, 2005). Alpha-cypermethrin is harmful if swallowed (MSDS, n.d.). Inhalation and dermal exposure are the most likely human exposure routes (HSDB, 2005). Environmental levels of significance are unlikely if alpha-cypermethrin is applied at recommended rates (IPCS, 1992).

Description of Data Quality and Quantity

Comprehensive reviews on the toxicity of alpha-cypermethrin are not widely available but include the following:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003)
- Environmental Health Criteria 142: Alpha- Cypermethrin (IPCS, 1992)

EPA and ATSDR have developed quantitative oral human health benchmarks (EPA's chronic RfD and ATSDR's acute oral MRL) for cypermethrin. Alpha-cypermethrin makes up one quarter of the racemic mixture cypermethrin and has a similar mode of action. Alpha-cypermethrin is also similar to cypermethrin with regard to the signs of intoxication, target organs effects, and metabolic pathways (IPCS, 1992).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	4	mg/kg/day	Inhalation NOAEL in rats with UF of 100 applied	
Acute	Oral	0.02	mg/kg/day	Acute oral MRL for cypermethrin based on neurological effects in rats with UF of 1000 applied	ATSDR (2003)
Intermediate	Oral	0.01	mg/kg/day	Adopt chronic RfD as intermediate duration	
Chronic	Oral	0.01	mg/kg/day	Chronic oral RfD for cypermethrin based on neurological effects in dogs with UF of 100 applied	U.S. EPA (2005)
Acute, Intermediate, Chronic	Dermal	5	mg/kg/day	Dermal NOAEL in rats with UF of 100 applied	

For inhalation exposure, a NOAEL of 400 mg/m^3 (447 mg/kg/day)[1] was identified for neurological and respiratory effects in rats exposed to alpha-cypermethrin via inhalation for 4 hours (IPCS, 1992). An uncertainty factor of 100 to account for intra- and interspecies variation was applied, for an inhalation benchmark of 4 mg/kg/day. This value is appropriate for all exposure durations.

Due to limited low-dose oral data for alpha-cypermethrin, health benchmarks for cypermethrin were used and are expected to be protective of human health. The acute oral MRL for cypermethrin of 0.02 mg/kg/day is based on a LOAEL of 20 mg/kg for neurological effects (altered gait and decreased motor activity) in rats with an uncertainty factor of 1,000 applied. Long-Evans rats were given single gavage doses of up to 120 mg/kg cypermethrin. Motor activity and FOB were assessed at 2 and 4 hours post-dosing. A NOAEL was not identified (ATSDR, 2003). The chronic oral RfD for cypermethrin of 0.01 mg/kg/day is based on a NOEL of 1 mg/kg/day for systemic effects with an uncertainty factor of 100 applied. Beagle dogs were dosed with up to 15 mg/kg/day cypermethrin in corn oil for 52 weeks. During the first week, increased vomiting was observed in dogs at all dose levels. Additionally, throughout the study all dogs passed liquid feces; however, the incidence was 10- and 30-fold higher in the 5 and 15 mg/kg/day groups, respectively. The NOEL identified for this study was 1 mg/kg/day (U.S. EPA, 2005).

For dermal exposure, a NOAEL of 500 mg/kg/day was identified in rats dermally exposed to alpha-cypermethrin once for 24 hours (IPCS, 1992). An uncertainty factor of 100 to account for intra- and interspecies variation was applied, for a dermal benchmark value of 5 mg/kg/day. This value is appropriate for all exposure durations.

Insecticide Background

CASRN: 67375-30-8

[1] Conversion between mg/m^3 and mg/kg/day assumes, for Fischer-344 rats, an average body weight of 0.152 kg and inhalation rate of 0.17 m^3/day (U.S. EPA, 1988).

Synonyms:	alfamethrin, alphamethrin, alphacypermethrin, alpha-cypermethrin, alfa-cipermetrina, alfacypermetrin, alfa cipremetrin,[1alpha(S*),3alpha]-(+ -)-Cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)- 2,2-dimethylcyclopropanecarboxylate, (1R cis S) and (1S cis R) Enantiomeric isomer pair of alpha-cyano-3- phenoxybenzyl-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate, Pesticide Code 209600(S)-alpha-cyano-3-phenoxybenzyl-(1R)-cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate and (R)-alpha-cyano-3-phenoxybenzyl-(1S)-cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate, WL 85871, cyano(3-phenoxyphenyl)methyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (+)-cis isomer, alphametrin, numerous other systematic and non-systematic names (HSDB, 2005; PAN 2005; ATSDR, 2003; MSDS, n.d.)
Chemical Group:	pyrethroid (PAN, 2005)
Registered Trade Names:	Bestox, Fastac, Concord, Dominex, Fendona, Fendona 1.5 SC, Fendona 10 SC, Fendonal WP, Renegade (HSDB, 2005, IPCS, 1992, WHO, 2002), Tenopa SC (alphacypermethrin + flufenoxuron) (HSDB, 2005; PAN 2005; ATSDR, 2003; MSDS, n.d.)

Usage

Alpha-cypermethrin is a pyrethroid insecticide used to combat a wide variety of chewing and sucking insects on field crops, fruits and vegetables, and in forestry uses. It may be applied to crops as either a curative or preventative treatment. Alpha-cypermethrin is also used in public health applications to control mosquitoes, flies, and other pests. For animal husbandry it is used as an ectoparaciticide and to control flies (HSDB, 2005; IPCS, 1992). Alpha-cypermethrin belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies (ATSDR, 2003). For mosquito protection, it is used in bed nets and other materials that are dipped into the alpha-cypermethrin to protect the user. Alpha-cypermethrin has been available since 1983 (IPCS, 1992); however, it not currently registered for use in the United States (HSDB, 2005).

Formulations and Concentrations

Alpha-cypermethrin is available in technical grade, emulsifiable concentrates, wettable powder, suspension concentrates, ultra-low-volume liquids, tablets, and in mixtures with other insecticides (HSDB, 2005; IPCS, 1992). Technical grade alpha-cypermethrin is greater than 90 percent pure (HSDB, 2005). Common formulations of alpha-cypermethrin include Fastac, which is available as an emulsifiable concentrate (20–100 g/L), a wettable powder (50 g/kg), a suspension concentrate (15–250 g/L), and an ultra-low-volume liquid (6–15 g/L); and Fendona and Renegade, which are available as an emulsifiable concentrate (50 or 100 g/L), a suspension concentrate (250 g/L), and a wettable powder (50 g/kg). Alpha-cypermethrin is combined with other active ingredients to form other products (IPCS, 1992). WHO has indicated that the content of alpha-cypermethrin in the formulated products must be declared and shall not exceed the listed standards. Technical grade alpha-cypermethrin must have no less than 910 g/kg alphacypermethrin cis 2 ([IR cis] S and [IS cis] R isomers), and the combined content of the cis and trans isomers of alpha-cyano-3-phenoxybenzyl-2,2-dimethyl-3-(2,2-dichlorovinyl-) cyclopropanecarboxylate must be at least 975 g/kg. No more than 1 g/kg

of volatile hydrocarbon solvent and 1 mg/kg of triethylamine is permitted. The aqueous suspension concentrate should contain alphacypermethrin cis 2 ([IR cis] S and [IS cis] R isomers) as follows: up to 25 g/kg, ± 15 percent of the declared content; 25 to 100 g/kg, ± 10 percent of the declared content. The alphacypermethrin cis 1:cis 2 isomer ratio must be lower than 5:95 (WHO, 1999).

Shelf Life

Alpha-cypermethrin is stable in acidic and neutral environments. However, it hydrolyzess at pH 12–13 and decomposes at temperatures greater than 220 °C. For practical purposes, field studies have indicated that it is stable to sunlight (IPCS, 1992). It is not compatible with strong oxidizing agents (MSDS, n.d.).

Degradation Products

Based on its structure, alpha-cypermethrin is expected to readily biodegrade in the environment. However, in two tests it did not degrade and therefore cannot be considered readily biodegradable. One of the major transformation products in the microbial transformation of technical alpha-cypermethrin is 3-phenoxybenzoic acid, which is then transformed to 4-hydroxy-3-phenoxybenzoic acid (IPCS, 1992).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Based on its Koc value, alpha-cypermethrin binds tightly to soil, making it almost immobile in most soil types. In moist soil, volatilization is expected to be the major fate process; however its bond to soil lessens this effect. Volatilization is not a major fate process for dry soil. Biodegradation by environmental organisms in non-sterile soil and by sunlight is expected (HSDB, 2005; IPCS, 1992). Studies have shown that within 2 weeks of treatment with 0.5 kg ai/ha (active ingredient per hectare) of a diluted alpha-cypermethrin emulsifiable concentrate formulation in sandy-clay soil, residues of alpha-cypermethrin were 50 percent less. After 1 year, they were below detection or < 0.01 mg/kg. Similar results were seen after a second and third application to the site indicating that alpha-cypermethrin did not build up in the surface soil. Additionally, no leaching to subsurface soils was observed. Alpha-cypermethrin also does not build up in peat soils (IPCS, 1992).

Fate and Transport in Aquatic Systems

Alpha-cypermethrin binds tightly to suspended solids and sediments in water. It is expected to volatilize from water; however, volatilization is lessened by alpha-cypermethrin's bond with soil. Reported volatilization half-lives are 8 days for a river models and 65 days for a lake model. If adsorption is taken into consideration, the estimated volatilization half-life in a pond model is 125 years. Estimated hydrolysis half-lives are 36 and 4 years at pH 7 and 8 respectively. Alpha-cypermethrin is also expected to undergo photodecomposition. Based on its bioconcentration factor, alpha-cypermethrin has a high potential to bioconcentrate in aquatic organism; however, its potential may actually be lower than this suggests because of the ability of aquatic organisms to rapidly metabolize alpha-cypermethrin (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Limited data exist on the acute toxicity of alpha-cypermethrin in humans (IPCS, 1992; HSDB, 2005). Occupationally exposed workers reported only mild skin irritation (IPCS, 1992). The main effects reported from acute exposure to alpha-cypermethrin in humans include skin rashes, eye irritation, itching and burning

sensation on exposed skin, and paraesthesia (a result of the direct action of this type of pyrethroid on sensory nerve endings, causing repeated firings in these fibers). Acute inhalation exposures may cause upper and lower respiratory tract irritation. Ingestion of alpha-cypermethrin is also harmful (HSDB, 2005; MSDS, n.d.). No acute poisonings have been reported (IPCS, 1992).

In rodents, alpha-cypermethrin has moderate to high oral toxicity (HSDB, 2005; IPCS, 1992). Oral LD_{50} values in rats and mice vary greatly and depend on the formulation, concentration, and the vehicle (IPCS, 1992). Acute oral LD_{50} values for technical alpha-cypermethrin range from 79 to 400 mg/kg (in corn oil) in rats (HSDB, 2005; IPCS, 1992; MSDS, n.d.). Although the LD_{50} of 80 mg/kg is considered representative, higher values have been reported. In mice, the reported acute oral LD_{50} of technical alpha-cypermethrin is 35 mg/kg (in corn oil). Oral LD_{50} values for formulated alpha-cypermethrin in rats range from 101 to 174 mg/kg for an emulsifiable concentrate formulation (100 g/L), while 1,804 mg/kg was reported for a suspension concentrate formulation (100 mg/L) and 5,838 mg/kg for an ultra-low-volume liquid formulation (15 g/L) (IPCS, 1992). Clinical signs reported in orally exposed animals are associated with central nervous system activity and included ataxia; gait abnormalities; choreoathetosis; "tip-toe" walk; and increased salivation, lacrimation, piloerection, tremor, and clonic convulsions. Acute dermal exposures are minimally irritating to the skin and eyes of rabbit skin. However, some formulations can cause severe eye irritation that includes corneal opacity and iris damage. Stimulation of the sensory-nerve endings of the skin has been observed in guinea pigs. Reported dermal LD_{50} values of greater than 2,000 mg tech/kg are reported for rats and rabbits (HSDB, 2005; IPCS, 1992). No mortality or signs of toxicity were observed in rats or mice after single dermal applications of up to 500 mg/kg or 4-hour inhalation exposure of mice to 400 mg/m^3. Alpha-cypermethrin is not a dermal sensitizer in guinea pigs (IPCS, 1992).

Treatment

Pyrethroid insecticides and their metabolites can be detected in blood and urine; however, the methods are not practical to use given how quickly these compounds are broken down in the body (ATSDR, 2003). Alpha-cypermethrin poisoning should be treated the same as a pyrethroid poisoning. There are no antidotes for alpha-cypermethrin exposure. Treatment is supportive and depends on the symptoms of the exposed person. Decontamination is all that is necessary for most exposures. If a person exhibits signs of typical pyrethroid toxicity following alpha-cypermethrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. The application of topical vitamin E helps to relieve the symptoms of paraesthesia. Eye exposures should be treated by rinsing with copious amounts of saline or room temperature water for at least 15 minutes. Contact lenses should be removed. Medical attention should be sought if irritation, pain, swelling, lacrimation, or photophobia persists. The treatment of ingestion exposures is mostly symptomatic and supportive. Care should be taken to monitor for the development of hypersensitivity reactions with respiratory distress. Gastric decontamination is recommended if large amounts have been very recently ingested, and oral administration of activated charcoal and cathartic are recommend for ingestion of small amounts or if treatment has been delayed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible. For inhalation exposures, removal to fresh air and monitoring for breathing difficulties, respiratory tract irritation, bronchitis, and pneumonitis are recommended. Oxygen should be administered as necessary (PAN, 2005; HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to alpha-cypermethrin. Chronic exposure to pyrethrins may cause hypersensitivity pneumonitis characterized by chest pain, cough, dyspnea, and bronchospasm. Because alpha-cypermethrin belongs to this class of chemicals, similar effects may be expected (HSDB, 2005).

Chronic toxicity data are also lacking in animals. No animal data are available for long-term toxicity, reproductive toxicity, teratogenicity, or immunotoxicity (HSDB, 2005; IPCS, 1992). However, chronic toxicity data are available for cypermethrin, including rodent multigenerational reproduction, embryotoxicity, and teratogenicity studies. At doses that produced systemic toxicity, no effects on reproductive parameters or fetal development were observed. Therefore, it is likely that alpha-cypermethrin would also cause no reproductive or developmental effects in rodents because it is a component of cypermethrin. Available data do not indicate that alpha-cypermethrin is mutagenic (IPCS, 1992).

Cancer Endpoints

No data are available on the carcinogenic potential of alpha-cypermethrin (IPCS, 1992).

Toxicokinetics

Like other pyrethroid insecticides, orally administered alpha-cypermethrin, is absorbed via the intestinal tract of mammals, and dermally applied doses are absorbed through intact skin. Little or none is absorbed by inhalation exposures (HSDB, 2005). Most pyrethroids are rapidly broken down by liver enzymes and their metabolites are quickly excreted (HSDB, 2005). The metabolism of synthetic pyrethroids in mammals is generally through hydrolysis, oxidation, and conjugation. Metabolism of alpha-cypermethrin occurs by the cleavage of the ester bond. Studies in rats show that the phenoxybenzyl alcohol and cyclpropan carboxylic ac parts of the molecule are conjugated with sulfate and glucuronide, respectively, before being excreted in urine. Esteric hydrolysis and oxidative pathways occur in rats, rabbits, and humans with esteric hydrolysis being the predominant pathway in humans and rabbits (IPCS, 1992). Within 24 hours of an oral dose of 0.25–0.75 mg in humans, 43 percent was excreted in the urine as free of conjugated cis-cyclprpane carboxlic acid (HSDB, 2005; IPCS, 1992). Orally administered alpha-cypermethrin is eliminated in the urine of rats as the sulfate conjugate of 3-(4-hydroxyphenoxy) benzoic acid. In the faces it is eliminated partly as unchanged compound. Alpha-cypermethrin levels in tissues are low except for fatty tissues. The reported half-life for elimination from fat is 2.5 days for the first phase of elimination and 17 to 26 days for the second phase (IPCS, 1992).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Alpha-cypermethrin, like other pyrethroids, is very unlikely to harm terrestrial organisms other than its targets (e.g., mosquitoes and other pests). No toxicity data are available for alpha-cypermethrin in birds. However, cypermethrin has a very low toxicity in birds with acute oral LD_{50} values of greater than 2,000 mg/kg body weight. In feed, the reported LC_{50} values are greater than 10,000 mg/kg diet (IPCS, 1992). As with other pyrethroid insecticides, alpha-cypermethrin is extremely toxic to honey bees. The reported 24-hour oral LD_{50} for alpha-cypermethrin emulsifiable concentrate is 0.13 µg/bee and the 24-hour oral LD_{50} for alpha-cypermethrin in acetone was 0.06 µg/bee. The reported dermal LD_{50}s are 0.03 µg/bee for technical alpha-cypermethrin and 0.11 µg/bee for emulsifiable concentrate (IPCS, 1992). The very high toxicity in bees was not observed in the field, likely as a result of the repellent effect of alpha-cypermethrin, which would limit

exposure (IPCS, 1992; HSDB, 2005). Mortality was seen in only 15 percent of honey bees exposed to flowers treated with an emulsifiable concentrate formulation within 48 hours. Other studies using oil-enhanced suspension concentrate formulations showed similarly low toxicity. Additionally, a similar pattern of toxicity was seen in leaf-cutting bees. The toxicity of alpha-cypermethrin to earthworms, Carabid beetles, Syrphid larvae and neuropteran larvae is low while it is relatively high for Linyphiid spiders and Coccinellids (IPCS, 1992).

Toxicity in Non-Targeted Aquatic Systems

Alpha-cypermethrin is very toxic to fish under laboratory conditions, with emulsifiable concentrate formulations being the most toxic (IPCS, 1992); however, these effects are not seen in field studies. Therefore, the hazard to fish from contamination of waterbodies due to overspraying and drift is negligible (IPCS, 1992). Depending on the formulation, the reported 96-hour LC_{50} values range from 0.7 to 350 µg/L (IPCS, 1992). For rainbow trout, the reported 96-hour LC_{50} values range from 2.8 to 350 µg/L (HSDB, 2005; IPCS, 1992). The emulsifiable concentrate formulation is 10 to 70 times more toxic to rainbow trout than the wettable powder or suspension concentrate formulations. However, in field studies, the 14-day LC_{50} for rainbow trout was just 29 g ai/ha for emulsifiable concentrate formulations and greater than 1,000 g ai/ha for suspension concentrate, wettable powder, and micro-encapsulated formulations. For fathead minnows, the reported 96-hour LC_{50} value for technical alpha-cypermethrin was 0.93 µg/L, while the reported 96-hour LC_{50} values for carp range from 0.8 to 11 µg/L depending on the formulation. For fish in the early stages of life, alpha-cypermethrin and cypermethrin toxicity are similar (IPCS, 1992). Alpha-cypermethrin has the potential to accumulate in fish, with a bioconcentration factor of 990 (HSDB, 2005). It has also been shown to be highly toxic to some aquatic invertebrates and aquatic insects (IPCS, 1992).

Chronic Exposure

Due to low rate of application and low persistence of alpha-cypermethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005). The hazard of alpha-cypermethrin to fish and aquatic invertebrates is in its acute toxicity. There is no evidence of chronic exposure causing cumulative effects (IPCS, 1992).

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Profile for Bendiocarb:

CAS Registry Number 22781-23-3

Summary of Insecticide

Chemical History

Bendiocarb is a broad spectrum carbamate insecticide first registered in the United States in 1980 for use to control a wide variety of nuisance and disease vector insects, such as mosquitoes, flies, wasps, ants, fleas, cockroaches, silverfish, and ticks. It is also effective against a variety of agricultural insects and to treat seeds against pests (U.S. EPA, 1999a, 1999b; EXTOXNET, 1996). The registration for bendiocarb was voluntarily canceled in 1999 (U.S. EPA, 1999a).

Bendiocarb exhibits its toxic effects through fast-acting, but reversible, cholinesterase inhibition. It has moderate toxicity in mammals (WHO/FAO, 1982), moderate toxicity in birds, and moderate to high toxicity in fish (EXTOXNET, 1996). In humans, symptoms of poisoning are neurological and include headache, blurred vision, nausea, vomiting, giddiness, slurred speech, excessive sweating and salivation, chest tightness, and twitching muscles (WHO/FAO, 1982). Bendiocarb pesticides were formulated as dusts, granules, wettable powders, pellets, and ultra low volume (ULV) sprays (U.S. EPA, 1999a; EXTOXNET, 1996).

Description of Data Quality and Quantity

Review data for bendiocarb are limited. Relevant resources include

- Bendiocarb: Revised HED Chapter for the Reregistration Eligibility Decision (RED) Document (U.S. EPA, 1999b)
- Data Sheet on Pesticides No. 52: Bendiocarb (WHO/FAO, 1982)
- Pesticide Information Profile for Bendiocarb (EXTOXNET, 1996).

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks) for bendiocarb.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.002	mg/kg/day	Inhalation NOAEL (0.00018 mg/L) for neurological effects with UF of 100 applied	U.S. EPA (1999b)
Acute, Intermediate, Chronic	Oral	0.00125	mg/kg/day	Acute and chronic oral RfDs based on neurological effects; adopt chronic for intermediate duration	U.S. EPA (1999b)
Acute	Dermal	0.5	mg/kg/day	Dermal NOAEL for neurological effects of 50 mg/kg/day with UF of 100 applied	U.S. EPA (1999b)
Intermediate	Dermal	0.2	mg/kg/day	Dermal LOAEL for neurological effects of 50 mg/kg/day with UF of 300 applied	U.S. EPA (1999b)
Chronic	Dermal	0.00125	mg/kg/day	Oral NOAEL for neurological effects of 0.125 mg/kg/day with UF of 100 applied	U.S. EPA (1999b)

For inhalation exposure, a NOAEL of 0.00018 mg/L (0.2 mg/kg/day)[2] was identified for whole blood cholinesterase inhibition in rats exposed to bendiocarb via inhalation for 6 hours per day, 5 days per week, for 90 days (Coombs et al., 1995). An uncertainty factor of 100 to account for interspecies and intrahuman variation was applied, for an inhalation benchmark of 0.002 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 1999b).

The acute and chronic oral RfDs of 0.00125 mg/kg/day were based on a NOAEL of 0.125 mg/kg for whole blood cholinesterase inhibition (about 25 percent) in rats exposed via gavage five days per week for two weeks (EPA MRID No. 00059269, no additional citation provided), with an uncertainty factor of 100 applied (10 each for interspecies and intrahuman variability). This value was also adopted for intermediate exposure (U.S. EPA, 1999b).

For acute dermal exposures, a NOAEL of 50 mg/kg/day in rats for whole blood cholinesterase inhibition from a single exposure was identified (EPA MRID No. 00122308, no additional citation provided) and an uncertainty factor of 100 was applied (10 each for interspecies and intrahuman variability). For intermediate dermal exposures, a LOAEL of 50 mg/kg/day for whole blood cholinesterase inhibition from repeated dermal exposures was identified (EPA MRID No. 00122308, no additional citation provided) and an uncertainty factor of 300 was applied (10 each for interspecies and intrahuman variability and 3 for the use of a LOAEL). For chronic dermal exposures, the NOAEL that was used to develop the oral RfDs was used with an uncertainty factor of 100 applied (10 each for interspecies and intrahuman variability) (U.S. EPA, 1999b).

[2] Conversion between mg/m^3 and mg/kg/day assumes, for Wistar rats, an average body weight of 0.187 kg and inhalation rate of 0.2 m^3/day (U.S. EPA, 1988).

Insecticide Background

CAS #:	22781-23-3
Synonyms:	2,3-isopropylidenedioxyphenyl methylcarbamate (EXTOXNET, 1996), Ent-27695; OMS 1394; (WHO/FAO, 1982), 1,3-Benzodioxol-4-ol, 2,2-dimethyl-, methylcarbamate , 1,3-Benzodioxole, 2,2-dimethyl-4-(N-methylamino-carboxylato)- , 105201 (U.S. EPA PC Code) , 1924 (CA DPR Chem Code) , 2,2-Dimethyl-1,3-benzodioxol-4-yl methylcarbamate, Carbamic acid, methyl-, 2,3-(dimethylmethylenedioxy)-phenyl ester, Carbamic acid, methyl-, 2,3-(isopropylidenedioxy)phenyl ester (PAN, 2005), bencarbate, 1,3-benzodioxole,2,2,-dimethyl-4(n-methylcarbamato), 2,2-dimethyl-1,3-benzodioxol-4-ol methcarbamate, 2,3-isopropylidenedioxyphenyl methylcarbamate, methylcarbamic acid 2,3,-(isopropylidenedioxy)phenyl ester (HSDB, 2005)
Chemical Group:	n-methyl carbamate (PAN, 2005)
Registered Trade Names:	Compounds containing bendiocarb: Ficam, Dycarb, Garvox, Multamat, Multimet, Niomil, Rotate, Seedox, Tattoo, Turcam (EXTOXNET, 1996), NC-6897, Ficam D, Ficam plus, Ficam W, Ficam ULV (HSDB, 2005).

Usage

Bendiocarb is a residual carbamate insecticide that has a variety of indoor and outdoor uses, including the control of mosquitoes, household and ornamental plant pests, and fire ants. It has no registered uses on either food of feed crops (U.S. EPA, 1999b). Most products containing bendiocarb are General Use Pesticides (EXTOXNET, 1996) and are meant for homeowner/residential use. However, some formulations (e.g., wettable powders) are recommended to be used only by pest control operators. Bendiocarb is not a Restricted Use Pesticide (U.S. EPA, 1999b); however, the formulations Turcam and Turcam 2.5 G are classified as *restricted* and may only be used by certified applicators (EXTOXNET, 1996).

Common bendiocarb formulations for both agricultural and public health program uses include wettable powders (800, 500 and 200 g active ingredient/kg [g a.i./kg]), granules for soil and turf treatment (30, 50, and 100 g a.i./kg), dust (10 g a.i./kg), suspension concentrate (500 g a.i./1) for spray or seed treatments, suspension in oil for ULV application (250 g a.i./1), residual sprays, and paint on and granular preparations with bait. The use patterns for bendiocarb in agricultural, horticultural, or forestry applications are reported as follows: soil treatment (300–2,000 g a.i./ha), seed treatment (1–10 g a.i./kg), residual spray (100–1,000 g a.i./ha), and ULV spray (50–500 g a.i./ha). In public health programs, it is reported that the 80 percent wettable powder should be applied only by a professional applicator (WHO/FAO, 1982).

Formulations and Concentrations

- Common formulations of pesticides containing bendiocarb include technical grade, dusts, granules (for soil and turf treatment: 30, 50, and 100 g a.i./kg), wettable powders (800, 500, and 200 g a.i./kg), dust (10 g a.i./kg), suspension concentrate (for spray or seed treatment: 500 g a.i./L) and ULV sprays (in oil: 250 g, a.i./L) (WHO/FAO, 1982; EXTOXNET, 1996). WHO (1999) indicated that the bendiocarb content in various preparations should be declared and contain the following:

- Technical grade bendiocarb: not less than 940 g/kg

- Wettable Powder: above 250 up to 500 g/kg ± 5% of the declared content or above 500 g/kg ± 25 g/kg
- Dustable Powder: shall not differ from the declared content by more than -10% to + 35%.
- ULV Liquid: Above 100 up to 200 g/kg ± 6% of the declared content (WHO, 1999)

Shelf Life

Bendiocarb is reported to be stable below 40°C. Its half-life in aqueous solutions at 25°C is reported as 48 days at pH 5, 81 hours at pH 7, and 45 minutes at pH 9. Bendiocarb degrades slowly at pH 5. Bendiocarb is resistant to oxidation on nonabsorbant surfaces and at low humidity. In sunlight, bendiocarb photo-oxidizes (WHO/FAO, 1982).

Degradation Products

In moist soils and water, a major fate process for bendiocarb is hydrolysis. This is particularly true in neutral and alkaline environments. In neutral hydrolysis, the products are 2,3-isopropylidenedioxyphenol, methylamine, and carbon dioxide (HSDB, 2005). At pHs less than 5, bendiocarb slowly degrades into pyrogallol and acetone (WHO/FAO, 1982). The major degradation product of terrestrial field dissipation on turf is NC-7312 (U.S. EPA, 1999b).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Insecticidal carbamates that are applied to plants reach the soil both directly and indirectly. Degradation of carbamates in soil depends on volatility, leaching, soil moisture, absorption, pH, temperature, photodecomposition, microbial degradation, and soil type (IPCS, 1986). With a Koc range of 28 to 200, moderately to very high mobility is expected if bendiocarb is released in soil (HSDB, 2005). The major fate processes are hydrolysis in moist soils and biodegradation, with volatilization being an unimportant fate process for both dry and moist soils due to the low vapor pressure of bendiocarb. In moist soils, bendiocarb may undergo hydrolysis, and hydrolytic degradation depends on pH (HSDB, 2005; U.S. EPA, 1999b). Biodegradation of bendiocarb is expected to be rapid (HSDB, 2005). The half-life of bendiocarb in soil varies from less than 1 week up to 4 weeks, depending on the type of soil and the pH (EXTOXNET, 1996). The estimated hydrolysis half-life of bendiocarb is 46.5 days at pH 5, 2 days at pH 7, and 0.33 days at pH 9 (U.S. EPA, 1999b). Soil photolysis is important in the photodegradation of bendiocarb in soil. In field dissipation studies on turf, bendiocarb and its degradate NC-7312 are not highly mobile, with intermediate half-lives of 20 days (bendiocarb) and 21 days (NC-7312) (U.S. EPA, 1999b). Bendiocarb degrades before leaching through soil, and degradates remain in the upper layers of soil in low concentrations (U.S. EPA, 1999a, 1999b). It is unlikely that bendiocarb will move through soil to groundwater or to surface water through runoff (U.S. EPA, 1999a). Bendiocarb is of low persistence in soil (EXTOXNET, 1996).

Fate and Transport in Aquatic Systems

Water is an important factor in the transport of carbamates; however, the hazard posed by carbamates under these conditions is limited due to their rapid decomposition under aqueous conditions (IPCS, 1986). In water, bendiocarb is not expected to adsorb to suspended soils and sediments based on its Koc range (28 to 200). The major fate processes in water are hydrolysis and biodegradation; volatilization is an unimportant fate process due to the low vapor pressure of bendiocarb. Additionally, direct photolysis is not a major degradation pathway in water (U.S. EPA, 1999b) and depends on the turbidity of the water (IPCS, 1986). In alkaline and neutral environments, hydrolysis is expected to be a major fate process. Half-lives have been

reported of 48 days at pH 5, 4 days at pH 7, and 45 minutes at pH 9 (HSDB, 2005). Bendiocarb does not accumulate in water (EXTOXNET, 1996), and based on soil studies, biodegradation in water is expected to be rapid (HSDB, 2005). Because bendiocarb degrades rapidly in water, bioconcentration in fish is unlikely (U.S. EPA, 1999a). The estimated bioconcentration factor is 12 (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Bendiocarb causes toxic effects by the rapid, but reversible, inhibition of cholinesterase in the blood. It is moderately toxic if absorbed through the skin or ingested (EXTOXNET, 1996). Typical signs of acute poisoning are neurological, and include weakness, excessive sweating and salivation, headache, blurred vision, nausea, vomiting, stomach pain, tightness in the chest, muscular twitching, giddiness, slurred speech, confusion, and muscular incoordination (WHO/FAO, 1982; EXTOXNET, 1996). Death from bendiocarb poisoning can result from paralysis of the respiratory system, severe constriction of the lung openings, or stopped breathing (EXTOXNET, 1996). Little data exist on the human health effects of acute exposure to bendiocarb. In humans, the threshold for mild symptoms and blood cholinesterase inhibition is 0.15–0.20 mg a.i./kg for ingestion. No symptoms were reported following repeated hourly doses of 0.1 mg a.i./kg. Studies in human volunteers have shown that both the onset and recovery from cholinesterase inhibition are very rapid (WHO/FAO, 1982). Case reports of accidental bendiocarb exposures report typical symptoms with reversible cholinesterase inhibition. In one case, cholinesterase was inhibited by 63 percent, and the exposed person recovered in less than 3 hours without any medical treatment. Cholinesterase levels returned to normal within 24 hours. In another case, recovery from symptoms occurred within 2 hours after being decontaminated and treated with atropine, with complete recovery by the next day. Bendiocarb is also a mild irritant to the skin and eyes (EXTOXNET, 1996).

In animals, bendiocarb is acutely toxic via the oral, inhalation, and dermal routes (U.S. EPA, 1999b). The oral LD_{50} values of unformulated bendiocarb in various animal species include 34–156 mg/kg in rats, 35–40 mg/kg in rabbits, and 35 mg/kg in guinea pigs. The reported dermal LD_{50} value in rats is greater than 566 mg/kg (EXTOXNET, 1996; IPCS, 1986; WHO/FAO, 1982) and the reported 4-hour LC_{50} in rats is 0.55 mg/L (EXTOXNET, 1996). For formulated bendiocarb compounds, an LD_{50} of 143–179 mg/kg was reported in rats for an 80 percent a.i. water dispersible powder. A dermal LD_{50} of greater than 1,000 mg/kg was reported for an 80 percent a.i. liquid formulation (WHO/FAO, 1982).

As in humans, acute exposure to bendiocarb in animals causes symptoms typical of cholinesterase inhibition (U.S. EPA, 1999a, 1999b). No acute delayed neurotoxicity was observed in hens. Although bendiocarb causes slight eye irritation in animals, it is not considered a skin or eye irritant or a dermal sensitizer (U.S. EPA, 1999b).

Treatment

Exposure to bendiocarb may be determined through laboratory tests that determine cholinesterase levels in blood; however, the enzyme will only be inhibited for a few hours following exposure. Additionally, bendiocarb metabolites may be identified in urine (WHO/FAO, 1982). Bendiocarb poisoning should be treated in the same way as high-toxicity carbamate poisoning (PAN, 2005). First removing any contaminated clothing and wash affected areas with soap and water. If bendiocarb gets in the eyes, they should be rinsed immediately with isotonic saline or water. Oral exposure to bendiocarb should be treated by rapid gastric lavage with 5 percent sodium bicarbonate if the patient is not already vomiting. Medical attention should be sought. Adults showing signs of bendiocarb toxicity should be treated with 1–2 mg atropine sulfate given

intramuscularly or intravenously as needed. Oxygen may be necessary for unconscious patients or those in respiratory distress. Pralidoxime is not effective in treating bendiocarb poisoning (WHO/FAO, 1982).

Chronic Exposure

Noncancer Endpoints

The effects of chronic exposure to bendiocarb in humans have not been well described in the literature, although it is not expected to be toxic at the levels applied to control mosquitoes. When used as a residual mosquito insecticide, few adverse effects were reported by occupationally exposed workers. Those effects that were reported were transient and mild. Additionally, no effects were reported by residents of villages where it was applied (WHO/FAO, 1982).

Subchronic and chronic exposure studies in rats, mice, and dogs have shown that bendiocarb inhibits cholinesterase activity in whole blood, plasma, red blood cells, and the brain (U.S. EPA, 1999a, 1999b; WHO/FAO, 1982). No macroscopic pathology or histological evidence of dermal irritation or treatment-related mortality was observed in a 21-day dermal study in rats. Rats exposed to bendiocarb for 90 days via inhalation showed whole-blood cholinesterase inhibition (U.S. EPA, 1999b). Additionally, bendiocarb does not accumulate in mammalian tissue. There was no evidence of cumulative toxicity in rats or dogs fed bendiocarb for 90 days (WHO/FAO, 1982).

Bendiocarb is not expected to cause reproductive effects in humans. In rats, no effect on fertility and reproduction was seen in rats fed diets containing bendiocarb for three generations. However, very high doses were toxic to dams and pups, as indicated by decreased survival rate and decreased pup weight (EXTOXNET, 1996). No teratogenicity was seen in rats or rabbit fetuses or offspring following pre- and/or postnatal exposures to bendiocarb (U.S. EPA 1999a, 1999b; WHO/FAO, 1982). No evidence of mutagenicity was observed following *in vivo* or *in vitro* exposures to bendiocarb (U.S. EPA, 1999a, 1999b; EXTOXNET, 1996; WHO/FAO, 1982). No irreversible or delayed neurotoxicity has been reported in animals following long-term bendiocarb exposure (WHO/FAO, 1982).

Cancer Endpoints

EPA has classified bendiocarb as a Group E chemical, noncarcinogenic to humans (U.S. EPA, 1999b). The classification is based on the lack of increase in tumors in rat and mouse studies and is supported by the lack of mutagenicity in somatic cells (U.S. EPA, 1999b). No human data are available.

Toxicokinetics

Bendiocarb can be absorbed through oral, dermal, and inhalation pathways; dermal absorption is especially rapid and is the main route of absorption. Absorption from inhalation, except inhalation of airborne dusts or fine spray mists, is unlikely due to bendiocarb's low vapor pressure (EXTOXNET, 1996; WHO/FAO, 1982). Animal metabolism studies indicate that bendiocarb is rapidly absorbed following oral exposure (U.S. EPA, 1999b). Liver microsome enzymes readily conjugate and metabolize bendiocarb, and it is rapidly excreted. Because of its rapid metabolism and excretion, bendiocarb does not accumulate in mammalian tissues (WHO/FAO, 1982). The majority of an orally administered dose is eliminated in the urine (U.S. EPA, 1999b). In rats fed diets containing up to 10 mg/kg bendiocarb, 89 to 90 percent of the dose was excreted in the urine, 2 to 6 percent was excreted in the feces, and 2 to 6 percent was exhaled. A human subject orally exposed to bendiocarb exhibited a similar excretion pattern (EXTOXNET, 1996). Bendiocarb is excreted mainly as sulfate and beta-glucuronide conjugates of the phenol derivative (WHO/FAO, 1982).

Ecological Effects

Acute Exposure

When applied at the maximum registered application rate, bendiocarb poses acute risk to nontarget terrestrial organisms, such as mammals and birds (WHO/FAO, 1982; U.S. EPA, 1999a). Single broadcast applications on turf may result in high risk to birds, and multiple applications may result in repeated acute effects (U.S. EPA, 1999a). Oral LD_{50} values range from 3.1 mg a.i./kg body weight in mallard ducks to 137 mg a.i./ kg body weight in domestic hens (WHO/FAO, 1982; U.S. EPA, 1999a). However, bendiocarb does not affect avian reproductive parameters (WHO/FAO, 1982). Additionally, bendiocarb has been found to be highly toxic to bees (WHO/FAO, 1982; EXTOXNET, 1996; U.S. EPA, 1999a), with an oral LD_{50} of 0.0001 mg/bee (EXTOXNET, 1996). Additionally, bendiocarb severely affects earthworms under treated turf (EXTOXNET, 1996).

Bendiocarb poses acute risks to freshwater fish, and estuarine and marine animals (U.S. EPA, 1999a). It is moderately to highly toxic to fish, with LC_{50} values ranging from 0.7 to 1.76 mg a.i./L in various species (U.S. EPA, 1999a; WHO/FAO, 1982). The 96-hour LC_{50} for rainbow trout is 1.55 mg/L (EXTOXNET, 1996). When applied at the maximum registered rate, bendiocarb also poses acute risks to freshwater invertebrates (U.S. EPA, 1999a).

Chronic Exposure

Very little data exist for chronic exposure to bendiocarb in nonterrestrial target organisms. In birds, multiple applications of the maximum registered application rate to turf are expected to result in repeated acute effects. The reproductive effects of chronic exposures cannot be assessed due to limited data (U.S. EPA, 1999a).

Little data exist for chronic exposure to bendiocarb in marine or estuarine organisms. When applied at the maximum registered rate, bendiocarb poses chronic risks to freshwater invertebrates. However, it poses no chronic risk to freshwater fish (U.S. EPA, 1999a).

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Profile for Bifenthrin:

CAS Registry Number 82657-04-3

Summary of Insecticide

Chemical History

Bifenthrin is a pyrethroid insecticide and acaricide used in agricultural and human health applications (EXTOXNET, 1995; WHO/FAO, 1992). It is primarily available as a wettable powder or an emulsifiable concentrate (EXTOXNET, 1995). Bifenthrin is used to control pests on crops and indoor pests (ATSDR, 2003). For mosquito protection, it is used on bed nets and other materials that are dipped in bifenthrin to protect the user. Bifenthrin is a restricted use pesticide due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003; EXTOXNET, 1995).

As a synthetic pyrethroid, bifenthrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels of nerve cells (Choi and Soderlund, 2006; EXTOXNET, 1995). Symptoms of acute exposure may include skin and eye irritation, headache, dizziness, nausea, vomiting, diarrhea, excessive salivation, fatigue, irritability, abnormal sensations of the face and skin, and numbness (PAN, 2005). Inhalation of pyrethrins may cause a localized reaction of the upper and lower respiratory tracts (HSDB, 2005). In mammals, pyrethroids are generally of low toxicity due to their rapid biotransformation (HSDB, 2005). EPA has classified bifenthrin as a Class II chemical or moderately toxic. EPA has not classified synthetic pyrethroids, including bifenthrin, as endocrine disruptors. Bifenthrin is highly toxic to fish and other aquatic organisms (EXTOXNET, 1995).

Description of Data Quality and Quantity

Several comprehensive reviews on the toxicity of bifenthrin have been prepared or updated in recent years:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003)
- Pesticide Residues in Food—1992 Evaluation, Part II: Toxicology—Bifenthrin (WHO/FAO, 1992)
- IRIS summary review (U.S. EPA, 2006)
- Pesticide Information Profile for Bifenthrin (EXTOXNET, 1995).

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs, intermediate-term oral, and short-, intermediate-, and long-term dermal and inhalation benchmarks) for bifenthrin.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate	Inhalation	0.007	mg/kg/day	Oral NOAEL for neurological effects in dogs at 2.21 mg/kg/day with UF of 300 applied	U.S. EPA (2003)
Chronic	Inhalation	0.004	mg/kg/day	Oral NOAEL for neurological effects in dogs at 1.3 mg/kg/day with UF of 300 applied	U.S. EPA (2003)
Acute	Oral	0.033	mg/kg/day	Acute RfD based on neurotoxicity in rats	U.S. EPA (2003)
Intermediate	Oral	0.007	mg/kg/day	Oral NOAEL for neurological effects in dogs at 2.21 mg/kg/day with UF of 300 applied	U.S. EPA (2003)
Chronic	Oral	0.004	mg/kg/day	Chronic RfD based on neurological effects in dogs	U.S. EPA (2003)
Acute, Intermediate, Chronic	Dermal	0.2	mg/kg/day	Dermal NOAEL for neurological effects in rats at 47 mg/kg/day with UF of 300 applied	U.S. EPA (2003)

For oral exposure, an acute RfD of 0.033 mg/kg/day was derived based on a NOAEL of 32.8 mg/kg/day for neurological effects observed in rats exposed to bifenthrin (study citations not provided), with an uncertainty factor of 1,000 applied to account for the lack of a developmental neurotoxicity study and for interspecies and intrahuman variability (U.S. EPA, 2003). An intermediate NOAEL of 2.21 mg/kg/day was identified for tremors in dogs exposed for 90 days and an uncertainty factor of 300 was applied, resulting in a benchmark of 0.007 mg/kg/day (U.S. EPA, 2003). A chronic oral RfD of 0.004 mg/kg/day was derived based on a NOAEL of 1.3 mg/kg/day for tremors in dogs exposed for 1 year, with an uncertainty factor of 300 applied (U.S. EPA, 2003).

For inhalation exposure, an oral NOAEL of 2.21 mg/kg/day was identified for tremors in dogs exposed for 90 days and an uncertainty factor of 300 was applied (U.S. EPA, 2003). This value (0.007 mg/kg/day) is appropriate to use for short- and intermediate-term inhalation exposures. An oral NOAEL of 1.3 mg/kg/day was identified for tremors in dogs exposed for 1 year and an uncertainty factor of 300 was applied (U.S. EPA, 2003). This value (0.004 mg/kg/day) is appropriate to use for long-term inhalation exposures.

For dermal exposure, a NOAEL of 47 mg/kg/day for neurological effects (staggered gait and exaggerated hind limb flexion) was identified in rats dermally exposed to bifenthrin for 21 days. An uncertainty factor of 300 was applied, for a dermal benchmark value of 0.2 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 2003).

Insecticide Background

CASRN: 82657-04-3

Synonyms: (2-methyl[1,1'-biphenyl]-3-yl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate, [1alpha, 3alpha(z)]-(+ -)-3-(2-Chloro-3,3,3-trifluoro-1-propenyl)-2,2-

	dimethylcyclopropanecarboxylic acid (2-methyl[1,1'-biphenyl]-3-yl)methyl ester, 2-Methylbiphenyl-3-ylmethyl (z)-(1RS,3RS)-3-(2-chloro-3,3,3-trifluoroprop-1- enyl)-2,2-dimethylcyclopropanecarboxylate, [1 alpha, 3 alpha(z)]-(+ -)-(2-Methyl[1,1'-biphenyl]-3-yl)methyl 3-(2-chloro- 3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate (ATSDR, 2003; EXTOXNET, 1995; HSDB, 2005)
Chemical Group:	pyrethroid (PAN, 2005; EXTOXNET, 1995)
Registered Trade Names:	Talstar, Bifenthrine, Biphenate, Brigade, Bifentrina, Biflex, Capture, FMC 54800, FMC 54800 Technical, OMS3024, Torant (with Clofentezine), and Zipak (with Amitraz), Tarstar (HSDB, 2005; EXTOXNET, 1995; ATSDR, 2003; PAN, 2005)

Usage

Bifenthrin is used as a broad spectrum insecticide and acaricide to combat indoor pests and those on a variety of crops (EXTOXNET, 1995; ATSDR, 2003). It is used to control mosquitoes, beetles, weevils, houseflies, lice, bedbugs, aphids, moths, cockroaches, and locusts. Crops on which bifenthrin is used include alfalfa hay, beans, cantaloupes, cereals, corn, cotton, field and grass seed, hops, melons, oilseed rape, potatoes, peas, raspberries, watermelons, and squash. Bifenthrin belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies. For mosquito protection, it is used on bed nets and other materials that are dipped into the bifenthrin to protect the user. Bifenthrin for agricultural use is restricted by EPA due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003).

Formulations and Concentrations

Bifenthrin is available in technical grade, emulsifiable concentrate, suspension concentrate, wettable powder, ultra-low volume (ULV) liquid, and granules (HSDB, 2005; EXTOXNET, 1995; WHO, 2001). Technical grade bifenthrin may be mixed with carriers or solvents, resulting in the commercial formulations. The label of products containing bifenthrin must contain the word "warning" (EXTOXNET, 1995). Technical grade bifenthrin must have no less than 920 g/kg bifenthrin. The wettable powder should contain > 25–100 g/kg +/- 10% of the declared content, 100–250 g/kg +/- 6% of the declared content, or > 250–500 g/kg +/- 5% of the declared content (WHO, 2001). Bifenthrin that is used on bed nets for malaria control comes in a suspension concentrate dose of 25 mg a.i./m^2 (WHO, n.d.).

Shelf Life

Bifenthrin is photostable and stable to hydrolysis. It volatilizes minimally and is generally stable when stored (EXTOXNET, 1995). Bifenthrin is stable for 2 years at 25–50°C. It is most stable in acidic environments and at pHs from 5 to 9, it is stable for 21 days. Pyrethrins, in general, are stable for a long time in water-based aerosols (HSDB, 2005).

Degradation Products

Pyrethroid insecticides are often formulated with synergists that prevent the breakdown of enzymes and thus enhance the activity of the pyrethroid (ATSDR, 2003). The primary metabolic pathway for the breakdown of bifenthrin is ester hydrolysis (HSDB, 2005). The major degradate of bifenthrin metabolism in soil, biota, and water is 4'-hydroxy bifenthrin (Fecko, 1999).

Environmental Behavior

Fate and Transport in Terrestrial Systems

With Koc values ranging from 131,000 to 320,000, the mobility of bifenthrin in soil ranges from low to immobile (HSDB, 2005; EXTOXNET, 1995). Bifenthrin has a low mobility in soils with large amounts of clay, silt, organic matter and in sandy soils without much organic matter (EXTOXNET, 1995). In moist soils, volatilization is a major fate process, although this is lessened by absorption in the soil (HSDB, 2005). Depending on soil type and the amount of air in the soil, the half-life of bifenthrin ranges from 7 days to 8 months (EXTOXNET, 1995). Bifenthrin is expected to biodegrade readily based on its structure and the biodegradation rates of pyrethroids in general (HSDB, 2005). It is not absorbed by plants and dose not translocate in plants (EXTOXNET, 1995).

Fate and Transport in Aquatic Systems

Bifenthrin is fairly insoluble in water, so it is unlikely to leach to groundwater and cause significant contamination (EXTOXNET, 1995). Volatilization is a major fate process from surface water; however, because bifenthrin is expected to adsorb to suspended soils and sediments, volatilization is attenuated. Volatilization half-lives of 50 days for a model river and 555 days for a model lake have been reported, but if adsorption is considered, the volatilization half-life of a model pond is 3,100 years. Bifenthrin has a high potential to accumulate in aquatic organisms, with an estimated bioconcentration factor of 190. However, bioconcentration is likely to be lower due to the ability of aquatic organisms to readily metabolize bifenthrin (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of bifenthrin in humans. Bifenthrin is classified as having moderate acute toxicity in mammals (EXTOXNET, 1995; WHO/FAO, 1992; PAN, 2005). Incoordination, irritability to sound and touch, tremors, salivation, diarrhea, and vomiting have been caused by high doses. In humans, no skin inflammation or irritation has been observed; however, bifenthrin can cause a reversible tingling sensation (EXTOXNET, 1995).

In animals, the main signs of acute toxicity include clonic convulsions, tremors, and oral discharge (WHO/FAO, 1992). Reported LD_{50} values for bifenthrin include 54–56 mg/kg in female rats, 70 mg/kg in male rats (EXTOXNET, 1995; WHO/FAO, 1992; HSDB, 2005) and 43 mg/kg in mice (WHO/FAO, 1992). Bifenthrin is slightly toxic through dermal contact, with dermal LD_{50}s of over 2,000 mg/kg in rabbits (WHO/FAO, 1992; HSDB, 2005). Neurotoxicity is a key effect of pyrethroids and is caused by interfering with the sodium channels of nerve cells (ATSDR, 2003; Choi and Soderlund, 2006). In mammals, acute exposure to pyrethroids causes tremors, hyperexcitability, salivation, paralysis, and choreoathetosis. However, delayed neurotoxicity has not been observed (HSDB, 2005). Bifenthrin is not a dermal sensitizer in guinea pigs (EXTOXNET, 1995; HSDB, 2005; WHO/FAO, 1992) and did not irritate either abraded or non-abraded skin of rabbits (WHO/FAO, 1992). In rabbits, it is only slightly irritating to the eyes (EXTOXNET, 1995; WHO/FAO, 1992; HSDB, 2005). Bifenthrin is also a suspected endocrine disruptor (ATSDR, 2003; PAN, 2005).

Treatment

Bifenthrin and its metabolites can be detected in blood and urine during the first few days following exposure (but not later, because these compounds are rapidly broken down in the body) (ATSDR, 2003). Treatment

depends on the symptoms of the exposed person. Most casual exposures require only decontamination and supportive care (HSDB, 2005). If a person exhibits signs of typical pyrethroid toxicity following bifenthrin exposure, affected skin areas should be washed promptly with soap and warm water. Medical attention should be sought if irritation or paresthesia occurs. Paresthesia may be prevented or stopped with Vitamin E oil preparations. Corn oil and Vaseline® are less effective and less suitable, and zinc oxide should be avoided (PAN, 2005; HSDB, 2005).

Eye exposures should be treated by rinsing with copious amounts of water or saline. Contact lenses should be removed. Medical attention should be sought if irritation persists (PAN, 2005; HSDB, 2005). Following oral exposures, the person should be kept calm and medical attention should be sought as quickly as possible. Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts of bifenthrin should be treated with gastric lavage, and small ingestions should be treated with activated charcoal and cathartic (PAN, 2005). For sublethal exposures, vomiting may be induced by ipecac and followed by saline cathartic and an activated charcoal slurry, as long as the person is alert and has a gag reflex (HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

No data are available for humans following chronic exposures to bifenthrin (EXTOXNET, 1995). Dietary studies in dogs, rats, and mice indicate that oral exposure to bifenthrin causes neurological effects such as tremors (U.S. EPA, 2006; WHO/FAO, 1992) but not cholinesterase inhibition (PAN, 2005). In a 1-year feeding study in dogs and a lifetime feeding study in mice, intermittent tremors were observed (U.S. EPA, 2006; WHO/FAO, 1992). In subchronic duration exposure studies in dogs and rats, tremors were also seen at higher exposure levels (U.S. EPA, 2006; WHO/FAO, 1992).

Bifenthrin has the potential to be reproductive toxin (PAN, 2005). Reproductive toxicity has been observed in rats and rabbits at doses lower than those that cause tremors (EXTOXNET, 1995). Teratogenicity was not observed in a 2-generation rat study (EXTOXNET, 1995) or a rabbit teratogenicity study (WHO/FAO, 1992; HSDB, 2005).

Additional effects observed in chronic exposure animal studies include increased body weight and organ-to-body ratios (U.S. EPA, 2006). The mutagenicity data are inconclusive for bifenthrin (EXTOXNET, 1995), but it is unlikely to pose a genetic hazard (WHO/FAO, 1992).

Cancer Endpoints

EPA has classified bifenthrin as Class C, possible human carcinogen (EXTOXNET, 1995; PAN 2005). A 2-year, high dose dietary exposure study in rats reported no evidence of cancer. In mice, however, a significant dose-related increase in urinary bladder tumors was observed in male mice. An increased incidence of lung tumors was observed in female mice (U.S. EPA, 2003; EXTOXNET, 1995).

Toxicokinetics

Bifenthrin is readily absorbed through intact skin (EXTOXNET, 1995; HSDB, 2005) and the gastrointestinal tract (WHO/FAO, 1992). It breaks down in the same way as other pyrethroids (EXTOXNET, 1995). Hydrolysis and hydroxylation are the primary steps in the transformation of bifenthrin. In poultry, bifenthrin metabolism begins with hydroxylation of the 2-methyl carbon of the cyclopropane ring, followed by fatty acid conjugation (WHO/FAO, 1992). Oral administration of radioactive pyrethroids have been shown to distribute to every tissue examined (HSDB, 2005). Bifenthrin can accumulate in fatty tissues such as skin and ovaries (EXTOXNET, 1995). Bifenthrin metabolism and excretion are rapid. In rats given 4–5 mg/kg

bifenthrin, 70 percent of the dose was excreted in urine within 7 days, and 20 percent was excreted in feces (EXTOXNET, 1995). However, another study in rats showed that following oral administration of bifenthrin, 70 to 80 percent was eliminated in the feces within 48 hours while only 5 to 10 percent was eliminated in the urine. Biliary excretion raged from 20 to 30 percent (WHO/FAO, 1992).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Bifenthrin, like other pyrethroids, is unlikely to harm terrestrial organisms other than its targets, such as mosquitoes and other pests, due to its low persistence in the environment (HSDB, 2005). Bifenthrin has a moderate toxicity in birds (EXTOXNET, 1995). The 8-day dietary LC_{50} values range from 1,280 ppm in mallard ducks to 4,450 ppm in bobwhite quail. Oral LD_{50} values range from 1,800 mg/kg in bobwhite quail to 2,150 mg/kg in mallard ducks. Additionally, concerns about bioaccumulation in birds have been reported. As with other pyrethroid insecticides, bifenthrin is extremely toxic to honey bees (EXTOXNET, 1995; HSDB, 2005).

Toxicity in Non-Targeted Aquatic Systems

Bifenthrin is also known to be toxic to a wide variety of aquatic organisms, including fish, crustaceans, aquatic insects, mollusks, nematodes, flatworms, phytoplankton, and zooplankton (PAN, 2005). Bifenthrin is very toxic to fish (EXTOXNET, 1995); however, because it is not very water soluble and has a high affinity for soil, the risk to aquatic systems is not expected to be high (EXTOXNET, 1995). The high toxicity in fish is illustrated by the low exposures that cause lethality. The reported 96-hour LC_{50} is 0.00015 mg/L in rainbow trout and 0.00035 mg/L in bluegill sunfish (EXTOXNET, 1995; HSDB, 2005). Average LC_{50} values are 17.5 µg/L in sheepshead minnow and 0.36 µg/L in gizzard shad (PAN, 2005). In Daphnia, the reported 48-hour LC_{50} is 0.0016 mg/L (HSDB, 2005). The risk of bioaccumulation of the bifenthrin formulation Talstar®100EC in aquatic organisms is reported to be very high (ASTRACHEM, n.d.). The whole-body bioconcentration factor values for fathead minnow in water T a concentration of 0.0037 µg/L were 21,000 (over 127 days) and 28,000 (over 254 days) (CalDFG, 2000).

Chronic Exposure

Toxicity in Non-Targeted Terrestrial Organisms

No data were located on the chronic toxicity to nontarget terrestrial organisms.

Toxicity in Non-Targeted Aquatic Systems

Chronic exposure of fathead minnow to a 95.7 percent bifenthrin formulation for 246 days resulted in a reported LOEC of 0.41 µg/L, NOEC of 0.30 µg/L, and MATC of 0.351 µg/L. Chronic exposure of fathead minnow to a 96.2 percent bifenthrin formulation for 346 days resulted in a reported LOEC of 0.090 µg/L, NOEC of 0.050 µg/L, and MATC of 0.067 µg/L (CalDFG, 2000).

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Profile for Chlorfenapyr:

CAS Registry Number 122453-73-0

Summary of Insecticide

Chemical History

Derived from a natural product, chlorfenpyr was discovered in 1985 following the isolation of a toxin from the *Streptomyces fumanus* an actinomycete bacterium. chlorfenpyr rate of intoxication is species-specific with a range that covers minutes to days depending on formulation, duration of exposure and target pest. Against carmine spider mite, it has efficacy for over 30 days. Chlorfenapyr is a pro-insecticide (meaning it is metabolized into an active insecticide after entering the host). (Raghavendra et al. 2010)

The United States Environmental Protection Agency (USEPA) initially denied registration in 2000 for use on cotton primarily because of concerns that the insecticide was toxic to birds and because effective alternatives were available. It was registered by EPA in 2001 for use on non-food crops in greenhouses, landscaping nurseries, as well as in structures such as warehouses. It is effective against cockroaches and termites. In 2005, EPA established a tolerance for residues of chlorfenapyr in or on all food commodities. Chlorfenapyr has a unique mode of action. It is a pro-insecticide that is converted (or metabolized) to the active form by mixed function oxidases (MFOs) in the target pest. The active form acts on the mitochondria and uncouples oxidative phosphorylation which stops the production of ATP, the primary source of cellular energy. This action causes cell death, paralysis, and ultimately organism mortality. (USEPA 2001)

Due to its unique mode of action, it is very effective against insects and mites that are resistant to organophosphates, carbamates, pyrethroids, and chitin-synthesis inhibitors. No instances of target site cross-resistance have been observed anywhere in the world. It was found to be effective against mosquitoes and is a candidate for IRS programs. Chlorfenapyr has a long residual life after applied on all internal surfaces. One of the reasons for this is the fact that it has very low water solubility which means it will not be easily wiped or washed off surfaces. (Oliver et al. 2010) Chlorfenapyr is a slow action non-repellant insecticide.

Ths molecule has low mammalian toxicity and is classified as only slightly hazardous. Efficacy of chlorfenapyr on different substrates spread at 12.5 to 200 mg/m^2 has shown a drastic reduction in efficacy against mosquitoes within two weeks after spraying. Residual activity of chlorfenapyr a.i. of 400 mg/m^2 on five fabricated substrates, namely wood, mud, mud+lime, cement and cement +distemper was found to be effective up to 24 weeks against *An. culicifacies* against *An. culicifacies* and up to 34 weeks against An. stephensi. (Raghavendra et al.2011, Oxborough et al. 2010). Chlorfenapyr belongs to a new group of insecticides, thus would fit well in an insecticide resistance program (Oliver et al. 2010).

Insecticide Background

Chemical name and class

Chemical name for chlorfenapyr is 4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5 (trifluoromethyl)-1H-pyrrole-3-carbonitrile.

Chlorfenapyr is derived from a class of microbial compounds known as halogenated pyrroles.

Synonyms, trade names, and formulations

Synonyms are Pirate; Alert; CL303,630; AC303,630.

Chlorfenapyr is now made by BASF who bought the rights from the original manufacturer, American Cyanamid.

Two products were registered in the USEPA since 2001 by BASF and both are emulsifiable concentrates. Pylon is at 21.4% and is an insecticide, miticide, and nematicide for use in greenhouses and nurseries against pests of vegetables, fruits, and ornamentals. Phantom 21.5% SC is an insecticide, miticide against household pests for use in domestic and commercial buildings. There are five products registered with EPA within the trade names Phantom and Pylon with BASF (www.pesticideinfo.org).

Usage

Chlorfenapyr can kill wide range of harmful insects and mites, has good effect to prevent and control 70 kinds of harmful insects belonging to Lepidoptera, Coleoptera, and Homoptera as well as spider mites in cotton, vegetable, oranges and tangerines. It is also useful as a protective barrier between soil and structures to control household insects via premises protection on floors, walls and has effectiveness against termites, ants, cockroaches, bedbugs etc. It is labeled for use on landscaping and outdoor nurseries against pests of ornamental crops in commercial greenhouses such as mites, caterpillars, and fungus gnats. (www.pesticideinfo.org)

Shelf Life

Chlorfenapyr is a stable insecticide and if stored sealed tightly and away from light in a cool and dry place it should last three years.(BASF MSDS for chlorfenapyr)

Degradation Products

The acute toxicity of four metabolites to rats was determined. Of those tested only AC 303,268 resulted in higher toxicity than the parent compound (e.g., combined sex LD_{50}s of 28.7 and 626 mg/kg for metabolite and parent, respectively). Of the 40 rats exposed to AC 303,268 at concentrations higher than 31.25 mg/kg, 39 died within 8 hours of dosing. Mortality occurred at a slower rate in tests with the other 3 metabolites but still most was observed within 3 days. Survivors of exposure to the metabolites exhibited no lasting clinical effects or notable findings during gross necropsy. No weight changes were reported for survivors. Clinical signs reported for exposure to the metabolites included decreased activity, prostration, ptosis, increased salivation and diuresis. Abnormalities found at necropsy included discolored livers and spleens, discolored and distended stomachs, and gas filled GI tracts. Striated muscle tissue was reported in animals killed by AC 303,268. (HSDB)

In the environment chlorfenapyr breaks down into three metabolites in the soil:

- 2-Pyrroline-3-carbonitrile, 2-(p-chlorophenyl)-5-hydroxy-4-oxo-5-
- Pyrrole-2-carboxylic acid, 3-bromo-5-(p-chlorophenyl)-4-cyano-
- Pyrrole-2-carboxylic acid, 5-(p-chlorophenyl)-4-cyano-

One degradate was found, CL357806, ranging from 55% to 73% of applied based on pH. (HSDB)

Environmental Behavior

Fate and Transport in Terrestrial Systems

Technical chlorfenapyr has a low vapor pressure, 1.0×10^{-7} mm Hg, volatilization will not contribute significantly to dissipation. Chlorfenapyr strongly bonds to soil and thus would not be expected to be mobile. The Kocs for the parent are 13214 in loamy sand, 14117 in sandy loam, 12321 in loam and 18095 in silt loam. Consequentially chlorfenapyr degrades slowly by both biotic and abiotic pathways, and is likely to remain in the soil as the parent compound for extended periods. Minimum field dissipation half-lives were stated to be

0.4 -0.6 years in loamy sand, 0.4-0.8 years in sandy loam, 0.6-0.9 years in silt loam, 0.6-1.4 years in clay loam, and 0.8-2.1 years in sand. Chlorfenapyr has a half-life of 0.8 years in the aqueous portion and 1.1 years in the soil portion. (HED)

Using a half-life of 1.4 years, and assuming repeated annual applications, chlorfenapyr is expected to build up to a level in the environment of 2.5 times the annual application rate (converted to ppm). Note that this assumes that 100% of the amount applied ultimately reaches the soil.

Fate and Transport in Aquatic Systems

Chorfenapyr is stable over a range of pH from 5-9 and has a water solubility of 0.14 mg/L at pH 7. Thus chlorfenapyr half-lives vary from 5.1 to 5.4, 6.9 to 8.1 and 4.8 to 4.9 days in sterile aqueous solutions of pH 5, 7 and 9, respectively. However, aqueous photolysis is not a major degradation route.

Human Health Effects

Acute Exposure

Clinical Symptoms

As chlorfenapyr is a rather new product there are not many cases of poisonings where the symptoms were described. One patient first exhibited general fatigue, hyperperspiration, nausea and vomiting. He was initially diagnosed as being dehydrated. (Hoshiko et al. 2007). Another patient entered the hospital due to exogenous intoxication with chlorphenapyr with suicidal purposes, initially presenting diaphoresis, headache and cough. Symptomatic management is initiated, but after seven days she presents neurological and respiratory deterioration, causing her death. (Suárez and Duque 2008)

Acute toxicity

Chlorfenapyr is moderate to highly toxic depending on the test. The acute oral $LD_{50}$for the technical or pure formulation for male rats 441mg/kg body weight which is toxicity level II. Female rats however are rated at toxicity level III at 1152 mg/kg, while the mouse is most toxic at 55 mg/kg at level I. With the formulated product however the toxicity rating is II using female rats at 563 mg/kg (www.pesticideinfo.org, USEPA 2001, HSDB)

Chlorfenapyr is a moderate but reversible eye irritant. Studies with rabbits found that corneal opacity, iritis, and conjunctivitis were present at 48 hours after the exposure. At 72 hours, iritis was resolved. By day 6 all rabbits were normal by Day-7. Eye exposure is rated as moderately toxic (III). Chlorfenapyr is not a skin irritant. Slight erythema was observed at 1 hour and persisted in a rabbit at 24 hours. All signs of irritation had resolved by 48 hours and thus chlorfenapyr is rated at level IV). Dermal toxicity was measured on rabbits and the LD_{50} was >2000 mg/kg which is rated at toxicity level III. Inhalation toxicity is rated at level II with an LC_{50} for rats at 1.9 mg tech. /l air. Therefore, risk via the inhalation route is not a concern at this time and no endpoint of concern was identified (HSDB).

Medical treatment for acute poisoning

Patients' symptoms following exposure to chlorfenapyr should be observed in a controlled setting until all signs and symptoms have fully resolved. If ingested, control any seizures first. Chlorfenapyr can produce abnormalities of the hematopoietic system, liver, and kidneys. Do not use emetics. Monitoring complete blood count, urinalysis, and liver and kidney function tests is suggested for patients with significant exposure. If respiratory tract irritation or respiratory depression is evident from inhalation, monitor arterial blood gases, chest x-ray, and pulmonary function tests. Significant esophageal or gastro-intestinal tract irritation or burns

may occur following ingestion. Consider gastric lavage after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Activated charcoal binds most toxic agents and can decrease their systemic absorption if administered soon after ingestion. Immediate dilution with milk or water may be of benefit in caustic or irritant chemical ingestions. Rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool (HSDB).

Observe patients with ingestion carefully for the possible development of esophageal or gastrointestinal tract irritation or burns. If signs or symptoms of esophageal irritation or burns are present, consider endoscopy to determine the extent of injury. Carefully observe patients with inhalation exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary. If exposure is to the eyes, immediately irrigate exposed eyes with copious amounts of room temperature water (better with 0.9% saline) for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.For dermal exposure remove contaminated clothing and wash exposed area thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists (HSDB).

Chronic Exposure

The EPA evaluated the risk to humans from chlofenapyr exposures from eating treated crops, drinking contaminated water, and from product mixing and spraying. Due to the types of products that are available, the EPA concluded that drinking water exposures would be negligible. The worst-case exposure to adults mixing and spraying chlorfenapyr insecticide is from the use of a pressurized hand-wand sprayer. The hazard from this type of exposure, from both inhalation and skin exposures, is rated as low. The post-application exposures to greenhouse worker would be after an indoor foliar application of chlorfenapyr for insect control, and is rated as high in hazard. (USEPA HED 1998)

Non-Cancer Endpoints

Occupational exposure to chlorfenapyr may occur through dermal contact with this compound at workplaces where chlorfenapyr is produced or used. The general population may be exposed to chlorfenapyr via ingestion of food and dermal contact with this compound near fields where chlorfenapyr is applied. The low toxicity from acute inhalation did not require the manufacturer to report the 28-day inhalation toxicity test. Exposure for 90 days at sub-chronic oral toxicity in the rat gave a The NOAEL endpoint of 24.1 mg/kg body weight/day with a range of exposure rates from 0-98 90 mg/kg/day. The endpoints for mice averaged 7.1 mg/kg/day (range of exposures from 0-63 mg/kg/day) and dog 4.2 mg/kg/day (range of exposures 0-6.1 mg/kg/day). The LOAEL endpoints for the same test averaged 48.4 mg/kg/day for the rat, 14.8 (range 0-63 mg/kg/day) for the mouse, and 6.1 mg/kg/day (range 0-6.1 mg/kg/day) for the dog. When exposed for 28 days at chronic oral toxicity for rabbits the NOAEL endpoint was 100 mg/kg/day and the LOAEL was 400 (with a range of exposures from 0-1000 mg/day). Exposure for 1 year produced a NOAEL of 4.0 mg/kg/day and a LOAEL 8.7 over a range of exposures from 0-9.4 mg/kg/day. Longer exposures of 80 weeks to 2 years produced a Rat: NOAEL 3.3 mg/kg/day and LOAEL 16.8 mg/kg/day (2 years) (range 0-33.9 mg/kg/day). Mice were exposed daily over 80 weeks giving a NOAEL of 3.3 mg/kg/day and LOAEL of 19.3 mg/kg/day over a range from 0-39.5 mg/kg/day. (HSDB, USEPA HED 1998)

In the rat chronic toxicity study there were increased trends in the incidence of hepatocellular adenomas, hepatocellular adenomas and/or carcinomas combined, malignant histiocytic sarcomas and testicular interstitial cell tumors in males rats. In female rats there were significant increasing trends in endometrial stromal polyps. Significant difference is pair-wise comparison of fibroadenomas at low dose and carcinomas

at the mid-dose existed for female rats. Chronic maternal systemic toxicity (administered throughout gestation) for the rat produced a NOAEL of 25 mg/kg/day and a LOAEL of 75 mg/kg/day over a range of exposures from 0-225 mg/kg/day). When rabbits were similarly tested the NOAEL was 5 mg/kg/day and LOAEL 15 mg/kg/day over a range 0-30 mg/kg/day. Reproductive toxicity measured over 2 generations in the rate produced a NOAEL endpoint of 5 mg/kg body weight (bodyweight bw)/day and a LOAEL endpoint of 22 mg/kg bw/day over a range of exposures from 0-44 mg/kg bw/day. Acute neurotoxicity was measured over 14 days observation in rats producing a NOAEL of 45 mg/kg bw/day LOAEL 90 mg/kg bw/day (range 0-180 mg/kg bw/day). Chronic neurotoxicity was 1 year in the rat and produced a NOAEL of 2.6 mg/kg bw/day and a LOAEL of 13.6 mg/kg bw/day over a range 0-32.8 mg/kg bw/day. (HSDB, USEPA 2001)

In summary reproductive toxicity was observed (decreased weight gains in offspring) at the same dose as maternal toxicity (decreased weight gains in mothers) was seen. Developmental toxicity was not observed at any dose level but neurotoxicity in the form of myelinopathic alterations (nerve disorder) was observed at the same dose as brain lesions and other adverse effects were observed. Results of experiments with laboratory mice and rats revealed a number of histological abnormalities, including vacuolation of brain, spinal cord, and optic nerve tissue in mice and vacuolation of spinal nerves and myelin sheath swelling in rats. (USEPA 1998)

The available mutagenicity studies clearly indicate that chlorfenapyr is neither mutagenic in bacterial or mammalian cells nor clastogenic in cultured mammalian cells in vitro or in male and female mice in vivo. There was also no evidence of genotoxicity in primary rat hepatocytes. There was also no evidence of tumorigenic potential in mice. Chlorfenapyr is a suspected endocrine disruptor (www.pesticideinfo.org)

Cancer Endpoints

Chlorfenapyr has not been found to be carcinogenic. In the carcinogenicity study using rats there were increased trends in the incidence of hepatocellular adenomas, hepatocellular adenomas and/or carcinomas combined, malignant histiocytic sarcomas and testicular interstitial cell tumors in male rats. In female rats there were significant increasing trends in endometrial stromal polyps. Significant difference is pair-wise comparison of fibroadenomas at low dose and carcinomas at the mid-dose existed for female rats. In accordance with the EPA proposed Guidelines for Carcinogenic Risk Assessment, chlorfenapyr was characterized as "cannot be determined, suggestive". The consensus of the CPRC to characterize the weight of evidence for chlorfenapyr as "cannot be determined, suggestive" was based on the absence of persuasive evidence; increases in tumors occurred with significant positive trends only, mainly at the highest dose and only in rats. Chlorfenapyr was not associated with increases in tumors in mice and, there was no apparent concern for mutagenic activity and an absence of structure-activity data. There is no human data for chlorfenapyr.(HSDB, USEPA 2001)

Toxicokinetics and Metabolism

In a metabolism study chlorfenapyr was administered to rats by oral gavage at dose levels of 20 mg/kg/day as a single dose or following a 14-day pre-treatment with non-radioactive chlorfenapyr, or at 200 mg/kg as a single dose. Low recoveries of the radioactive dose in urine and tissues indicate limited absorption of chlorfenapyr by rats. The radioactivity in urine from the high dosed rats was about half that from the single and multiple-low dosed rats. More than 80% of the doses were eliminated in the feces. Most of the radioactivity was eliminated in the feces and urine within 48 hours of dosing. After 7 days, 89-121% of the dosed radioactivity was recovered. At sacrifice, female rats had greater (about twice) recovery of radioactivity in the carcass, blood, and fat at all doses than did males. The highest recovery of radioactivity from a single organ was from the liver (0.15-0.48% of dose). Metabolite extraction and identification accounted for 72-91% of the radioactive doses. The parent was the major radioactive compound found in excreta, accounting for

approximately 40-70% of the administered doses. Minor amounts of eight primary and conjugated metabolites and four unidentified isolated components were detected, each at less than 10% of the dosed radioactivity. Liver and kidney contained several primary and conjugated metabolites and only minor levels of the parent compound (8.3% of the radioactivity in the sample). Based on the metabolites identified, the major deposition route of orally administered chlorfenapyr is fecal excretion of unaltered parent compound. Other pathways include cleavage of the ethoxymethyl sidechain, followed by de-alkylation and ring hydroxylation, and some degree of conjugation of the dealkylated, ring-hydroxylated metabolite. The two rings of the molecule are not cleaved. Metabolites are excreted primarily in urine; accumulation in tissues is minimal. (HSDB)

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Chlorfenapyr is highly to very highly toxic to birds. The acute oral LD_{50} for mallard ducks 10.3 mg/kg, bobwhite quail 34 mg/kg. The LC_{50} (8 d) for mallard ducks is 9.4 and for the bobwhite quail it was 132 ppm. Chlorfenapyr has high acute, sub-acute, and chronic (reproductive) toxicity in birds; and poses an acute poisoning hazard to aquatic organisms (definitive data are lacking for chronic effects). However, the process interrupted is a process common to all living organisms, and so is of concern for non-target organisms. The LD_{50} for bees is very highly toxic at 0.12 ug/bee and that for earthworms is 8.5 mg/kg (moderately toxic). (HSDB, BASF MSDS, USEPA HED 1998)

It appears that various wild species metabolize chlorfenapyr differently. For example, insects are more efficient in converting chlorfenapyr to its active form (and thus are more susceptible) than are vertebrate species. However, there are differences in sensitivity to chlorfenapyr between mammals and birds. One possible explanation for this difference comes from metabolism data that show the active form is metabolized in mammals to compounds which are more water soluble (or excretable in urine), but in birds less of these soluble metabolites of the active form are found. (USEPA 2001)

The following evidence was used to reject registration for use on cotton. Because of the persistence of chlorfenapyr, repeat applications, and evidence that it can be found in avian food items, the Agency required chronic toxicity studies for this compound. In a chronic toxicity study for birds, over a period of 22 weeks, the test species is subjected to continuous exposure to a pesticide at predetermined test levels, before and during its breeding season. The researchers found that chlorfenapyr is a persistent compound. If applied to the same fields for many consecutive years, EPA expects it will build up to levels that likely will present reproductive risks to birds. Since it will be applied as a foliar spray, the area containing residues will, in time, extend beyond the boundaries of the treated field. Further, even if use were discontinued after a number of years of application, it is expected that a significant amount of time will pass before residue levels drop to levels that are below levels of concern. (USEPA 2001)

Toxicity in Non-Targeted Aquatic Systems

Chlorfenapyr poses an acute poisoning hazard to aquatic organisms. Chlorfenapyr is very highly toxic or highly toxic to fish. The LC_{50} (96 h) value for rainbow trout was 7.44 ppb, bluegill sunfish 11.6 ppb, 12.3 ppb for catfish, and 60.2 ppb for sheepshead minnow, and 500 ppb for carp. The Daphnia LC_{50} (96 h) was 6.11 mg/l also very highly toxic. The LC_{50} for mysid shrimp was 2.0 ppb, 19.6 ppb for two amphipods Hyallela and 0.2 ppb for for Leptocheirus, all VHT. For a green alga Selenastrum capricornuntum the EC_{50} was 132 ppb, very highly toxic. (HSDB, BASF MSDS, USEPA HED 1998)

In studies, chlorfenapyr did not concentrate in fish tissue but it did metabolize to AC312,094 which concentrated up to 2,300 times. The metabolite is 97% eliminated, through depuration, from the fish 21 days after being moved to clean water. Since chlorfenapyr is very persistent in aquatic environments, organism may not be able to get to "clean" water or sediment, therefore the bioaccumulation hazard is rated as high. (Thurston County Health Department 2009)

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Profile for Cyfluthrin:

CAS Registry Number 68359-37-5

Summary

Chemical History

Cyfluthrin is a synthetic pyrethroid insecticide first registered by EPA in 1987. It is used in agricultural and human health applications against a wide variety of pests. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (ATSDR, 2003). Cyfluthrin has both contact and stomach poison action (EXTOXNET, 1998) and it interferes with nervous system transmissions through inhibition of the sodium channel system (Choi and Soderlund, 2006; WHO, 2004). It is available as the technical product, emulsifiable concentrate, wettable powder, aerosol, granule, liquid, oil-in-water emulsion, dust, concentrate, and ultra-light-volume oil spray (EXTOXNET, 1998; IPCS, 1997). For mosquito control, it is used in bed nets and other materials that are treated with cyfluthrin to protect the user (WHO, 1998). Cyfluthrin can be found in both restricted use pesticides and general use pesticides (EXTOXNET, 1998). When used, it is applied by spraying, dusting, fogging, or impregnation (WHO, 2004; IPCS, 1997). It is considered moderately toxic to mammals (EXTOXNET, 1998). EPA has not classified synthetic pyrethroids, including cyfluthrin, as endocrine disruptors. Typical symptoms of acute human exposure are skin and eye irritation. Dermal irritation may include itching, burning, or stinging, which may lead to a numbness that lasts up to 24 hours. Skin irritation may occur immediately following exposure or be delayed for 1 to 2 hours (EXTOXNET, 1998). In animals, very high doses have been shown to cause nervous system effects, including irritability, excessive salivation, uncoordinated gait, tremors, convulsions, and death (EXTOXNET, 1998; ATSDR, 2003).

Description of Data Quality and Quantity

EPA has developed a quantitative human health benchmark for cyfluthrin (EPA's chronic oral RfD). Several reviews on the toxicity of cyfluthrin have been prepared or updated in recent years and recommended resources include the following:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003)
- IRIS summary review (U.S. EPA, 2005b)
- Pesticide Information Profiles: Cyfluthrin (EXTOXNET, 1998)
- Toxicological Evaluation of Certain Veterinary Drug Residues in Food. WHO Food Additives Series 39: Cyfluthrin (IPCS, 1997)
- Specifications and Evaluations for Public Health Pesticides: Cyfluthrin (WHO, 2004).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute	Inhalation	0.0007	mg/kg/day	Inhalation NOAEL in rats with UF of 100 applied	U.S. EPA (2005a)
Intermediate, Chronic	Inhalation	0.0002	mg/kg/day	Inhalation NOAEL in rats with UF of 100 applied	U.S. EPA (2005a)
Acute	Oral	0.02	mg/kg/day	Acute RfD based on mammalian neurotoxicity	U.S. EPA (2005a)
Intermediate	Oral	0.024	mg/kg/day	Adopt chronic RfD for intermediate duration	
Chronic	Oral	0.024	mg/kg/day	Chronic RfD based on neurological effects in dogs	U.S. EPA (2005a)
Acute, Intermediate, Chronic	Dermal	3	mg/kg/day	Dermal NOAEL in rabbits with UF of 100 applied	

For inhalation exposure, a NOAEL of 0.00026 mg/L (0.07 mg/kg/day) was identified for body weight effects in rats exposed to beta-cyfluthrin via inhalation for 28 days. A NOAEL of 0.00009 mg/L (0.02 mg/kg/day) was identified for neurological and body weight effects in rats exposed to cyfluthrin via inhalation for 13 weeks. An uncertainty factor of 100 to account for inter- and intraspecies variation was applied, for a short-term inhalation benchmark of 0.0007 mg/kg/day and an intermediate- and long-term inhalation benchmark of 0.0002 mg/kg/day.

For oral exposure, an acute oral RfD of 0.02 mg/kg/day was derived based on a NOAEL of 2 mg/kg/day for acute mammalian neurotoxicity following exposure to beta-cyfluthrin. An uncertainty factor of 100 was applied for inter- and intraspecies variability (U.S. EPA, 2005a). A chronic oral RfD of 0.024 mg/kg/day was derived based on a NOAEL of 2.4 mg/kg/day for neurological effects in dogs exposed to cyfluthrin for 53 weeks. An uncertainty factor of 100 was applied for inter- and intraspecies variability (U.S. EPA, 2005a). An intermediate oral RfD of 0.024 mg/kg/day was derived based on a NOAEL of 2.4 mg/kg/day for neurological effects in dogs exposed to beta-cyfluthrin for 90 days. An uncertainty factor of 100 was applied for inter- and intraspecies variability (U.S. EPA, 2005a).

For dermal exposure, a NOAEL of 250 mg/kg/day (85 percent purity) was identified in rabbits dermally exposed to cyfluthrin 5 times a week for 6 hr/day for 3 weeks (IPCS, 1997). An uncertainty factor of 100 to account for inter- and intraspecies variation was applied, for a dermal benchmark value of 3 mg/kg/day. This value is appropriate for all exposure durations.

Insecticide Background

CASRN: 68359-37-5

Synonyms: Cyano(4-fluoro-3-phenoxyphenyl) methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate; BAY-FCR 1272; (R,S)-alpha-Cyano-4-fluoro-3-phenoxybenzyl-(1R,S)-cis,trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate; 3-(2,2-Dichloroethenyl)-2,2-diethylcyclopropanecarboxylic acid cyano(4-fluoro- 3-phenoxyphenyl)methyl ester; Cyfluthrine; FCR 1272;

	(RS)-alpha-Cyano-4-fluoro-3-phenoxybenzyl (1RS, 3RS: 1RS, 3SR)-3-(2,2- dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (ATSDR, 2003; HSDB 2005)
Chemical Group:	pyrethroid (ATSDR, 2003)
Registered Trade Names:	Attotox, Baythroid, Baygon aerosol, Baythroid H, Cyfoxlate, Contur, Laser, Responsar, Solfac, Tempo, Tempo H (ATSDR, 2003; EXTOXNET, 1998)

Usage

Cyfluthrin is effective in combating a broad spectrum of insect pests in agricultural, public health, and structural applications (WHO, 2004; EXTOXNET, 1998). The main agricultural use of cyfluthrin is against chewing and sucking insects on crops (EXTOXNET, 1998; HSDB, 2005; ATSDR 2003). In public health applications, it is used to control mosquitoes, houseflies, and cockroaches (HSDB, 2005). It is primarily a contact insecticide and is applied by residual spraying, fogging, or impregnation (WHO, 2004).

Formulations and Concentrations

Cyfluthrin is available in technical grade, emulsifiable concentrate, wettable powder, aerosol, granules, liquid, oil-in-water emulsion, and ultra-light-volume oil sprays (EXTOXNET, 1998; HSDB 2005). Technical grade cyfluthrin may be mixed with carriers or solvents resulting in the commercial formulations. These commercial formulations may also include ingredients that may potentiate the toxicity compared to technical grade cyfluthrin (EXTOXNET, 2005). WHO indicates that the content of cypermethrin in the formulated products must be declared and shall not exceed the listed standards. Technical grade cyfluthrin must have no less than 920 g/kg cyfluthrin and should contain the four diastereoisomers as follows:

- Diastereoisomer I, (R)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)-cis -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate + (S)-alpha, (1S)-cis: 23–27 percent
- Diastereoisomer II, (S)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)-cis -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate + (R)-alpha, (1S)-cis: 17–21 percent
- Diastereoisomer III, (R)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)-trans -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate + (S)-alpha, (1S)-trans: 32–36 percent
- Diastereoisomer IV, (S)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)- trans -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate + (R)-alpha, (1S)-trans: 21–25 percent.

The wettable powder should contain 100 g/kg cyfluthrin +/- 10 percent of the declared content. The oil-in-water emulsion shall contain 50 g/kg or g/L cyfluthrin +/- 10 percent of the declared content at 20 +/- 2 ^{o}C (WHO, 2004, ATSDR, 2003). For malaria control, a 10 percent wettable powder formulation has been found to be safe and effective for indoor residual spraying against malaria vectors at target doses of 15 to 50 mg/m^2, while a 5 percent oil in water emulsion is effective and safe for use in impregnation of bed nets at a dose of 50 mg/m^2 (WHO, 1998).

Shelf Life

Cyfluthrin in water-based aerosols is stable for a long time. It is thermally stable at room temperature. Topical cyfluthrin preparations made with piperonyl butoxide should be stored at temperatures below 40 ^{o}C (and optimally at 15 to 30 ^{o}C) and in tightly closed containers (HSDB, 2005). Australian researchers reported that

cyfluthrin is stable and does not break down for up to 52 weeks when used on stored wheat (EXTOXNET, 1998).

Degradation Products

Pyrethroid insecticides are often formulated with synergists that act to prevent the breakdown of enzymes and thus enhance the activity of the pyrethroid (ATSDR, 2003). Cyfluthrin's breakdown products include 4-fluoro-3-phenoxybenzoic acid (PAN, 2005). In soil, the primary breakdown products include carbon dioxide and 4-fluoro-3-phenyl-benzaldehyde (a compound of considerably lower toxicity than the parent compound) (EXTOXNET, 1998).

Environmental Behavior

Fate and Transport in Terrestrial Systems

The use of cyfluthrin as an insecticide may result in its release into the environment via a variety of waste streams (HSDB, 2005). Once in the environment, cyfluthrin is expected to be highly immobile in the soil based on its Koc value (HSDB, 2005; EXTOXNET, 1998). Because it is immobile in soil, cyfluthrin does not easily leach into groundwater (EXTOXNET, 1998).

Cyfluthrin is one of the more persistent pyrethroids and as a result, it is used more often in agricultural applications (ATSDR, 2003). It can be broken down by sunlight, and in surface soils, the reported half-life ranges from 48 to 72 hours. Reported half-lives in German loam and sandy loam soils are 51 to 63 days. Persistence under anaerobic conditions is similar. The persistence of cyfluthrin in soil is not significantly affected by soil moisture content (EXTOXNET, 1998; ATSDR, 2003).

The major fate processes for cyfluthrin in soil are biodegradation and photolysis. Under anaerobic conditions, more than 90 percent biodegradation was reported during an incubation period of 140 days. Anaerobic biodegradation of cyfluthrin initially produces 3-(2,2-dichlorovinyl)2,2-dimethylcyclopropancarboxcylic acid and 4-fluoro-3-phenoxybenzoic acid. Photodegradation was observed when cotton fabric was irradiated for 96 hours in simulated natural sunlight, resulting in almost 75 percent photo-degradation (HSDB, 2005). Volatilization is not expected to be a major fate process from either moist or dry soils (HSDB, 2005).

Fate and Transport in Aquatic Systems

Cyfluthrin binds tightly to soil, is practically insoluble in water, and is less dense than water, allowing it to float on the surface film of natural water (EXTOXNET, 1998; HSDB, 2005). It is stable in water under acidic conditions but hydrolyzes rapidly under basic conditions (EXTOXNET, 1998). On surface waters, cyfluthrin breaks down by photolysis and is not expected to volatilize (EXTOXNET, 1998; HSDB, 2005). In aqueous solutions, an experimental half-life of 16 hours was identified when irradiated by environmentally significant wavelengths of light (HSDB, 2005). Aqueous hydrolysis does not play an important role in the environmental fate of cyfluthrin. Hydrolysis half-lives of 231 days and 2 days were identified at pH 7 and 8, respectively (ATSDR, 2003). Cyfluthrin has a high potential to bioconcentrate in aquatic organisms (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Limited data are available on the acute toxicity of cyfluthrin in humans, because pyrethroid poisonings are uncommon. Cases of acute occupational or accidental exposure to pyrethroids resulted in burning, itching, and tingling of the skin which resolved after several hours. Reported systemic symptoms included dizziness,

headache, anorexia, and fatigue. Vomiting occurred most commonly after ingestion of pyrethroids. Less commonly reported symptoms included tightness of the chest, paresthesia, palpitations, blurred vision, and increased sweating. In serious cases, coarse muscular fasciculations (twitching), convulsions, and coma were reported (IPCS, 1997). Cyfluthrin is of low toxicity to humans largely due to its poor absorption from the bloodstream and rapid breakdown and excretion. Acute effects of cyfluthrin exposure in humans consist primarily of immediate or delayed skin irritation and immediate eye irritation. Itching, burning, and stinging of exposed skin can progress to cutaneous paresthesias, which can last up to 24 hours. Sweating, heat, and water can make dermal symptoms worse (WHO, 2004; EXTOXNET, 1998; HSDB, 2005; IPCS, 1997).

As a pyrethroid, cyfluthrin inhibits cholinesterase (HSDB, 2005), and symptoms of acute toxicity in animals may include irritability, excessive salivation, uncoordinated gait, tremors, convulsions, and death (HSDB, 2005; EXTOXNET, 1998). Cyfluthrin is a type II pyrethroid, a class which is known to produce a complex poisoning syndrome involving a progressive development of symptoms. In rats, this manifests as burrowing behavior, coarse tremors, clonic seizures, sinuous writhing, and profuse salivation without lacrimation (HSDB, 2005). Nervous system effects have been reported in acute high-dose exposures of animals to cyfluthrin by oral routes (EXTOXNET, 1998). Neurological effects (e.g., disturbed posture, abnormal motor activity, restlessness, and agitated gate) have also been seen following acute inhalation exposures (ATSDR, 2003). Neurological symptoms following daily dermal doses of $\geq$ 1,845 mg/kg in rats for up to 7 days included pawing and whole body tremors (ATSDR, 2003).

The vehicle used in formulating cyfluthrin significantly affects its toxicity (WHO, 2004). Reported LD_{50} values range from 16 to 1,189 mg/kg body weight, depending on the vehicle used (WHO, 2004). The reported oral LD_{50}s range from 500 to 1,271 mg/kg in rats, 1,401 to 609 mg/kg in mice, greater than 100 mg/kg in dogs, greater than 1,000 mg/kg in rabbits, and greater than 1,000 mg/kg in sheep (EXTOXNET, 1998; HSDB, 2005).The oral LD_{50}s for cyfluthrin in polyethylene glycol and xylene are 500 and 270 mg/kg, respectively (HSDB, 2005), while the oral LD_{50} for a 5 percent water emulsion preparation is reported as 2,100 mg/kg body weight in rats (WHO, n.d.). Inhalation exposures in rats have resulted in 4-hour LC_{50}s ranging from 469 to 592 µg/L and a reported 1-hour LC_{50} greater than 1,089 µg/L (EXTOXNET 1998). The 4-hour LC_{50}s for aerosol and dust exposures in rats are reported as 0.1 mg/L and 0.53 mg/L, respectively (HSDB, 2005). Cyfluthrin is not considered highly toxic via the dermal route of exposure, with a dermal LD_{50} of greater than 5,000 mg/kg in rats (EXTOXNET, 1998; HSDB, 2005). Additionally, it is not a dermal sensitizer or irritant in guinea pigs and rabbits (WHO, 2004; EXTOXNET, 1998; HSDB, 2005) but did induce eye irritation in rabbits (WHO, 2004; HSDB, 2005).

Treatment

Cyfluthrin and its metabolites can be detected in blood and urine; however, the methods are not practical given how quickly these compounds are broken down in the body (ATSDR, 2003). There are no antidotes for cyfluthrin exposure. Treatment depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following cyfluthrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible. Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts of cyfluthrin should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent; exposure to light should be avoided (PAN, 2005; HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to cyfluthrin, although it is not likely to cause long-term problems when used under normal conditions (ATSDR, 2003). Available animal data suggest that chronic toxicity is highest by inhalation exposure, with lower toxicity by oral exposure. Dermal exposure has the lowest chronic toxicity (WHO, 2004). Cyfluthrin does not appear to be a reproductive or developmental toxin in animals (HSDB, 2005; WHO, 2004; ATSDR, 2003; EXTOXNET, 1998; WHO/FAO, 1997). However, treatment-related reductions in viability, decreased lactation, and deceased birth weight or weight gain were observed in one 3-generation rat study (ATSDR, 2003; EXTOXNET, 1998; U.S. EPA, 2005b). No developmental or teratogenic effects were observed in several animal studies (HSDB, 2005; EXTOXNET 1998; U.S. EPA, 2005b). In a 1-year dog feeding study, high doses of cyfluthrin caused slight ataxia, increased vomiting, and increased pasty or liquid feces. Decreased body weights were seen in males (U.S. EPA, 2005b). Cyfluthrin does not show any mutagenic potential (HSDB, 2005; WHO, 2004; EXTOXNET, 1998; WHO/FAO, 1997). Decreased weight gain and organ weight changes secondary to body weight are the only significant effects observed in long-term feeding studies in rats, mice, and dogs (WHO/FAO, 1997; EXTOXNET, 1998; U.S. EPA, 2005b). Additionally, reversible damage to the sciatic nerve was observed (EXTOXNET, 1998).

Cancer Endpoints

No evidence of carcinogenic potential has been reported in rats and mice exposed to cyfluthrin (WHO, 2004; EXTOXNET, 1998; WHO/FAO, 1997).

Toxicokinetics

Pyrethroids are rapidly absorbed via inhalation as is indicated by the excretion of their metabolites within 30 minutes of exposures. In workers, plasma cyfluthrin levels confirmed absorption. Oral exposure to pyrethroids results in absorption from the gastrointestinal tract. Cyfluthrin metabolites were identified in the urine of an orally exposed volunteer. Minimal oral absorption was estimated based on the recovery of urinary cyfluthrin metabolites (ATSDR, 2003).

As with other synthetic pyrethroids, biotransformation in mammals exposed to cyfluthrin occurs through hydrolysis of the central ester bond, oxidative attacks at several sites, and conjugation reactions that produce water-soluble metabolites that are excreted in urine and feces. For cypermethrin, the rapid hydrolytic cleavage of the ester bond is followed by oxidation, which results in carboxylic acid derivatives and phenoxybenzoic acid derivatives that are then excreted as alcohols; phenols; carboxylic acids; and their glycine, sulfate, glucuronide, or glucoside conjugates (ATSDR, 2003). The metabolism of cyfluthrin is biphasic with a rapid initial phase and a slower second phase. This is demonstrated by the elimination of 60 percent of an intravenous dose within the first 24 hours followed by 6 percent elimination during the second 24 hours. Similarly, in feces 20 percent was eliminated on the first day and 3 to 4 percent was eliminated on the second day. Additionally, a single oral dose of cyfluthrin was shown to be 98 percent eliminated within 48 hours (EXTOXNET, 1998). Inhalation of a single dose of cyfluthrin in humans resulted in urinary metabolites within 30 minutes of exposure (ATSDR, 2003; WHO/FAO, 1997).

Elimination of cyfluthrin following inhalation exposure follows first-order kinetics with 93 percent of the dose being excreted within 24 hours of exposure. The elimination half-times for cis-/trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (DCCA) and, 4-fluoro-3-phenoxybenzoic acid (FPBA) metabolites and their isomers range from 5.3 to 6.9 hours and remain constant over a range of exposure levels (ATSDR, 2003). Based on occupational human exposure studies, the elimination half-time for

cyfluthrin is estimated at 0.5 to 2 hours for plasma and 5 hours for urine (ATSDR, 2003). Oral exposures to cyfluthrin resulted in approximately 60 to 70 percent of the dose being eliminated in the urine and the rest eliminated in the feces (WHO/FAO, 1997).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Cyfluthrin has a very low toxicity in birds (EXTOXNET, 1998; HSDB, 2005). Oral LD_{50} values range from greater than 2,000 mg/kg in acute tests in bobwhite quail to greater than 5,000mg/kg in subacute tests in mallards and bobwhite quail (EXTOXNET, 1998). Other reported oral LD_{50}s are 4,500 to greater than 5,000 mg/kg in hens (depending on the vehicle used), greater than 2,000 mg/kg in Japanese quail, and 250 to 1,000 mg/kg in canaries (EXTOXNET, 1998; HSDB, 2005). As with other pyrethroid insecticides, cyfluthrin is extremely toxic to honey bees in laboratory tests. The reported LD_{50} is 0.037 mg/bee (EXTOXNET, 1998). However, in the field, serious adverse effects have not been seen due to low application rates and low environmental persistence (HSDB, 2005). Cyfluthrin is also highly toxic to other beneficial insects (EXTOXNET, 1998) but of low toxicity to earthworms (WHO, 2004).

Toxicity in Non-Targeted Aquatic Systems

As with other pyrethroids, cyfluthrin is very toxic to marine and freshwater fish and invertebrates (EXTOXNET, 1998; WHO, 2004). The high toxicity in fish is illustrated by the low exposures that cause lethality. The reported 48-hour LC_{50} for rainbow trout is 0.00068 mg/L, while in bluegill, carp, and golden orfe, the reported LC_{50}s are 0.0015, 0.022, and 0.0032 mg/L, respectively. In sheepshead minnow, an LC_{50} of 0.004 mg/L is reported (EXTOXNET, 1998). The 96-hour LC_{50} values range from 28 ng/L in bluegill sunfish to 330.9 ng/L in golden orfe (HSDB, 2005). In marine and estuarine invertebrates, extreme sensitivity to cyfluthrin is also seen. Reported LC_{50}s include 2.42 ng/L for mysid shrimp. An EC_{50} of 3.2 ng/L was seen in eastern oysters (EXTOXNET, 1998). Cyfluthrin has a high potential to bioconcentrate in aquatic organisms based on the measured BCF of the structurally similar insecticide cypermethrin (HSDB, 2005).

Chronic Exposure

Due to low rate of application and low persistence of cyfluthrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005).

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Profile for DDT:

CAS Registry Number 50-29-3

Summary

Chemical History

Dichlorodiphenyltrichloroethane (DDT) is a broad range pesticide used since the late 1930s on agricultural crops and to control disease-carrying insects, such as those that spread malaria and typhus. In 1955, a global campaign to eradicate malaria was adopted based on the use of DDT, and endemic malaria in developed countries, subtropical Asia, and Latin America was eradiated by 1967. However, few African countries participated, and the campaign ended in 1969 due to lack of support and developing mosquito resistance to DDT (Rogan and Chen, 2005). DDT was banned in the United States and other industrialized countries in the early 1970s, largely due to its persistence in the environment. However, DDT is still in use today in sub-Saharan African countries to control malaria (ATSDR, 2002). Some studies indicate that DDT (as well as DDE) is an endocrine disruptor in humans. Recent data have indicated that exposure to DDT in amounts necessary for malaria control may cause preterm birth, decreased birth weight, early weaning, and pregnancy loss (IPCS, 2004; Longnecker, 2005; Rogan and Chen, 2005). Acute exposure to high levels of DDT by any route causes neurological effects, including excitability, headache, nausea, vomiting, and dizziness (ATSDR, 2002).

Data on Mexican workers who use DDT show very high levels of DDT in adipose (fat) tissues and serum (Rogan and Chen, 2005). Children are also at risk for increased exposure to DDT and its metabolites via consumption of breast milk and cow's milk. DDT exhibits its toxic effects in humans on the nervous system and liver (ATSDR, 2002).

Description of Data Quality and Quantity

EPA and ATSDR have developed quantitative human heath benchmarks (EPA's chronic RfD and oral and inhalation CSFs and ATSDR's acute and intermediate oral MRLs). Several comprehensive reviews on the toxicity of DDT are available and recommended:

- Toxicological Profile for DDT, DDE, and DDD (ATSDR, 2002)
- IRIS summary review (U.S. EPA, 2005a)
- A recent review article by Rogan and Chen (2005).

Other relevant resources include

- Specifications for Pesticides Used in Public Health (WHO, 1999)
- Environmental Health Criteria 9: DDT and its Derivatives (IPCS,1979)
- Pesticide Information Profile for DDT (EXTOXNET, 2003)
- The Pesticide Action Network (PAN) Pesticide Database (PAN, 2005).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute	Inhalation	0.0005	mg/kg/day	Adopt acute oral MRL as acute inhalation; assume no portal of entry effects	
Intermediate	Inhalation	0.0005	mg/kg/day	Adopt intermediate oral MRL as intermediate inhalation; assume no portal of entry effects	
Chronic	Inhalation	0.0005	mg/kg/day	Adopt chronic RfD as chronic inhalation; assume no portal of entry effects	
Cancer	Inhalation	0.034	per mg/kg/day	Inhalation CSF (calculated from oral data) for benign and malignant liver tumors in rats and mice	U.S. EPA (1997)
Acute	Oral	0.0005	mg/kg/day	Acute oral MRL based on neurodevelopmental effects in mice	ATSDR (2002)
Intermediate	Oral	0.0005	mg/kg/day	Intermediate oral MRL based on liver effects in rats	ATSDR (2002)
Chronic	Oral	0.0005	mg/kg/day	Chronic oral RfD based on liver effects in rats	U.S. EPA (2005a)
Cancer	Oral	0.034	per mg/kg/day	Oral CSF for benign and malignant liver tumors in rats and mice	U.S. EPA (2005a)
Acute	Dermal	0.0005	mg/kg/day	Adopt acute oral MRL as acute dermal; assume no first pass effects and 100% oral absorption	
Intermediate	Dermal	0.0005	mg/kg/day	Adopt intermediate oral MRL as intermediate dermal; assume no first pass effects and 100% oral absorption	
Chronic	Dermal	0.0005	mg/kg/day	Adopt chronic RfD as chronic dermal; assume no first pass effects and 100% oral absorption	
Cancer	Dermal	0.034	per mg/kg/day	Adopt oral CSF as chronic dermal; assume no first pass effects and 100% oral absorption	

For oral exposure, the acute oral MRL of 0.0005 mg/kg/day was derived for DDT based on the LOAEL for neurodevelopmental effects in mice perinatally exposed to DDT (ATSDR, 2002). The intermediate oral MRL of 0.0005 mg/kg/day was derived for DDT based on the NOAEL for liver effects in rats exposed to DDT in the diet (ATSDR, 2002). A chronic RfD of 0.0005 mg/kg/day was derived for DDT based on liver lesions in male and female rats exposed to DDT in the diet for 27 weeks. An oral CSF of 3.4E-1 per mg/kg/day was also derived based on benign and malignant liver tumors in male and female rats and mice chronically exposed to DDT in the diet (U.S. EPA, 2005a).

For inhalation exposure, no noncancer toxicity factors were derived for DDT because adequate experimental data do not exist for this route (ATSDR, 2002; U.S. EPA, 2005a). An inhalation unit risk of 9.75E-5 per

μg/m³ and an inhalation cancer slope factor of 3.4E-1 per mg/kg/day were calculated from oral data for benign and malignant liver tumors in male and female rats and mice chronically exposed to DDT in the diet (U.S. EPA, 2005a).

For dermal exposure, no dermal toxicity factors have been derived because EPA and ATSDR have not yet identified a method suitable for this route of exposure. However, EPA has developed a simplified paradigm for making route-to-route extrapolations for systemic effects via percutaneous absorption in which complete oral absorption is assumed, thereby eliminating the need to adjust the oral toxicity value (U.S. EPA, 2004). This approach may result in underestimating risk. No adjustment was made and oral toxicity values were used for the dermal assessment.

Background

CASRN:	50-29-3
Synonyms:	(p-chlorophenyl)ethane; dichlorodiphenyl trichloroethane; DDT; 1,1'-(2,2,2-trichloroethylidene)bis(4-chlorobenzene); α-α-bis(p-chlorophenyl)-β, β, β –trichloroethane (ATSDR, 2002)
Chemical Group:	organochlorine (ATSDR, 2002)
Registered Trade Names:	Genitox, Anofex, Detoxan, Neocid, Gesarol, Pentachlorin, Dicophane, Chlorophenothane (ATSDR, 2002) Cesarex, p,p'-DDT, Dichlorodiphenyltrichloroethane, Dinocide, Didimac, Digmar, ENT 1506, Guesapon, Guesarol, Gexarex, Gyron, Hildit, Ixodex, Kopsol, Neocid, OMS 16, Micro DDT 75, Rukseam, R50 and Zerdane (EXTOXNET, 2003).

Usage

DDT is a broad spectrum insecticide that was once widely used. In World War II, it was used extensively to control insect-borne diseases such as malaria and typhus. In the early 1970s, it was banned in the United States and most industrial countries due to its persistence in the environment. Today it is used only in sub-Saharan Africa and in emergency cases to control malaria (ATSDR, 2002).

Formulations and Concentrations

Technical grade DDT is generally used as an insecticide. It is made up of three isomers of DDT, including p,p'-DDT (up to 85 percent), o,p'-DDT (15 percent), and o,o-DDT (trace amounts) (ATSDR, 2002). DDT is available as an aerosol, a dustable powder, an emulsifiable concentrate, in granules, or as wettable powders (EXTOXNET, 2003). DDT that is used for indoor residual spraying is usually a wettable powder that has 75 percent active ingredient. WHO (1999) indicated that the content of p,p'-DDT in the DDT formulation should be declared and contain the following:

- Technical grade DDT: no less than 700 g/kg p,p'-DDT
- Dustable powder: over 25–100 g/kg p,p'-DDT with a permitted tolerance of +/- 10% of the declared content
- Wettable powder: 100–250 g/kg p,p'-DDT with a permitted tolerance of +/- 6% of the declared content, or 250–500 g/kg p,p'-DDT with a permitted tolerance of +/- 5% of the declared content, or greater than 500 g/kg with a permitted tolerance of +/- 25 g/kg.

Shelf Life

DDT has a long shelf life. It is resistant to destruction by light or oxidation (HSDB, 2005).

Degradation Products

DDT breaks down very slowly by dehydrohalogenation into DDE [1,1-dichloro-2,2-bis(p-dichlorodiphenyl)ethylene] and DDE [1,1-dichloro-2,2-bis(p-chlorophenyl)ethane]. In animal systems, these metabolites are stored in body fat and either leave the body slowly if exposure decreases, remain constant in the tissues, or increase with continued exposures (ATSDR, 2002). Stored DDE and DDD are slowly transformed to DDA [bis(dichlorodiphenyl) acetic acid] by other metabolites. DDA and its metabolites are then excreted in the urine (EXTOXNET, 2003).

Environmental Behavior

Fate and Transport in Terrestrial Systems

DDT and its metabolites are highly persistent and bioaccumulate in the environment (ATSDR, 2002). The persistence of DDT in the environment is mainly due to its being soluble in fat and virtually insoluble in water (IPCS, 1979). DDT is released into the air as a result of spraying operations in countries where it is still being used. DDT and its metabolites may also enter the air when they evaporate from contaminated soil and water. They may then be deposited back onto land and surface waters. This cycle of volatilization and deposition may be repeated numerous times resulting in the movement of DDT in the atmosphere. As a result, DDT and its metabolites have been found in air, sediment, and snow, and accumulated in biota in the Arctic and Antarctic regions. As a result of this ability to undergo long-range global transport, the actual lifetime of DDT and its metabolites is substantially longer than indicated by their estimated half-lives. In the atmosphere, DDT and its metabolites occur as a vapor or are attached to particulates in the air. As a vapor, DDT and its metabolites are broken down by sunlight. DDT is also broken down slowly by microorganisms (ATSDR, 2002).

In most soils, DDT is practically immobile due to its strong affinity to soil, especially organic soil matter (EXTOXNET, 2003). Because DDT and its metabolites (DDD and DDE) stick strongly to the soil, they remain mostly in the surface layers of soil. Soil with DDT bound to it may enter waterways via runoff (ATSDR, 2002). Other routes of loss and breakdown of DDT in soil include volatilization, photolysis, and aerobic and anaerobic biodegradation. Loss from volatilization depends on how much DDT was applied, the amount of organic material in the soil, proximity to the soil-air interface, and the amount of sunlight (EXTOXNET, 2003). Very little DDT will seep into groundwater. The persistence of DDT is soil varies with the type of soil, temperature, and soil moisture (ATSDR, 2002). The typical half-life of DDT in soil ranges from 2 years to 15 years (EXTOXNET, 2003). DDT and its metabolites last for a shorter time in soils that contain more microorganisms, wet soils, and warmer soils (ATSDR, 2002). Because DDT persists in the soil, bioaccumulation in plants has been observed, especially in the root.

Fate and Transport in Aquatic Systems

The two main ways that DDT may be released into surface waters are by direct application for the control of mosquito-borne malaria and by runoff from sprayed areas. Atmospheric transport and drift represent lesser scenarios (EXTOXNET, 2003). DDT is a highly persistent compound with low volatility and low solubility in water, leading to great potential to bioaccumulate in the environment. DDT binds to particles in surface water, settles, and then deposits in the sediment (ATSDR, 2002). Studies have shown that DDT dose not readily break down in estuary sediments. Additionally, DDT has been widely detected in ambient surface water samples in the United States. The reported half-life of DDT in lake and river water is 56 and 28 days, respectively; the half-life in river water is shorter because river water usually has more organic soil matter

(EXTOXNET, 2003). The main fate processes in the aquatic environment are volatilization, photodegradation, absorption to water-borne particles, and sedimentation, with the dominant fate process being volatilization. In surface waters, DDT is transformed via biotransformation and photolysis (ATSDR, 2002). DDT is also readily taken up by and accumulates in aquatic organisms (EXTOXNET, 2003).

Human Health Effects

Acute Exposure

Effects/Symptoms

DDT has been used in large populations for more than 60 years with little acute toxicity except from accidental exposures (Rogan and Chen, 2005). DDT impairs the conduction of nerve impulses. In humans, this can cause effects ranging from mild altered sensations to tremors, convulsions, and respiratory depression (ATSDR, 2002). Additional effects observed in humans following acute DDT exposure include headaches; nausea; vomiting; diarrhea; numbness; paresthesia; increased liver enzyme activity; irritation of the eyes, nose, or throat; altered gait; and malaise or excitability (EXTOXNET, 2003; PAN, 2005).

The toxicity of DDT varies with formulation and the exposure pathway. In humans, the oral route is thought to be the most significant. Fatalities have been documented following ingestion of commercial preparations that also contain substances other than DDT (ATSDR, 2002). Children appear to be more susceptible to the fatal effects of DDT than adults (EXTOXNET, 2003). Dermal and inhalation exposures to DDT are more likely in humans if the compound is in solution form (dermal) or aerosol form (inhalation). Exposure through dermal contact is more likely when DDT is in an oily solution than when it is in a wettable powder form, which is the formulation used most often in indoor residual spraying (ATSDR, 2002).

In animals, the toxicity DDT and its analogues have been studied extensively. Acute exposure to high doses of DDT can cause death, with the toxicity dependent upon the formulation. Acute oral LD_{50} values range from 150 to 200 mg/kg in mice, 113 to 800 mg/kg in rats, and 500 to 750 mg/kg in dogs (EXTOXNET, 2003). Deaths were usually a result of respiratory arrest (ATSDR, 2002). DDT is most known for its neurotoxic effects in animals. Similar to its effects in humans, DDT causes hyperactivity, tremor, and seizures in animals. Acute exposure to low doses of DDT can cause subtle neurodevelopmental effects in neonatal mice (EXTOXNET, 2003). Liver effects such as increased liver weights, induction of liver enzymes, and hepatic-cell hypertrophy and necrosis have also been observed (Rogan and Chen, 2005). Because of the hormone altering action of DDT isomers, reproductive and developmental effects have also been seen in laboratory animals. Acute exposure to DDT and its metabolites in food may have negative effects on reproduction (ATSDR, 2002). DDT is very slightly toxic to laboratory animals via acute dermal exposure. LD_{50} values range from 2,500 to 3,000 mg/kg in rats, 1,000 mg/kg in guinea pigs, and 300 mg/kg in rabbits. Acute inhalation exposure of animals to DDT does not result in significant absorption in the lungs (EXTOXNET, 2003).

Treatment

Exposure to DDT may be measured through laboratory tests. DDT and its metabolites (DDE and DDD) may be detected in the blood/plasma, semen, urine, liver, kidney, fatty tissue, skin lipids, breastmilk, and lymphatic tissues (ATSDR, 2002). DDT exposure should be treated with anticonvulsants (benzodiazepines), oxygen, and cardiopulmonary monitoring. Epinephrine, other adrenergic amines, atropine, and orally administered fats are all contraindicated (PAN, 2005; Reigart and Roberts, 1999).

Chronic Exposure

Noncancer Endpoints

Most chronic exposure human data come from studies of workers who are exposed to DDT in manufacturing facilities or as spray applicators and from epidemiological studies. These studies indicate that chronic oral exposure to small amounts of DDT does not produce toxic effects in humans. However, DDT and its metabolite DDE may alter hormonally mediated endpoints such as lactation duration, maintenance of pregnancy, and fertility. Recent data have indicated that exposure to DDT in amounts necessary for malaria control may cause preterm birth, decreased birth weight, early weaning, and pregnancy loss (Farhang et al., 2005; IPCS, 2004; Longnecker, 2005; Rogan and Chen, 2005; Venners et al., 2005). Increased chances of premature birth, infants that are small for their gestational age, and height abnormalities in children have also been associated with high DDE levels in the blood (ATSDR, 2002). DDT and its metabolites affect male reproductive parameters such as semen volume, sperm count, testosterone ratios, sperm motility, and sperm morphology and DNA damage; these data indicate the possibility of reduced male fertility as a result of occupational and non-occupational exposure to DDT used in IRS (De Jager et al., 2006; IPCS, 2004; Rogan and Chen, 2005). Residential exposure (*in utero* and from breastfeeding) to DDT may delay neurodevelopment in children during their first two years of life (Eskenazi et al., 2006).

In animals, liver effects have been seen following chronic exposure to moderate levels of DDT (ATSDR, 2002). The main effect was localized liver damage. Additional chronic effects in animals include nervous system (tremors, central nervous system cellular chemistry changes, loss of equilibrium), kidneys (adrenal gland and kidney damage), and immune system (reduced antibody formation, reduced immune cells). Those effects were seen at levels much higher than expected human exposure levels (EXTOXNET, 2003).

Cancer Endpoints

IARC has classified DDT in group 2B; a probable human carcinogen (IARC, 1991). EPA has also determined that DDT is a probable human carcinogen (U.S. EPA, 2005a). The available epidemiological evidence regarding carcinogenicity in humans is inconclusive. A slight increase in risk from lung cancer was observed in workers at two DDT production facilities. No other cancer incidences were found in sufficient numbers for analysis. Inconsistent results have been found when comparing serum DDT/DDE levels in people with and without cancer (IARC, 1991). One study indicated a potential link between chronic, high dose DDT exposure and pancreatic cancer in chemical workers but the reliability of the study is questionable. The association between p,p'-DDE and breast cancer has been studied extensively, but studies have failed to show an association (Rogan and Chen, 2005). Studies have indicated that DDT and its metabolites are not mutagenic (ATSDR, 2002). In animals, DDT has been shown to cause liver and lung cancers (ATSDR, 2002).

Toxicokinetics

DDT is absorbed via inhalation, the gastrointestinal tract, and dermally. In humans, oral exposure to DDT is considered the most significant. Orally, DDT is absorbed from the gastrointestinal tract into the lymphatic system. There is also some absorption into the portal blood. Distribution of DDT to all body tissues then occurs from the lymphatic system and blood. In the tissues, DDT is stored in proportion to the lipid (fat) content of the tissue (ATSDR, 2002). DDT is initially metabolized into DDE and DDD, however these are ultimately transformed into DDA (EXTOXNET, 2003). DDA and its metabolites are eventually excreted in the urine. DDT may also be excreted via feces, semen, and breastmilk (ATSDR, 2002).

Ecological Effects

Acute Exposure

DDT is only slightly toxic to birds. Acute oral LD_{50} values in various bird species include the following: Japanese quail (841 mg/kg), pheasant (1,334 mg/kg), and mallard (2,240 mg/kg). Most avian exposures are a result of the food chain and consumption of aquatic (e.g., fish) or terrestrial (e.g., earthworms or other birds) species that have an accumulated body burden of DDT. However, earthworms are not susceptible to the acute toxic effects of DDT. Additionally, DDT is not toxic to bees. DDT may, however, be toxic to bats as DDT may be released from fat stores during migration (EXTOXNET, 2003).

DDT is highly toxic to many aquatic species. On average, acute exposure to DDT is only slightly toxic to amphibians and phytoplankton; moderately toxic to annelida, mollusks, and zooplankton; highly to very highly toxic to fish; and very highly toxic to crustaceans (PAN, 2005). In fish, the 96-hour LC_{50} values range from 1.5 µg/L in northern pike to 21.5 µg/L in fathead minnows. DDT is very highly toxic to stoneflies, midges, crayfish, sow bugs, and other aquatic invertebrate with 96-hour LC_{50} values ranging from 0.18 to 7.0 µg/L. In aquatic invertebrates, DDT adult stages are less susceptible than developmental stages (EXTOXNET, 2003).

Chronic Toxicity

Chronic exposure to DDT has been linked to reproductive effects in birds. Eggshell thinning and embryo death are two of the main concerns especially in birds of prey. The mechanism of eggshell thinning is thought to be from the major metabolite DDE. Additionally, the reproductive behavior of birds may also be subtlety altered by DDT and DDE exposure. In laboratory studies, changes in courtship behavior, delays in pairing and egg laying, and decreases in egg weight have been observed in some bird species, though it is not clear what these effects mean for the survival of wild bird species. A synergism may exist between DDT metabolites and organophosphate pesticides to produce greater neurotoxicity and increased deaths (EXTOXNET, 2003).

Chronic exposure to DDT may occur in fish and aquatic species through bioaccumulation. This occurs from the uptake of DDT in sediments and water, with smaller fish taking up higher amounts of DDT. It has been estimated that the half-time elimination of DDT for rainbow trout is 160 days. Bioaccumulation can occur at very low environmental concentrations and the bioconcentration factor for DDT is 1,000 to 1,000,000, depending on the aquatic species (EXTOXNET, 2003).

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Profile for Deltamethrin:

CAS Registry Number 52918-63-5

Summary of Insecticide

Chemical History

Deltamethrin is a broad spectrum synthetic pyrethroid insecticide used in agricultural and human health applications. It was first marketed in 1977 (IPCS, 1990; EXTOXNET, 1995; WHO/FAO, 2001) and has been in use longer than any alpha-cyano pyrethroid with an excellent safety record (WHO/FAO, 1999). It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (EXTOXNET, 1995; WHO/FAO, n.d.; IPCS, 1990). Deltamethrin is considered the most powerful synthetic pyrethroid (EXTOXNET, 1995). For mosquito control, it is used on bed nets and other materials that are dipped in deltamethrin to protect the user (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, 2001). Deltamethrin is typically formulated as emulsifiable concentrates, wettable powders, ultra-light-volume (ULV) and flowable formulations, and granules either alone or combined with other pesticides (EXTOXNET, 1995; IARC, 1991). A dispersible tablet is also used to treat mosquito nets (Barlow et al., 2001). Deltamethrin is of moderate toxicity to mammals because metabolizes rapidly and does not accumulate (WHO/FAO, n.d.; WHO/FAO, 1999). It is of low risk to humans when used at levels recommended for its designed purpose (ATSDR, 2003; WHO, 2004). General population exposures are expected to be very low and to occur mostly through public health uses and dietary residues. As a synthetic pyrethroid, deltamethrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels of nerve cells (Choi and Soderlund, 2006). EPA has not classified synthetic pyrethroids, including deltamethrin, as endocrine disruptors. Typical symptoms of acute exposure are irritation of skin and eyes, severe headaches, dizziness, nausea, anorexia, vomiting, diarrhea, excessive salivation, and fatigue. Tremors and convulsions have been reported in severe poisonings. Inhaled deltamethrin has been shown to cause cutaneous paraesthesia (a burning, tingling, or stinging). However, these effects are generally reversible and disappear within a day of removal of the exposure (Barlow et al., 2001; WHO, 2004; ATSDR, 2003; IPCS, 1989, 1990). In animals, the critical effect is neurotoxicity (WHO, 2004).

Description of Data Quality and Quantity

Adequate dose-response studies on the toxicity of deltamethrin exist for oral, dermal, and inhalation exposures. Most are oral exposure studies (WHO, 2004). Several comprehensive reviews on the toxicity of deltamethrin have been prepared or updated in recent years:

- Environmental Health Criteria 97: Deltamethrin (IPCS, 1990)
- Health and Safety Guide No. 30: Deltamethrin Health and Safety Guide (IPCS, 1989)
- A review article by Barlow et al. (2001)
- Pesticide Information Profiles (PIP) for Deltamethrin (EXTOXNET, 1995)
- Data Sheets on Pesticides No. 50—Deltamethrin (WHO/FAO, n.d.)
- A Generic Risk Assessment Model for Insecticide Treatment and Subsequent Use of Mosquito Nets (WHO, 2004)
- Malaria Vector Control—Insecticides for Indoor Spraying (WHO/FAO, 2001)

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs, intermediate-term oral, and short-, intermediate-, and long-term dermal and inhalation benchmarks) for deltamethrin.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.01	mg/kg/day	Oral NOAEL for clinical signs in dogs at 1 mg/kg/day with UF of 100 applied	U.S. EPA (2004)
Acute	Oral	0.01	mg/kg/day	Acute RfD based on neurological effects in rats	U.S. EPA (2004)
Intermediate	Oral	0.01	mg/kg/day	Oral NOAEL for clinical signs in dogs at 1 mg/kg/day with UF of 100 applied	U.S. EPA (2004)
Chronic	Oral	0.01	mg/kg/day	Chronic RfD based on clinical signs in dogs	U.S. EPA (2004)
Acute, Intermediate, Chronic	Dermal	10	mg/kg/day	Dermal NOAEL of 1000 mg/kg/day in rats with a UF of 100 applied	Barlow et al. (2001)

For oral exposure, an acute RfD of 0.01 mg/kg/day was derived based on a NOAEL of 1 mg/kg/day for neurological effects (reduced motor activity) observed in rats exposed to deltamethrin (Crofton et al., 1995), with an uncertainty factor of 100 applied to account for interspecies and intrahuman variability (U.S. EPA, 2004). A chronic oral RfD of 0.01 mg/kg/day was derived based on a NOAEL of 1 mg/kg/day for clinical signs and reduced weight gain in dogs (study citation not provided), with an uncertainty factor of 100 applied (U.S. EPA, 2004). The chronic RfD is appropriate to use for intermediate-term exposures (U.S. EPA, 2004).

For inhalation exposures, the chronic RfD is also appropriate for short-, intermediate-, and long-term exposures (U.S. EPA, 2004).

For dermal exposure, a NOAEL of 1,000 mg/kg/day was identified in rats dermally exposed to deltamethrin for 21 days (study citation not provided). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability, for a dermal benchmark value of 10 mg/kg/day. This value is appropriate for all dermal exposure durations (Barlow et al., 2001). The large difference between the oral and dermal NOAELs is due to rapid absorption of deltamethrin from the gastrointestinal tract versus low dermal absorption (WHO, 2004; Barlow et al., 2001).

Insecticide Background

CASRN:	52918-63-5
Synonyms:	cyano(3-phenoxy-phenyl)methyl;2-(2,2dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate (CA); alpha-cyano-m-phenoxybenzyl,(1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropanl-carboxylate, (S)-alpha-cyano-3-phenoxybenzyl (1R)-cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane-carboxylate, decamethrine, FMC 45498, NRDC 161, OMS 1998, RU 22974, RUP 987 (EXTOXNET, 1995; IARC, 1991; WHO/FAO, n.d.).
Chemical Group:	pyrethroid (PAN, 2005)

Registered Trade Names:	Products containing deltamethrin (NRDC 161 and RU 22974): Butoflin, Butoss, Butox, Cislin, Cislin 2.5% EC, Cislin 2.5% WP, Cislin RTU, Crackdown, Cresus, Decis, Decis-Prime, K-Othrin, K-Orthine, K-Otek, Kordon, Sadethrin (EXTOXNET, 1995; WHO/FAO, n.d.; ATSDR, 2003; IPCS, 1989; IARC, 1991; FPA, 2002).

Usage

Deltamethrin is used to combat pests on a variety of crops, including cotton, fruit, vegetables, coffee, maize, wheat, rapeseed, hops, and soybeans (ATSDR, 2003; EXTOXNET, 1995; IPCS, 1989, 1990). It is also used to control insects in stored grains, to protect cattle from infestation, and in public health applications. It may be applied to foods, field crops, gardens, orchards, and vineyards (WHO/FAO, n.d.). Public health uses include malaria control in Central America and Africa (IPCS, 1990). Deltamethrin belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies (ATSDR, 2003). For mosquito protection, it is used on bed nets and other materials that are dipped into the deltamethrin to protect the user. All concentrated formulations of deltamethrin were restricted by EPA due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003).

Formulations and Concentrations

Deltamethrin is available in technical grade (> 98 percent pure), suspension concentrate, emulsifiable concentrate (25–100 g/L), ultra-low-volume (ULV) concentrate (1.5–30 g/L), wettable powder (25–50 g/kg), flowable powder (7.5–50 g/L), dust powder (0.525 g/kg), and granules (0.5 and 1.0 g/kg) alone or combined with other pesticides (IPCS, 1989, 1990; WHO/FAO, n.d.). Deltamethrin that is marketed for use as a bed net treatment comes in a single 400 mg tablet form (WHO, 2004).

Shelf Life

In storage conditions at 40°C, deltamethrin is stable to light, heat, and air for 6 months and to light and air for 2 years. It is most stable in acidic media and unstable in alkaline environments (EXTOXNET, 1995; IPCS, 1989, 1990; WHO/FAO, n.d.).

Degradation Products

Deltamethrin's major metabolites are free and conjugated Br_2CA, *trans*-hydroxymethyl-Br_2CA, and 3-(4-hydroxyphenoxy)benzoic acid formed by ester cleavage, oxidation, and conjugation (IPCS, 1990).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Deltamethrin is not expected to be mobile in soil, with a Koc ranging from 46,000 to 1,630,000 (HSDB, 2005). Additionally, it binds tightly to soil particles, is insoluble in water, and has low application rates (IPCS, 1989, 1990). Volatilization is a major environmental fate process from moist soils but this is lessened by its adsorption to soil. Another major fate process is biodegradation, with a half-life of several weeks to greater than 100 days (HSDB, 2005). As with other synthetic pyrethroids, deltamethrin degrades rapidly in soil and plants (IPCS, 1990). Degradation occurs within 1 to 2 weeks for soil, and no residues remain on plants after 10 days (EXTOXNET, 1995). Deltamethrin does not bioaccumulate in terrestrial systems (IPCS, 1990).

Fate and Transport in Aquatic Systems

Because deltamethrin binds tightly to soil and is practically insoluble in water, very little leaching into groundwater is expected. In pond water, deltamethrin was absorbed rapidly by sediment, uptake by plants, and evaporation (EXTOXNET, 1995). Volatilization is a major environmental fate process in surface waters but is lessened by soil adsorption. Deltamethrin breaks down quickly in water with reported half-lives of 2 to 4 hours. The estimated volatilization half-life in a model river is 30 hours, and in a model lake, 500 hours. In a model pond, the estimated volatilization half-life is 7 years if adsorption is considered. Deltamethrin has a high potential to bioconcentrate in aquatic organisms. It has an estimated bioconcentration factor of 270. The reported estimated hydrolysis half-life was 36 years at pH 7 and 3.6 years at pH 8 (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of deltamethrin in humans. Acute effects in humans include irritability, headache, salivation, sweating, fever, anxiety, rapid heart beat, diarrhea, dyspnea, tinnitus, runny nose, vomiting, edema, hepatic microsomal enzyme induction, peripheral vascular collapse, serum alkaline phosphatase elevation, tremors, ataxia, convulsions leading to muscle fibrillation and paralysis, and death due to respiratory failure (EXTOXNET, 1995; WHO/FAO, n.d.; IPCS, 1990). Dermatitis is expected after dermal exposures, which often occur as a result of inadequate handling safety precautions during agricultural use (EXTOXNET, 1995; IPCS, 1990). Coma was caused within 15 to 20 minutes at oral exposure levels of 100 to 250 mg/kg (EXTOXNET, 1995). Facial paraesthesia is a common indicator of exposure of humans to high levels (WHO/FAO, n.d.).

In clinical studies in humans, slight irritation but no skin damage was reported in patch tests of deltamethrin put on faces of volunteers (IPCS, 1990). Acute occupational exposures to deltamethrin have resulted mostly in dermal symptoms including itching, burning, and paraesthesia. These are an early, reversible signs of exposure and are due to local, not systemic, exposures (Barlow et al., 2001; IPCS, 1990; EXTOXNET, 1995). Neurological signs such as headaches, dizziness, fatigue, nausea, anorexia, transient EEG changes, muscular fasciculation, and convulsions have also been reported following acute occupational exposures (Barlow et al., 2001; EXTOXNET, 1995). Loss of consciousness, muscle cramps, myosis, and tachycardia were reported in a 13-year-old girl who attempted suicide by ingesting 5 g of deltamethrin (200 mL of a 2.5% EC formulation). After appropriate medical intervention, she recovered completely within 48 hours. Only digestive and hepatic signs were observed in a 23-year-old man who attempted suicide by ingesting 1.75 g of deltamethrin (70 mL of a 2.5% EC formulation) (IPCS, 1990).

Animal studies have indicated that deltamethrin has low acute toxicity; however, this varies greatly depending on the route of administration and the vehicle used (WHO, 2004; Barlow et al., 2001). In acute exposure studies, the mouse is the species most susceptible to deltamethrin toxicity (WHO/FAO, n.d.). Reported oral LD_{50} values range from 19 to 34 mg/kg in mice, 52 to over 5,000 mg/kg in male rats, 30 to 139 mg/kg in female rats, and over 300 mg/kg in dogs (EXTOXNET, 1995; IPCS, 1990; WHO/FAO, n.d.; WHO/FAO, 2001; Barlow et al., 2001). Following acute dermal exposure, the reported LD_{50} is greater than 2,940 mg/kg in rats and dogs and greater than 2,000 mg/kg in rabbits (EXTOXNET, 1995; IPCS, 1990; WHO/FAO, n.d.; WHO/FAO, 2001). The reported inhalation 6-hour LD_{50} in rats is 600 mg/m^3 (IPCS, 1990).

Hyperactivity and hypersensitivity are general characteristics of pyrethroid poisonings. However, the signs of acute deltamethrin poisoning are different from other pyrethroids in that it produces a unique set of effects that occur in a specific sequence in animals. They begin with chewing, pawing, and burrowing behavior;

excessive salivation; and coarse tremors advancing to choreoathetosis and sometimes terminal clonic seizures. Rolling convulsions are especially characteristic of deltamethrin poisoning (WHO/FAO, n.d.; EXTOXNET, 1995). In rabbits and guinea pigs, no primary skin irritation or sensitization was observed following acute dermal exposure to 0.5 g/animal, although transitory ocular irritation was seen in rabbits without immediate rinsing (EXTOXNET, 1995; WHO/FAO, n.d.). However, another study reported skin irritation in rats and guinea pigs (EXTOXNET, 1995). Cardiovascular effects include a rapid fall in blood pressure, severe bradycardia, and EKG changes in intravenously exposed dogs (WHO/FAO, n.d.)

Treatment

Deltamethrin and its metabolites can be detected in blood and urine; however, the methods are not practical given how quickly these compounds are broken down in the body (ATSDR, 2003; WHO/FAO, n.d.). Levels of the degradation products bromide, cyanide, and 3-phenoxybenzyl in urine may be useful indicators in cases of severe toxicity (WHO/FAO, n.d.).

There are no antidotes for deltamethrin exposure (IPCS, 1989; WHO/FAO, n.d.). Treatment depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following deltamethrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible (PAN, 2005; WHO/FAO, n.d.). Medical personnel will treat severe intoxications with a sedative and anticonvulsant (IPCS, 1989). Ingestion of large amounts of deltamethrin should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent and exposure to light should be avoided (WHO/FAO, n.d.)

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to deltamethrin; however, it is not likely to cause long-term problems when used under normal conditions. In humans, suspected chronic effects include choreoathetosis, hypotension, prenatal damage, and shock (EXTOXNET, 1995). Chronic occupational exposure to deltamethrin caused skin and eye irritation; however, no long-term effects were seen (Barlow et al., 2001; EXTOXNET, 1995). After 1 year of using bednets treated with a target does of 25 mg/m^2 deltamethrin, skin irritation occurred one week after treatment, and runny nose and sneezing in the first days of use were reported for target does of 10–30 mg/m^2. No chronic effects were reported (Barlow et al., 2001). Data in animals indicate that oral exposure to deltamethrin is not highly toxic (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, n.d.).

In studies of reproductive toxicity in rats, no effects were seen on male or female fertility; number of implantation sites; litter size at birth; or pre- or postnatal survival in rats, mice, and rabbits (Barlow et al., 2001). No effects on reproduction were observed in a 3-generation rat study, but slight embryotoxicity was seen (EXTOXNET, 1995; Barlow et al., 2001). Dose-related decreases in maternal weight gain were seen in pregnant mice dosed with deltamethrin on gestational days 7 to 16. However, no effect on the number of implants, fetal mortality, fetal weight, or malformations was seen (EXTOXNET, 1995). Deltamethrin is not teratogenic in mice, rats, or rabbits at doses that produced clinical signs of toxicity in pregnant dams (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, n.d.). Mutagenicity studies in mice, rats, and rabbits indicate that deltamethrin is not mutagenic (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, n.d.)

Cancer Endpoints

IARC (1991) has classified deltamethrin as a Group 3 chemical, "not classifiable as to its carcinogenicity in humans." No human carcinogenicity data are available for deltamethrin (IARC, 1991; EXTOXNET, 1995). Long-term dietary studies in rats, mice, and dogs did not find evidence of carcinogenicity (IPCS, 1990). Microbial, mammalian cell, and *in vivo* mammalian mutagenicity studies support the evidence that deltamethrin is not carcinogenic (WHO/FAO, n.d.).

Toxicokinetics

Deltamethrin metabolism has not been well studied in humans. It is expected to be similar to metabolism in rodents (Barlow et al., 2001). Deltamethrin is readily absorbed via the gastrointestinal tract, inhalation, and less so through intact skin. The rate at which it is absorbed depends on the carrier or solvent used. Once absorbed, deltamethrin is readily metabolized and excreted (Barlow et al., 2001; IPCS, 1989, 1990; WHO/FAO, n.d). Similar metabolism and excretion patterns have been observed in extensive studies in rats, mice, and cows. Deltamethrin is metabolized in the liver by microsomal esterases and oxidases. It is distributed to the gut wall and liver. The parent compound is cleaved into cyclopropanecarboxylic acid and 3-phenoxybenxyl alcohol, which is then oxidized to 3-phenolbezoic acid. 3-Phenoxybenxoic acid is the major excretion compound. Hydroxylation of this moiety can occur before or after hydrolysis (Barlow et al., 2001; WHO/FAO, n.d.; EXTOXNET, 1995; IPCS, 1990). In rats, approximately 13 to 21 percent of deltamethrin is eliminated unchanged in the urine and feces within 2 to 4 days; however, the metabolites of the cyano substituent are eliminated more slowly. The half-life of deltamethrin in the brains of rats is 1 to 2 days. Levels of the metabolites remain higher, especially in the skin, stomach, and body fat, with a half-life of 5 days in body fat (Barlow et al., 2001; EXTOXNET, 1995). Following oral exposure, deltamethrin is completely eliminated within 6 to 8 days (WHO/FAO, n.d.). In feces, 7 to 15 percent of the oral dose is found as the parent compound and its hydroxylates; the hydrolysis products are mainly excreted in the urine. A smaller amount is found in the skin as thiocyanate (WHO/FAO, n.d.)

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Deltamethrin, like other pyrethroids, is very unlikely to harm terrestrial organisms other than its targets, such as mosquitoes and other pests (EXTOXNET, 1996). It has a very low toxicity in birds (IPCS, 1990; IPCS, 1989). Oral LD_{50} values range from greater than 1,800 mg/kg in grey partridge to greater than 4,000 mg/kg in ducks (IPCS, 1989). An 8-hour LD_{50} of more than 4,640 mg/kg diet was reported in ducks, and the 8-hour LD_{50} in quail was greater than 10,000 mg/kg diet (EXTOXNET, 1995). As with other pyrethroid insecticides, deltamethrin is extremely toxic to honey bees, with a 24-hour LD_{50} of 0.079 for technical deltamethrin and 0.4 μg ai/bee for the EC formulation. The contact LD_{50} for bees is reported to be 0.05 μg ai/bee. However, in real-life applications, serious effects have not been noticed due to low application rates and lack of environmental persistence. Deltamethrin is also very toxic to *Typhodromum pyri*, a predatory mite; *Encarsia Formosa*, a parasitic wasp; and spiders (EXTOXNET, 1995; IPCS, 1990).

Toxicity in Non-Targeted Aquatic Systems

In the laboratory, deltamethrin is very toxic to fish and aquatic arthropods. However, under normal use conditions in the environment, no deleterious effects have been observed due to its low application rates and lack of persistence (EXTOXNET, 1995; IPCS, 1990). The reported 96-hour LC_{50} value for technical deltamethrin ranges from 0.39 μg/L in rainbow trout to 3.5 μg/L in *Sarotherodon mossambicus*. For the

emulsifiable concentrate, LC_{50} values range from 0.59 μg/L in *Salmo salar* (96-hour) to 4.7 μg/L in brown trout (48-hour). For ultra-light volume concentrate, LC_{50} value ranges from 82 μg/L in bleak to 210 μg/L in common carp. In Daphnia, the reported 48-hour LC_{50} for technical deltamethrin is 5 μg/L (IPCS, 1990). Deltamethrin can accumulate in fish. Fathead minnows accumulated deltamethrin without any effect on mortality (EXTOXNET, 1995). Deltamethrin is also highly toxic to aquatic macroinvertebrates such as lobster (IPCS, 1989).

Chronic Exposure

Due to low application rates and low persistence of deltamethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005)

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Profile for Etofenprox:

CAS Registry Number 80844-07-1

Summary of Insecticide

Chemical History

Etofenprox is a non-ester pyrethroid-like insecticide and acaricide used in agricultural, horticultural, and public health applications. Its toxicity and mode of action (acting on the central nervous system) are similar to other pyrethroids (WHO/FAO, 1993; WHO, 1999; NIH, 2005). For mosquito control, etofenprox is used on bed nets and other materials that are dipped in it to protect the user. WHO has classified etofenprox as low risk for acute toxicity in humans under normal use conditions (WHO, 1999). Typical symptoms of acute exposure are likely to be similar to other pyrethroid insecticides. At high doses, hunched posture, lethargy, body tremors, and respiratory distress were reported in laboratory animals. Etoxfenprox does not inhibit cholinesterase activity. At high doses, long-term exposure can affect organs such as the thyroid and kidneys. Reproductive and developmental effects are not expected. Etofenprox is available as the technical product and formulated wettable powders and emulsifiable concentrates. Etofenprox is classified as Group C, possible human carcinogen.

Description of Data Quality and Quantity

The available data on etofenprox are limited. Relevant references include the following:

- Pesticide Residues in Food – 1993. Evaluation Part II Toxicology. Etofenprox (WHO/FAO, 1993)
- Etofenprox Evaluation (FAO, 1993)
- Summary of Toxicology Data: Etofenprox (CalEPA, 2003)

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.1	mg/kg/day	NOAEL for systemic effects in rats with UF of 100 applied	NYSDEC (2005)
Acute, Intermediate, Chronic	Oral	0.037	mg/kg/day	Proposed chronic RfD based NOEL in rats with UF of 100 applied	NYSDEC (2005)
Acute, Intermediate	Dermal	0.4	mg/kg/day	LOAEL (skin lesions) in rats with UF of 1,000 applied	NYSDEC (2005)
Chronic	Dermal	0.037	mg/kg/day	Adopt chronic oral RfD; assume no first pass effects and 100% absorption	NYSDEC (2005)
Cancer	Inhalation, Oral, Dermal	0.0051	per mg/kg/day	CSF for thyroid adenomas and carcinomas in rats	NYSDEC (2005)

For inhalation exposure, a NOEL of 0.04 mg/L (equivalent to 10.6 mg/kg/day) was identified for hematological and systemic effects in rats (study citation not provided) exposed to etofenprox for 90 days

(NYSDEC, 2005). An uncertainty factor of 100 was applied to account for intrahuman and interspecies variation. This value is appropriate for all exposure durations.

For oral exposure, EPA calculated a chronic RfD of 0.037 mg/kg/day based on a NOEL in a chronic rat feeding study (study citation not provided). An uncertainty factor of 100 was applied. EPA's Integrated Risk Information System (IRIS) has not yet adopted this value (NYSDEC, 2005). This value is appropriate for all exposure durations.

For dermal exposure, a LOAEL of 400 mg/kg/day for skin lesions was reported (study citation not provided) in a 28-day dermal study in rats (no systemic effects were observed). An uncertainty factor of 1,000 was applied to account for the use of a LOAEL and intrahuman and interspecies variation (NYSDEC, 2005). This value is appropriate for short- and intermediate-term exposures. For long-term exposures, the chronic oral RfD was adopted for dermal exposures.

EPA has classified etofenprox as Group C, possible human carcinogen. To assess potential carcinogenic risks, EPA derived a cancer slope factor (CSF) of 5.1 x 10^{-3} per mg/kg/day based on increased thyroid follicular cell adenomas and carcinomas in a two-year rat feeding study (NYSDEC, 2005).

Insecticide Background

CASRN:	80844-07-1
Synonyms:	Ethofenprox. Ethophenprox, Ephofenprox, 1-((2-(4-Ethoxyphenyl)-2-methylpropoxy)methyl)-3-phenoxy benzene, 3-Phenoxybenzyl 2-(4-ethoxyphenyl)-2-methylpropyl ether, MTI 500, BRN, 707478121 percentEtofenprox aerosol , 1 percentEtofenprox Fogger, 2-(4-Ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether , Benzene, 1-((2-(4-ethoxyphenyl)-2-methylpropoxy)methyl)-3-phenoxy- , Benzene, 1-((2-(4-ethoxyphenyl)-2-methylpropoxy)methyl)-3-phenoxy- (9CI) RF 316 , SAN 811 I (NIH, 2005; FAO, 1993; PAN, 2005)
Chemical Group:	non-ester pyrethroid (Hemingway, 1995)
Registered Trade Names:	Carancho 2.5 EC, Polido 2.5 EC, Trebon 10 EC, Trebon 10 EW, Trefic 20 WP, Vectron 10 EW, Vectron 20 WP, Zoecon RF-316 (WHO, 2002; FAO, 1993; PAN, 2005)

Usage

Etofenprox is used as a broad spectrum insecticide to combat a wide variety of pests on an assortment of crops including rice, fruits, vegetables, corn, soybeans, and tea. Etofenprox is effective against Lepidoptera, Hemiptera, Coleoptera, Diptera, Thysanoptera, and Hymenoptera at low rates. Because of its pyrethroid-like activity, it is active against insects that are resistant to carbamate or organophosphorus insecticides, including strains of rice green leafhopper and planthoppers (WHO/FAO, 1993; FAO, 1993). Etofenprox is also used in public health applications, including mosquito control, and on livestock (WHO/FAO, 1993; Hemingway, 1995). Etofenprox is a WHO Pesticide Evaluation Scheme (WHOPES)-recommended insecticide for the indoor spraying of malaria vectors. Application of 0.1 to 0.3 mg/m^2 is effective for 3 to 6 months (WHO, 2003). Technical grade etofenprox (97 percent etofenprox) is labeled for use in pesticide formulations for use in residential, commercial, and industrial uses. Etofenprox aerosol (1 percent) is labeled to kill cockroaches, ants, fleas, ticks, spiders, and other listed insects in residential, commercial, and industrial applications (NYSDEC, 2005). Etofenprox is not a restricted use chemical (PAN, 2005).

Formulations and Concentrations

Etofenprox is available in technical grade, emulsifiable concentrates, and wettable powder formulations (WHO, 1999; FAO, 1993). Technical grade etofenprox is typically 96.3 percent etofenprox with < 1 percent impurities (FAO, 1993). It may be mixed with carriers or solvents resulting in the commercial formulations. The most common formulations are a 20 percent wettable powder and a 20 percent emulsifiable concentrate. These may be used on all crops; however 10 percent or 30 percent formulations are used in some countries (FAO, 1993). WHO indicated that the content of etofenprox in the formulated products must be declared and shall not exceed the listed standards. Technical grade etofenprox must have no less than 985 g/kg etofenprox. The wettable powder should contain > 25–100 g/kg +/- 10% of the declared content, 100–250 g/kg +/- 6% of the declared content, or > 250–500 g/kg +/- 5% of the declared content (WHO, 1999). For mosquito netting treatment, etofenprox is a WHOPES-recommended insecticide at doses of 200 mg ai/m^2 of netting of a 10 percent EW formulation. The amount of etofenprox that is recommended for treatment of mosquito netting is 30 ml of a 10 percent EW formulation (WHO, 2003).

Shelf Life

Etofenprox is stable to temperatures up to 80°C for up to 3 months. At 100°C, it degrades partially. A half-life of 4 days was calculated for radiolabeled etofenprox exposed to high intensity heat lamps (FAO, 1993).

Degradation Products

In soil, etofenprox is broken down by oxidation. The main degradation products are 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate and 2-(4-ethoxyphenyl)-2-methylpropyl 3-hydroxybenzyl ether. It is metabolized by desethylation of the ethoxyphenyl group, hydroxylation of the phenoxy ring, and oxidation of the benzyl moiety followed by cleavage of the ether linkage to form polar compounds. In animals, conjugates are formed (FAO, 1993).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Studies of adsorption and leaching of etofenprox in Yamanashi sandy loam (78 percent sand, 11 percent silt, 11 percent clay), Chiba light clay (28 percent sand, 39 percent silt, 32 percent clay), and Shizuoka light clay (43 percent sand, 26 percent silt, 31 percent clay) revealed low translocation. Unchanged etofenprox was not found in deeper layers of the soil when it was applied just before application of glass columns. When radiolabeled soil was preincubated, the majority or the radioactivity remained in the top 5 cm of soil. Unchanged etofenprox was not found in the elutes (FAO, 1993).

Under laboratory conditions the half-life of etofenprox in soil is 6 to 9 days, with only minor differences between Yamanashi sandy soil, Chiba light clay soil, and Shizuoka light clay soil. Etofenprox content decreased 15 percent over 3 weeks. Degradation occurred by oxidation to 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate and 2-(4-ethoxyphenyl)-2-methylpropyl 3-hydroxybenzyl ether. In nonsterile soil, 80 percent of the applied etofenprox was decomposed within two weeks; no degradation occurred in sterile soil (FAO, 1993).

In field studies, the half-life of etofenprox was approximately 79 days in loam soil (8.2 percent clay, 7.5 percent organic carbon), 62 days in clayish loam soil (21 percent clay, 2.4 percent organic carbon), 39 days in volcanic ash loam (10 percent clay, 6.2 percent organic carbon), and 9 days in alluvial clayish loam (2 percent clay, 2.8 percent organic carbon) (FAO, 1993).

Photodegradation may be an important fate process for etofenprox on plant surfaces. Similar degradation pathways have been shown in laboratory studies of photodegradation from glass disc surfaces and in studies on bean leaves (FAO, 1993).

Fate and Transport in Aquatic Systems

Under laboratory conditions, etofenprox is stable in aqueous solutions of 1N NaOH or 1N HCl for a period equal to or greater than 10 days (FAO, 1993). It is stable in neutral and acidic environments at 25°C and in darkness, with an estimated half-life of greater than 1 year. However, a more rapid breakdown is seen under real life conditions. In city water treated with 200 g/L etofenprox, 70 percent degradation was observed after 1 week and 93 percent after 3 weeks. The rapid degradation was attributed to the presence of sunlight.

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of etofenprox in humans. Because its toxicity and mode of action are similar to other pyrethroids, the general symptoms of pyrethroid exposure are expected to occur following acute etofenprox exposure. Technical grade etofenprox is not expected to present an acute hazard to humans under normal use conditions (WHO, 2005; WHO/FAO, 1993).

In mice, rats, and dogs, etofenprox and 1 percent Etofenprox Aerosol have low acute toxicity by oral, dermal, and inhalation routes of exposure (WHO/FAO, 1993, PAN, 2005, NYSDEC, 2005). Reported LD_{50} values for mice exposed to etofenprox (96 percent) were >107.2 for oral exposures and >2.14 g/kg for dermal (24-hour) exposures. In rats, an oral LD_{50} of >42.88 g/kg, a dermal 24-hour LD_{50} of 2.14 g/kg bw, and an inhalation LC_{50} of > 5.9 g/m^3 were reported. The oral LD_{50} in dogs was reported as >5.0 g/kg. The oral LD_{50} of Trebon 20 EC (20 percent etofenprox emulsifiable concentrate) is reported as >5 g/kg in both mice and rats, and the dermal LD_{50} is reported as > 2 g/kg in rats (WHO/FAO, 1993).

Acute oral studies of high-dose exposure to etofenprox showed central nervous system effects in both mice and rats. Dose-related decreases in spontaneous motor activity were observed in mice at high doses. In rats, a dose-related effect on EEG of the frontal lobe was seen at a similarly high dose. In rabbits, a 1 percent etofenprox formulation did not produce much skin or eye irritation. However, technical etofenprox is moderately irritating to the skin but not the eyes. No dermal sensitization was observed in tests on guinea pigs (NYSDEC, 2005; WHO/FAO, 1993). In subchronic (13-week) dietary studies in mice and rats, growth retardation and increased liver weights were observed at lower doses and hunched posture, lethargy, body tremors, and respiratory distress were reported at the highest dose tested (WHO/FAO, 1993).

Treatment

Etofenprox's toxicity and mode of action are similar to other pyrethroids. No chemical-specific data were located on the treatment of etofenprox exposure; however, generalized treatment for pyrethroids should be appropriate. Treatment of etofenprox exposure depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following etofenprox exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible. Medical personnel will treat severe intoxications

with a sedative and anticonvulsant. Ingestion of large amounts of etofenprox should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent and exposure to light should be avoided (WHO, 1999)

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to etofenprox. No compound-related effects were reported in workers occupationally exposure to unspecified concentrations of technical etofenprox for 1.5 to 5.5 years. Blood pressure measurements, X-rays, hematology measurements, blood chemistry analysis, urinalysis, and EKGs were taken and interviews conducted (WHO/FAO, 1993).

In chronic animal studies, rodents appear to be the most sensitive species (WHO/FAO, 1993). Following long-term oral exposure, systemic organ toxicity has been observed, including effects on the thyroid, kidneys, and liver in rats, mice, and dogs (NYSDEC, 2005; CalEPA, 2003; WHO/FAO, 1993). A 90-day inhalation exposure of rats resulted in increased heart, lung, liver, and kidney weights (NYSDEC, 2005). Etofenprox is not a cholinesterase inhibitor (PAN, 2005).

Etofenprox exposure does not produce significant reproductive or developmental toxicity in animals (NYSDEC, 2005; CalEPA, 2003). No adverse effects on reproductive parameters were seen in a two-generation feeding study or in segment I and II gavage study where rats were exposed to high levels in the diet and by gavage, respectively (CalEPA, 2003; WHO/FAO, 1993; NYDEC, 2005). No significant developmental toxicity in the absence of maternal toxicity has been reported following etofenprox exposure in animals (NYSDEC, 2005; CalEPA, 2003). Some developmental effects (increased incidence of malformations and visceral abnormalities) have been reported in rat offspring; however, they only occurred at doses that also caused maternal toxicity (WHO/FAO, 1993). Reduced fetal body weight and increased postimplantation loss were observed in rabbits at maternally toxic levels (NYSDEC, 2005).

Etofenprox is not mutagenic. Results from genotoxicity studies in bacteria, mammalian cells, *in vitro*, and *in vivo* in mice were all negative (WHO/FAO, 1993; CalEPA, 2003).

Cancer Endpoints

EPA has classified etofenprox as Category C, possible human carcinogen, and calculated a cancer potency slope factor of 5.1×10^{-3} per mg/kg/day (NYSDEC, 2005). The available animal data show evidence of carcinogenicity in the absence of any human data (PAN, 2005). An increased incidence of thyroid follicular cell adenomas was seen in a two-year rat feeding study (WHO/FAO, 1993; CalEPA, 2003; NYSDEC, 2005).

Toxicokinetics

Etofenprox is readily absorbed from the gastrointestinal tract of rats given oral doses. Absorption ranged from 48–93 percent; absorption is dose dependent (WHO/FAO, 1993; FAO, 1993). Dermal absorption studies in male rats revealed that more than 90 percent of the total dose of 5, 59, or 184 g/cm^2 was recovered up to 96-hours after applications of ^{14}C-labeled etofenprox. Most of the radioactivity was recovered in the skin wash prior to sacrifice. The absorbed radioactivity was less than 7 percent after 96 hours (CalEPA, 2003). Etofenprox is distributed to fat as the parent compound, where the highest tissue concentrations are observed. Following oral administration, it is rapidly excreted, mainly in feces. Within 5 days, 85 to 90 percent was excreted in the feces, with lesser amounts (3 to 4 percent) in the urine. Only 3 to 4 percent remained in the body after 5 days. Etofenprox is not excreted in bile. It is excreted unchanged in the milk of dairy cows fed diets containing etofenprox. In rats, biotransformation mainly involves desethylation of the ethoxyphenyl group, hydroxylation of the phenoxy ring and oxidation of the benzyl methylene group. Although

gastrointestinal absorption occurred at a slower rate in dogs than rats, the major routes of biotransformation were the same (WHO/FAO, 1993; FAO, 1993; CalEPA, 2003).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

No data are available on the toxicity of etofenprox in birds or other non-target terrestrial organisms.

Toxicity in Non-Targeted Aquatic Systems

Etofenprox is toxic to aquatic organisms (WHO, 1999). In fish, etofenprox is slightly to moderately toxic. Slight toxicity is supported by the reported average LC_{50} of 49,000 µg/L in Japanese eel, while moderate toxicity is supported by the reported average LC_{50} of 1,845 µg/L in Mozambique tilapia. In addition to mortality, behavioral, biochemical, and physiological changes have been reported in fish exposed to etofenprox . Behavioral changes were reported in Mozambique tilapia exposed to 1,305 µg/L of the etofenprox formulation Trebon. Biochemical changes were seen in carp exposed to 600 µg/L of a 30 percent emulsifiable concentrate of Trebon for 24 hours, and effects were seen at a mean exposure of 300 µg/L for 15 days. Hematological effects and oxygen consumption changes were seen in Mozambique tilapia at concentrations of 1,400 µg/L of 96.3 percent etofenprox (PAN, 2005)

Chronic Exposure

Due to low application rates and low persistence of etofenprox in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005). No specific chronic data are available.

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Profile for Fenitrothion:

CAS Registry Number 122-14-5

Summary

Chemical History

Fenitrothion is a general use organophosphate insecticide that is nonsystemic and nonpersistent. It is mostly used in the control of chewing and sucking insects on a wide variety of agricultural crops and in forests, as well as for public health purposes. It is also used as a residual contact spray against mosquitoes, flies, and cockroaches. Fenitrothion is used residentially to control household and nuisance insects (EXTOXNET, 1995; WHO, 2003). Fenitrothion was introduced in 1959 as a less toxic alternative to parathion, with which it shares similar insecticidal properties. Fenitrothion is used heavily in countries that have banned parathion (EXTOXNET, 1995). In the United States, the use of fenitrothion for mosquito control was voluntarily cancelled by the manufacturer in 1995 (U.S. EPA, 1995) and the only registered use is for containerized ant and roach baits (U.S. EPA, 2000b).

The primary route of occupational exposure to fenitrothion is dermal, although inhalation exposures are also possible (U.S. EPA, 1995). Exposure to fenitrothion can cause overstimulation of the nervous system due to cholinesterase inhibition. This may result in nausea, dizziness, confusion, and respiratory paralysis and death at very high exposures (U.S. EPA, 2000b).

Description of Data Quality and Quantity

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs and inhalation and dermal benchmarks) for fenitrothion. Relevant review data resources include the following

- Reregistration Eligibility Decision (RED) Fenitrothion (U.S. EPA, 1995)
- Pesticide Information Profiles (PIP) for Fenitrothion (EXTOXNET, 1995)
- Specifications for Pesticides Used in Public Health: Fenitrothion (WHO, 1999)
- Pesticide Residues in Food 2000: Fenitrothion (IPCS, 2000).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.0004	mg/kg/day	Inhalation NOAEL of 0.2 µg/L (0.2 mg/kg/day) for neurological effects in rats with UF of 100 applied and adjusted for intermittent exposure	U.S. EPA (1999a)
Acute	Oral	0.13	mg/kg/day	Acute oral RfD based on neurological effects in rats	U.S. EPA (1999a)
Intermediate	Oral	0.0013	mg/kg/day	Adopt chronic RfD for intermediate duration	U.S. EPA (1999a)
Chronic	Oral	0.0013	mg/kg/day	Chronic oral RfD for based on NOEL for systemic and neurological effects in dogs	U.S. EPA (1999a)
Acute, Intermediate, Chronic	Dermal	0.01	mg/kg/day	Dermal LOAEL of 3 mg/kg/day for dermal effects in rabbits	U.S. EPA (1999a)

For inhalation exposure, a NOAEL of 0.2 µg/L (0.2 mg/kg/day)[3] was identified in rats (Coombs et al., 1988) exposed to fenitrothion via inhalation for 6 hours per day, 5 days per week, for 90 days (U.S. EPA, 1999a; IPCS, 2000). The concentration was adjusted for intermittent exposure[4] (0.04 mg/kg/day) and an uncertainty factor of 100 was applied to account for interspecies and intrahuman variation, for an inhalation benchmark of 0.0004 mg/kg/day. This value is appropriate for all exposure durations.

For oral exposure, an acute oral RfD was estimated at 0.13 mg/kg/day based on a NOAEL of 12.5 mg/kg/day for acute neurotoxicity in rats (Beyrouty et al, 1992). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability (U.S. EPA, 1999a). A chronic oral RfD of 0.0013 mg/kg/day was developed by EPA (1995, 1999a) based on a NOAEL of 0.125 mg/kg/day for systemic effects and plasma acetylcholinesterase inhibition in a long-term feeding study in dogs (Spicer, 1986). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability (U.S. EPA, 1995, 1999a). The chronic RfD was adopted to represent intermediate-term exposures.

For dermal exposure, a LOAEL of 3 mg/kg/day for dermal irritation and desquamation of the epidermis was identified from 21-day dermal rabbit study (Suetake, 1991); no neurological effects were observed at this concentration (U.S. EPA, 1995). An uncertainty factor of 300 was applied to account for interspecies and intrahuman variability and the use of a less serious LOAEL, resulting in a dermal benchmark of 0.01 mg/kg/day. This value is appropriate for all exposure durations.

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[3] Conversion between mg/m^3 and mg/kg/day assumes, for female Wistar rats, an average body weight of 0.156 kg and inhalation rate of 0.17 m^3/day (U.S. EPA, 1988).

[4] Adjustment for intermittent exposure is the product of air concentration and exposure of 6/24 hours/day and 5/7 days/week.

Insecticide Background

CAS#	122-14-5
Synonyms:	O,O-dimethyl O-(4-nitro-m-tolyl) phosphorothioate (U.S. EPA, 1995) methylnitrophos (Eastern Europe) (EXTOXNET, 1995)
Chemical Group:	Organophosphate (EXTOXNET, 1995; U.S. EPA, 2000a)
Registered Trade Names:	Accothion, Agrothion, Bay 41831, Bayer 41831, Bayer S 5660, Cyfen, Cytel, Dicofen, Dybar, Fenitox, Fenstan, Folithion, Kaleit, Mep, Metathion, Micromite, Novathion, Nuvanol, Pestroy, Sumanone, Sumithion, and Verthion (U.S. EPA, 1995; EXTOXNET, 1995)

Usage

Fenitrothion is a broad spectrum organophosphate insecticide and acaricide (IPCS, 2000) most commonly used in agriculture to control chewing and sucking insects on crops such as rice, cereals, fruits, vegetables, stored grains, and cotton. It is also used in forested areas and to control flies, mosquitoes, and cockroaches, and in public health programs (WHO, 2004). In the United States, fenitrothion is only registered for use as a containerized ant and roach bait. In Australia, it is used on stored wheat (U.S. EPA, 2000b).

Formulations and Concentrations

There are several formulations for fenitrothion, each containing varying amounts of the active ingredient. The typical formulations for fenitrothion are dusts (2 percent , 2.5 percent, 3 percent, or 5 percent), emulsifiable concentrate (50 percent), flowable, fogging concentrate (95 percent), and wettable powder (40 or 50 percent). It is also available in granules and ultra-low-volume, oil-based liquid spray (EXTOXNET, 1995). Registered formulation types include 0.01563 percent and 1 percent pellets and granular baits. Emulsifiable concentrates are not registered in the Unites States (U.S. EPA, 2000b). The fenitrothion content for various formulations should be declared as follows: technical grade fenitrothion (no les than 910 g/kg), fenitrothion emulsifiable concentrate and wettable powder (above 250 up to 500 g/kg + 5% of declared content, above 500 g/kg + 25 g/kg) (WHO, 1999).

Shelf-Life

Like many insecticides, fenitrothion should be stored in a locked, well-ventilated facility, preferably one designated only for insecticide storage. It should not be exposed to sunlight and should be stored away from animal feed and foodstuffs (IPCS, 1991).

Fenitrothion is stable for up to two years if stored between 20 and 25°C; storage temperatures should not exceed 40°C. Fenitrothion is unstable when heated above 100°C and may undergo Pishchemuka isomerization and decompose explosively. Decomposition of fenitrothion is promoted by iron. Therefore, fenitrothion should be stored in enamel, aluminum, or glass containers. Fenitrothion is not stable in alkaline environments (EXTOXNET, 1995). Residues of fenitrothion are stable for up to 147 days in wheat and 174 days in wheat gluten when frozen (-18°C) (U.S. EPA, 1995).

Degradation Products

In water, fenitrothion is degraded through photolysis and hydrolysis, with degradation accelerated in the presence of microflora. In soil, fenitrothion is primarily broken down by biodegradation with photolysis also

playing a role (WHO, 2003, 2004). Carbon monoxide is the major degradate for aerobic soil metabolism and photolysis. The major nonvolatile degradates for aerobic soil metabolism, anaerobic aquatic metabolism, and photolysis include 3-methyl-4-nitro-phenol (approximately 1 to 22 percent of applied); aminofenitrothion (approximately 13 percent of applied); acetyl-aminofenitrothion (approximately 13 percent of applied); formylaminofenitrothion (4.9 percent of applied); o,o-dimethyl o-(3-carboxy-4-nitrophenyl)phosphorothionte (12.4 percent of applied); fenitrooxon (≤ 4.3 percent of applied); demethylate fenitrothion (approximately 1 percent of applied); and desmethylfenitrooxon (≤ 4.3 percent of applied). Other degradates are present at concentrations less than or equal to 2 percent and include o,o-dimethyl o-(3-methyl-4-nitrophenyl)phosphorothioate-3-methyl-4-nitrophenol; o-methyl (5-methyl o-(3-methyl-4-nitrophenyl)phen-phorothioate; o-methyl o-hydrogen o-(3-methyl-4-nitro-phenyl)phosphate; o,o-dimethyl o-(3-carboxy-4-nitrophenyl)phosphate; 5-methylfenitrothion; and carboxyfenitrooxon. The major degradates in pH 5 and pH 9 solutions are demethylated fenitrothion (10.3 percent of applied) and 3-methyl-4-nitrophenol (1.7 percent of applied). In pH 9 solution, the major degradate is 3-methyl-4-nitrophenol (15.1 percent of the applied), while demethylated fenitrothion accounts for up to 5.6 percent of applied. The major degradate from hydrolysis in pH 5 and pH 7 buffered solutions is demethylated fenitrothion. The major degradate in pH 9 buffered solution is 3-methyl-4-nitrophenol. Seven degradates were identified from photodegradation in soil. In loam soil, the major nonvolatile degradates from aerobic soil metabolism was 3-methyl-4-nitrophenol. Additional degradates included fenitrooxon, desmethylfenitrooxon, and 3-methyl-4-nitroanisole. The major volatile degradate was carbon monoxide (U.S. EPA, 1995).

Environmental Behavior

Fate and Transport in Terrestrial Systems

In most soil types, fenitrothion degrades rapidly with a half-life ranging from 3 to 25 days (U.S. EPA, 1995). Fenitrothion is mostly found in the top six inches of soil and is not very mobile and only slightly persistent in soil (U.S. EPA, 1995). In nonsterile muck and sandy loam soils, a half-life of less than one week is reported. Fenitrothion is intermediately mobile in soils ranging from sandy loam to clay (EXTOXNET, 1995). However, when applied to silty clay loam, silty clay, and sandy loam under laboratory conditions, fenitrothion appears to be immobile (U.S. EPA, 1995). Fenitrothion leaches very slowly into groundwater from most soils; however, some runoff can occur (WHO, 2004).

Fate and Transport in Aquatic Systems

On lakes, surface foam can trap fenitrothion from aerial spraying (EXTOXNET, 1995). In water, fenitrothion is unstable in the presence of sunlight or microbial contamination (WHO, 2003). Laboratory studies at 23°C and pH 7.5 in the dark resulted in a half-life of 21.6 days for buffered lake water and 49.5 days for natural lake water. However, in field experiments, the half-life was 1.5-2 days at pH 7.0-7.5 and 19-23°C (EXTOXNET, 1995). Phenyl labeled [^{14}C]-fenitrothion had a half-life of 4-7 days, while the anaerobic aquatic half-life is reported at 0.82 days. In fish, fenitrothion accumulates rapidly but at low concentrations (U.S. EPA, 1995).

Human Health Effects

Acute Exposure

Effects / Symptoms

Acute oral and dermal experimental data are available for human exposures to fenitrothion. No effect on acetylcholinesterase activity was observed in volunteers following a single oral dose of up to 0.33 mg/kg body weight or repeated doses of up to 0.36 mg/kg body weight/day for 4 days. Volunteers ingested technical-

grade fenitrothion via capsule at doses of 0.18 mg/kg/day followed 2 weeks to 5 months later by 0.36 mg/kg/day, with each daily dose continued for 4 consecutive treatments. No significant effect of treatment was seen on blood pressure or pulse, and observed clinical signs were not considered to be treatment related. Transient decreases in erythrocyte cholinesterase activity were observed in two volunteers, but no treatment-related changes in hematological or clinical chemistry parameters were observed. No dermal irritation and no effects on cholinesterase activity were observed in volunteers exposed to up to 0.5 mg/kg/day fenitrothion orally followed by 0.1 mg/kg/day dermally to the arms and face for 9 days (IPCS, 2000).

Case reports of humans accidentally or intentionally ingesting fenitrothion indicate that fenitrothion is lethal at oral doses of 3 g. Additionally, death from respiratory insufficiency was observed 6 days after a man ingested 60 mL of a 50 percent emulsion in a suicide attempt. Other acute oral effects included paralysis at 1.5 to 6 g. In patients exhibiting paralysis, plasma cholinesterase was inhibited by 40 percent to more than 80 percent. In patients who consumed 50 to 100 mL of a 50 percent fenitrothion solution either accidentally or in suicide attempts, 6 of 16 died within 5 to 22 days, despite receiving medical attention. Intermediate syndrome, characterized by muscular weakness affecting the neck, proximal limb, and respiratory muscles, was observed in 7 of 10 survivors. Of those with intermediate syndrome, plasma cholinesterase activity was not observed at time of hospitalization. Recovery ranged from 5 weeks to more than10 weeks in patients with intermediate syndrome, versus 2 to 4 weeks in those without (IPCS, 2000).

No clinical signs were observed in spray operators or villagers one week after exposure to a 5 percent fenitrothion spray. However, a 40–60 percent decrease in cholinesterase activity was observed in spray operators using fenitrothion indoors for 4 weeks in the absence of clinical symptoms of organophosphate toxicity. Orchard spray operators who inhaled a mean concentration of 0.011 μg/L fenitrothion for 3 consecutive days also showed no clinical signs but had lower maximum plasma concentration of fenitrothion than unexposed operators, with relatively rapid clearance from plasma (IPCS, 2000).

In animals, the acute toxicity of fenitrothion is low. The oral LD_{50} ranges from 240 to 1,700 mg/kg in rats, 715 to 1,400 mg/kg in mice, and 500 mg/kg in guinea pigs (EXTOXNET, 1995; IPCS, 2000). The acute dermal LD_{50} is reported to be 890–5,000 mg/kg in rats and greater than 3,000 mg/kg in mice (EXTOXNET, 1995; IPCS 2000). The acute inhalation LC_{50} ranges from 2.2 to 5.0 mg/L in rats (EXTOXNET, 1995; IPCS 2000). In cats, acute oral toxicity was 142 mg/kg (IPCS, 2000). Toxicity is dependent on sex and vehicle used; males are sensitive than females (IPCS, 2000). This is illustrated by the reported acute toxicity of the fenitrothion preparation Sumithion Technical (97.2 percent); the oral LD_{50} is 330 mg/kg in males and 800 mg/kg in females, and the dermal LD_{50} is 890 mg/kg in males and 1,200 mg/kg in females (U.S. EPA, 1995).

The signs of acute fenitrothion toxicity in animals are consistent with cholinesterase inhibition (IPCS, 2000). In hens, no evidence of delayed neurotoxicity or increased neurological lesions was seen following a single dose (WHO, 2004) or acute administration of Sumithion Technical (97.2 percent) (U.S. EPA, 1995). However, the fenitrothion product Sumithion 50EC has been shown to cause delayed neurotoxicity in adult rats as well as humans (EXTOXNET, 1995). In rats, cholinergic signs and erythrocyte and brain cholinesterase inhibition were seen at a number of doses, but cholinergic signs were seen only when brain cholinesterase was inhibited by more than 58 percent or erythrocyte acetyl cholinesterase was inhibited by more than 38 percent (WHO, 2004).

Technical grade fenitrothion (95 percent) does not cause dermal or ocular irritation in rabbits or dermal sensitization in guinea pigs (IPCS, 2000; U.S. EPA, 1995). However, mild dermal irritation was seen following exposure to Sumithion 8-E (77 percent ai) (U.S. EPA, 1995). Other acute effects in animals include those caused by O,O,S-trimethyl phosphorothioate, one of the contaminants of fenitrothion, including cytotoxic effects in rat lungs and modulated immune response in mice (EXTOXNET, 1995).

Treatment

Dermal exposure to fenitrothion should be treated by removing contaminated clothing, rinsing the skin with water, washing the exposed areas with soap and water, then seeking medical attention. If fenitrothion gets into the eyes, they should be rinsed with water for several minutes. Contact lenses should be removed if possible and medical attention should be sought. Ingestion of fenitrothion should be treated by rinsing the mouth and inducing vomiting if the person is conscious. Inhalation exposures require removal to fresh air and rest in a half-upright position. Artificial respiration should be administered if indicated and medical attention should be sought (PAN, 2005).

Chronic Exposure

Noncancer Endpoints

Limited data are available on the chronic toxicity of fenitrothion in humans. Chronic symptoms of toxicity in humans include general malaise, fatigue, headache, loss of memory and ability to concentrate, anorexia, nausea, thirst, loss of weight, cramps, muscular weakness, and tremors. At sufficient exposure levels, typical symptoms of cholinergic poisoning may be seen (EXTOXNET, 1995). Mild clinical signs such as nausea and dizziness and whole-blood cholinesterase inhibition were observed in spray operators following occupational exposure to fenitrothion used during a 30-day malaria control operation. However, no treatment-related effects were seen in operators spraying fenitrothion for 5 hours/day, 5 days a week, intermittently for 2 years (IPCS, 2000).

The main toxicological finding from long-term animal studies was cholinesterase activity inhibition (red blood cell, plasma, and brain) in all species studied (IPCS, 2000; U.S. EPA, 1995; EXTOXNET, 1995). Signs of poisoning and cholinergic stimulation were also reported at higher levels.

In animals, reproductive and developmental toxicity are of concern. Developmental effects were seen at doses that were maternally toxic in rats. Reduced body weight, viability, and lactation indices were seen in offspring. In rats and rabbits, no fetal toxicity or treatment-induced malformations were seen at the highest dose tested in the presence of maternal cholinergic signs and decreased body weight gain (WHO, 2004). Others have reported an increase in fetal and skeletal variations at doses causing maternal toxicity (U.S. EPA, 1998). Behavioral effects were observed in rat pups following maternal exposure to Sumithion 50EC on gestation days 7 to 15 and included differences in simple behavioral measures and complex measures, which persisted up to 104 days after birth. No effects were seen at lower levels (EXTOXNET, 1995).

Fenitrothion is not teratogenic, mutagenic, or genotoxic in chronically exposed animals and is not expected to cause those effects in humans (EXTOXNET, 1995). Additionally, fenitrothion did not induce immunotoxicity (WHO, 2004).

Cancer Endpoints

Data on the carcinogenic potential of fenitrothion indicate that it is unlikely to pose a carcinogenic risk to humans. EPA has classified fenitrothion as a Group E chemical, "evidence of noncarcinogenicity for humans" (U.S. EPA, 1995, 1999a). Evidence from animal studies suggests that fenitrothion is not carcinogenic in animals.

Toxicokinetics

Fenitrothion is readily absorbed from the intestinal tract of most mammalian species, with about 90 to 100 percent of the dose absorbed (IPCS, 2000; EXTOXNET, 1995). In rats, oral absorption is approximately 90 to 100 percent within 72 hours, while in humans, it is about 70 percent in 96 hours (IPCS, 2000). Within 24 hours of dermal application, about 45 percent of the applied dose is absorbed (WHO, 2004; IPCS, 2000). In

rats, a dermal absorption rate of slightly over 1 percent is suggested as fenitrothion disappeared rapidly during the first hour (EXTOXNET, 1995). Fenitrothion is widely distributed in the body. In rats, the highest concentrations after 48 hours are found in the liver, kidneys, and fat. It is rapidly activated and deactivated (IPCS, 2000). In the liver, fenitrothion is activated by oxidative desulfuration to the activated metabolite fenitrooxon (WHO, 2004; IPCS, 2000). It is then rapidly degraded by demethylation and hydrolysis into the inactive metabolites 3-methyl-4-nitrophenol and dimethylphosphate. Further oxidation to 3-carboxyl-4-nitrophenol is involved in a minor metabolic pathway. In dermally exposed rats, the area of highest concentration (other than skin) of fenitrothion after 31 hours was the cartilaginous part of the bones (EXTOXNET, 1995). Within 24 hours of oral exposures, up to 93 percent of the dose is excreted via the urine, and 5 to 15 percent is excreted in the feces (WHO, 2004; IPCS, 2000; U.S. EPA, 1995). In rats, rabbits, and dogs, seventeen metabolites have been isolated in the urine, and the parent compound was not detected (U.S. EPA, 1995).

Toxicokinetic studies in humans have shown the time to maximal plasma concentration was 1 hour in volunteers who ingested two capsules 12 hours apart that contained 0.09 or 0.18 mg fenitrothion/kg body weight for 4 days. The elimination half-time ranged from 2 to 3 hours for both doses. The maximal plasma concentration following a single oral dose was 0.09 mg/kg body weight 1 day after exposure and 0.84 ng/mL 4 days after exposure. Higher doses resulted in higher maximal concentrations on days 1 and 4 after exposure (1.8 ng/mL and 7.7 ng/mL, respectively). In addition, the elimination half-time of fenitrothion was 2 to 4.5 hours (WHO, 2004; IPCS, 2000). Human studies also indicate that fenitrothion does not accumulate. In humans, doses of 2.5 and 5 mg/man/day administered for 5 days were all excreted within 12 hours without accumulation. Urinary excretion of the metabolite 3-methyl-4-nitrophenol was almost complete within 24 hours in subjects given single oral doses of approximately 0.042 to 0.33 mg/kg body weight fenitrothion. Peak excretion occurred after 12 hours and plasma cholinesterase inhibition was seen in only one subject at the highest dose (EXTOXNET, 1995).

Ecological Effects

Acute Exposure

Fenitrothion has been shown to be moderately to highly toxic to birds (WHO, 2004; U.S. EPA, 1995) and highly toxic to honeybees (U.S. EPA, 1995). It is also toxic to spider mites and has a long residual action (EXTOXNET, 1995). The toxicity of fenitrothion in birds ranges from highly toxic in game birds to slightly toxic in waterfowl. The oral LC_{50} in pheasants was reported as 450–500 ppm for 2-week-old pheasants fed fenitrothion in the diet for 5 days (EXTOXNET, 1995). In bobwhite quail, an LC_{50} of 157 ppm and an LD_{50} of 23.6 mg/kg have been reported (U.S. EPA, 1995; EXTOXNET, 1995). An LD_{50} of 1,190 mg/kg is reported in mallard ducks (EXTOXNET, 1995). The oral LD_{50} for chickens is reported as 28 mg/kg and fenitrothion was negative for delayed neurotoxicity in hens (EXTOXNET, 1995). In honeybees, the oral LD_{50} is reported between 0.02 and 0.38 μg/bee. In mammals, the acute oral toxicity data indicate that fenitrothion is moderately toxic to small mammals. Fenitrothion was acutely toxic to rats at 330 to 355 mg/kg (U.S. EPA, 1995). Additionally, fenitrothion was acutely toxic to mule deer at 727 mg/kg (EXTOXNET, 1995).

Fenitrothion has been shown to be moderately toxic to both warm and coldwater fish (WHO, 2004; U.S. EPA, 1995). Acute 96-hour LC_{50} values range from 1.7 ppm for brook trout to 3.8 ppm for bluegill sunfish, while the 48-hour LC_{50} ranges from 2.0 to 4.1 mg/L in carp. In various North American freshwater fish, the 96-hour LC_{50} values range from 2 to12 μg/L (EXTOXNET, 1995). Studies have shown that the toxicity of fenitrothion in rainbow trout was dependent on the developmental stage of the fish during exposure and the water temperature. Fingerlings and adult fish were the most sensitive, the sacfry stage was intermediate, and embryos were least sensitive to the toxic effects of fenitrothion. Additionally, the toxicity increased as water

temperatures increased. In fish, sublethal effects of fenitrothion exposure include morphological and anatomical changes, behavioral changes, biochemical changes, respiratory effects, and effects on growth (EXTOXNET, 1995). Because fenitrothion breaks down rapidly, it does not accumulate in fish (WHO, 2004).

Fenitrothion is highly toxic in freshwater invertebrates. Acute exposure to 95 percent fenitrothion resulted in EC_{50}/ LC_{50} values ranging from 4.3 ppb in *Gammarus* to 11 ppb in *Daphnia magna* (U.S. EPA, 1995). It is also moderately to very highly toxic to estuarine organisms. Acute exposure to 75 percent fenitrothion resulted in EC_{50}/ LC_{50} values ranging from 1.5 ppb in pink shrimp to > 1,000 ppb in Sheepshead minnow (U.S. EPA, 1995).

Chronic Exposure

Chronic toxicity data for non-target terrestrial organisms are limited. Fenitrothion has been shown to cause reproductive impairment in birds. Chronic exposure to 17 ppm fenitrothion reduced egg production in bobwhite quail, with a NOEL of 13 ppm (U.S. EPA, 1995).

Limited data for chronic duration exposures of aquatic organisms were located. In fish, the chronic toxicity of fenitrothion is generally considered to be low (EXTOXNET, 1995). In freshwater fish, studies have reported effects in rainbow trout chronically exposed to 94.5 percent fenitrothion. A LOEL of 88 ppb was determined for weight and length effects, with a NOEL of 46 ppm. In freshwater aquatic invertebrates, chronic exposure to 94.5 percent fenitrothion resulted in a 21 day LOEL of 0.23 ppb for adult daphnid survival in *Daphnia magna* with a NOEL of 0.087 ppb (U.S. EPA, 1995).

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Profile for Lambda-Cyhalothrin:

CAS Registry Number 91465-08-6

Summary

Chemical History

The synthetic pyrethroid lambda-cyhalothrin is a relatively new addition to this insecticide group. It was developed in 1977 and consists of one enantiomeric (i.e., nonsuperimposable, mirror image) pair of isomers and is a more biologically active form than cyhalothrin (IPCS, 1990a). It is used in the control of pests, including mosquitoes, in agricultural and public and animal health settings (EXTOXNET, 1996). The risks of occupational exposures and exposures to the general public are expected to be very low if proper precautions are followed. At the recommended application rates, lambda-cyhalothrin is not expected to cause adverse environmental effects. As is typical of synthetic pyrethroids, the typical symptoms for acute exposure are neurological and include tingling, burning, or numbness sensations (particularly at the point of skin contact), tremors, incoordination of movements, paralysis or other disrupted motor functions. These effects are generally reversible because lambda-cyhalothrin beaks down rapidly in the body (IPCS, 1990a; EXTOXNET, 1996). EPA has not classified synthetic pyrethroids, including lambda-cyhalothrin, as endocrine disruptors.

Description of Data Quality and Quantity

Lambda-cyhalothrin and cyhalothrin are basically the same chemical and differ only in their stereo chemistry and the number of isomers in each mixture (U.S. EPA, 2002a). Cyhalothrin consists of four stereo isomers while lambda-cyhalothrin is a mixture of only two isomers. The two lambda-cyhalothrin isomers are contained in cyhalothrin and they represent 40 percent of the cyhalothrin mixture. The majority of toxicity studies available were conducted using cyhalothrin as the test chemical. Evidence based on subchronic studies in rats suggests that the two mixtures are not biologically different with respect to their mammalian toxicity (U.S. EPA, 2002a).

EPA and ATSDR have developed quantitative human health benchmarks for cyhalothrin (EPA's acute and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks, and ATSDR's acute and intermediate oral MRLs).

Recommended resources include:

- Environmental Health Criteria 99: Cyhalothrin (IPCS, 1990a)
- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003a)
- Pesticide Information Profiles (PIP) for Lambda-cyhalothrin (EXTOXNET, 1996)
- Specifications and Evaluations for Public Health Pesticides for Lambda-cyhalothrin (WHO, 2003)
- Integrated Risk Information System (IRIS) summary review for cyhalothrin (U.S. EPA, 2005b).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.0008	mg/kg/day	Inhalation NOAEL for neurotoxicity in rats at 0.08 mg/kg/day (0.3 µg/L) with uncertainty factor (UF) of 100 applied	U.S. EPA (2002b)
Acute	Oral	0.005	mg/kg/day	Acute RfD based on neurotoxicity in dogs	U.S. EPA (2002b)
Intermediate	Oral	0.001	mg/kg/day	Adopt chronic RfD for intermediate duration	
Chronic	Oral	0.001	mg/kg/day	Chronic RfD based on neurological effects in dogs	U.S. EPA (2002b)
Acute, Intermediate, Chronic	Dermal	0.1	mg/kg/day	Dermal NOAEL in rats with UF of 100 applied	U.S. EPA (2002b)

For inhalation exposure, a NOAEL of 0.3 µg/L (0.08 mg/kg/day) was identified for neurotoxicity, decreased body weight, and slight changes in urinalysis parameters in rats exposed to lambda-cyhalothrin via inhalation for 21 days. An uncertainty factor of 100 was applied, for an inhalation benchmark value of 0.0008 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 2002a).

For oral exposure, an acute RfD of 0.005 mg/kg/day was derived based on a NOAEL of 0.5 mg/kg/day for neurotoxicity (ataxia) observed in dogs exposed to lambda-cyhalothrin, with an uncertainty factor of 100 applied (U.S. EPA, 2002a). A chronic oral RfD of 0.001 mg/kg/day was derived based on a NOAEL of 0.1 mg/kg/day for gait abnormalities in dogs exposed to lambda-cyhalothrin, with an uncertainty factor of 100 applied (U.S. EPA, 2002a). The chronic RfD was adopted to represent intermediate exposures.

For dermal exposure, a NOAEL of 10 mg/kg/day was identified in rats dermally exposed to lambda-cyhalothrin for 21 days. An uncertainty factor of 100 was applied, for a dermal benchmark value of 0.1 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 2002a).

Background

CAS #:	91465-08-6
Synonyms:	none (WHO, 2003)
Chemical Group:	synthetic pyrethroid
Registered Trade Names:	Charge, Excaliber, Grenade, Karate, Hallmark, Icon, OMS 0321, PP321, Saber, Samurai, Sentinel, and Matador (EXTOXNET, 1996)

Usage

Lambda-cyhalothrin is a synthetic pyrethroid (IPCS, 1990a) most commonly used for pest control, especially mosquitoes; the insecticide is usually sprayed on interior walls or used to impregnate bed nets (EXTOXNET, 1996). This insecticide is a restricted use pesticide, so it can be purchased and used only by certified applicators (EXTOXNET, 1996). Lambda-cyhalothrin has adulticidal, ovicidal, and larvicidal activity (IPCS,

1990a). In addition to mosquitoes, it is effectively used to control: cockroaches, ticks, fleas, aphids, Colorado beetles, cutworms and butterfly larvae (EXTOXNET, 1996; IPCS, 1990a).

Formulations and Concentrations

There are several formulations for lambda-cyhalothrin, each containing varying amounts of the active ingredient. The typical formulations for lambda-cyhalothrin are

- Technical grade (not less than 810 g/kg lambda-cyhalothrin)
- Emulsifiable concentrate (at 20 +/- 2°C: up to 25 g/l +/- 15% declared content; > 25 g/l to 100 g/l +/- 10% of declared content)
- Wettable powder (up to 25 +/- 15% of declared content: > 25-100 +/- 10 % of declared content)
- Slow release capsule suspension (at 20 +/- 2°C: up to 25 g/l +/- 15% declared content).

The main formulation used for agricultural purposes is the emulsifiable concentrate. The wettable powder formulation is mainly used for public health reasons (WHO, 2003). Lambda-cyhalothrin is commonly mixed with buprofezin, pirimicarb, dimethoate, or tetramethrin, resulting in the usual product (WHO, 2003; EXTOXNET, 1996).

Shelf-Life

This insecticide, like many others, needs to be stored in a cool, dry, and well-ventilated facility (IPCS, 1990a). Lambda-cyhalothrin should not be stored or transported with foodstuffs and household supplies to the limit the potential for cross contamination and human exposure (IPCS, 1990a).

Degradation Products

In the environment, lambda-cyhalothrin degrades through biological and photochemical reactions (IPCS, 1990a). Biological reactions are thought to be more important. Lambda-cyhalothrin will degrade rapidly in soils, remain relatively stable in water, and is usually not found in air due to its low vapor pressure. The main degradation products are 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2, 2-dimenthyl-cyclopropanecorboxylic acid, the amide derivative of cyhalothrin, and 3-phenoxybenzoic acid. The degradation is a result of the cleavage of the ester linkage to give two main degradation products, which are further degraded to carbon dioxide. Lambda-cyhalothrin degrades fairly quickly in alkaline conditions, in comparison to neutral or acidic media. It is strongly absorbed in soils and sediments with little tendency for bioaccumulation (IPCS, 1990a).

In water, lambda-cyhalothrin is stable at pH 5. Racemization at the alpha-cyano carbon occurs at pH 7 to pH 9, creating a one to one mixture of enantiomer pairs A and B. The ester bond is hydrolyzesd at pH 9. Additionally, a moderately high rate of photolysis is seen in dilute aqueous solutions (IPCS, 1990a).

Environmental Behavior

Fate and Transport in Terrestrial Systems

In most soil types, lambda-cyhalothrin is not very mobile. Its high reported organic carbon partitioning coefficient (Koc) value reflects its strong affinity for soil. It is retained more in soil with low sand content or high organic matter content (EXTOXNET, 1996). Studies have shown that lambda-cyhalothrin and its degradation products do not leach through soils into groundwater nor are they transported to other compartments of the environment following agricultural uses (IPCS, 1990a).

Lambda-cyhalothrin is moderately persistent in soil with a soil half-life ranging from 4 to 12 weeks. A longer in-field half-life of approximately 30 days is reported for most soils (EXTOXNET, 1996). The half-life is variable because it is dependent on the availability of sunlight, which speeds degradation (IPCS, 1990a).

Fate and Transport in Aquatic Systems

Lambda-cyhalothrin is not expected to be prevalent in surface or groundwater because it has extremely low water solubility and binds tightly to soil. Lambda-cyhalothrin enters surface water largely through surface runoff. Even so, lambda-cyhalothrin is most likely to stay bound to sediment and settle to the bottom. Studies have shown that hydrolysis of lambda-cyhalothrin occurs rapidly at a pH of 9 but not at a pH of 7, though isomerization was observed at a pH of 7. No hydrolysis or isomerization was seen at a pH of 5.

Human Health Effects

Acute Exposure

Effects/Symptoms

No data on accidental human poisonings have been reported. Additionally, no quantitative epidemiological studies are available (IPCS, 1990a). However, under normal use conditions, acute exposure to lambda-cyhalothrin is not expected to represent a hazard in humans. Transient skin sensations such as periorbital facial tingling and burning have been reported following direct skin exposure in laboratory workers and manufacturing workers handling synthetic pyrethroids. This sensation is possibly due to repetitive firing of sensory nerve terminals and usually lasts for a few hours up to 72 hours post-exposure. No neurological abnormalities have been observed upon medical examination (IPCS, 1990a). Lambda-cyhalothrin can irritate the eyes, skin, and upper respiratory tract. Additionally, oral exposure can cause neurological effects, including tremors and convulsions. Ingestion of liquid formulations may result in aspiration of the solvent into the lungs, resulting in chemical pneumonitis. Based on the acute oral toxicity data, lambda-cyhalothrin has been classified as "Moderately Hazardous" (Class II) (WHO, 2003).

In animals, the technical form of lambda-cyhalothrin is moderately toxic; however, toxicity depends on both the formulation (concentration of active ingredient and solvent vehicle) and the route of exposure (EXTOXNET, 1996). Laboratory data indicate that acute oral exposure to lambda-cyhalothrin is moderately to highly toxic in rats and mice and that mice are more susceptible to the toxic effects than rats (WHO, 2003). The oral LD_{50} for lambda-cyhalothrin in corn oil has been reported to range from 56 mg/kg in female rats up to 79 mg/kg in males. A similar LD_{50} is reported for technical grade lambda-cyhalothrin in rats at 64 mg/kg (EXTOXNET, 1996). The oral LD_{50} in mice is reported as 20 mg/kg (IPCS, 1990a). The effects of acute oral exposure are typical of pyrethroid toxicity, including abnormal motor function (WHO, 2003).

Acute inhalation exposures are also highly toxic to animals (WHO, 2003). In the formulated product Karate, the 4-hour LC_{50} in rats is reported as 0.175 mg/L in females and 0.315 mg/L in males (EXTOXNET, 1996).

Lambda-cyhalothrin is less toxic in animals via acute dermal exposure (WHO, 2003). In rats, dermal LD_{50}s of 632 mg/kg for males and 696 mg/kg for females have been reported for the technical product. Studies have also shown the technical product produced no skin irritation to rabbits and is nonsensitizing in guinea pigs. Mild eye irritation was observed in rabbits. However, dermal exposure to the formulated product Karate causes severe primary skin irritation in rabbits and mild skin sensitization in guinea pigs. Other acute dermal effects are related to the nervous system and include tingling, burning sensations, or numbness (EXTOXNET, 1996).

Treatment

Lambda-cyhalothrin and its breakdown products can be detected in blood and urine, but only within a few days of the last exposure (ATSDR, 2003a). Dermal exposure to lambda-cyhalothrin exposure should be treated by removing contaminated clothing and washing the exposed areas with soap and water. If lambda-cyhalothrin gets into the eyes, they should be rinsed with water for several minutes. Contact lenses should be removed if possible and medical attention should be sought. Vomiting should not be induced following ingestion of lambda-cyhalothrin, and medical attention sought. Inhalation exposures require removal to fresh air and rest (IPCS, 1990b)

Chronic Exposure

Noncancer Endpoints

Based on the available data, it is unlikely that lambda-cyhalothrin would cause chronic effects in humans under normal conditions. No specific target organs have been identified in the available chronic studies (EXTOXNET, 1996). Decreased body weight gain and mild neurological effects have been observed in some animal studies (EXTOXNET, 1996; IPCS, 1990a).

Lambda-cyhalothrin is not expected to be teratogenic, mutagenic, or genotoxic in humans. Studies in animals have found no teratogenic or fetotoxic effects in rats or rabbits. Additionally, it was negative in five test strains in the Ames mutagenicity assay (IPCS, 1990a). No mutagenic or genotoxic effects were seen in other in vitro cytogenic assays or chromosomal aberration tests (EXTOXNET, 1996).

Cancer Endpoints

Data on the carcinogenic potential suggest that lambda-cyhalothrin is not carcinogenic in humans. In rats and mice exposed to cyhalothrin, no carcinogenic effects were observed. EPA has classified lambda-cyhalothrin as a Group D chemical, "not classifiable as to human carcinogenicity" (U.S. EPA, 2002a).

Toxicokinetics

Animal studies have been have been conducted in various species to investigate the toxicokinetics of cyhalothrin and lambda-cyhalothrin. Oral cyhalothrin is readily absorbed, metabolized thoroughly, and eliminated as polar conjugates in the urine (IPCS, 1990a). Studies with lambda-cyhalothrin have shown that it also is rapidly metabolized into less toxic water-soluble compounds and excreted in the urine and feces (EXTOXNET, 1996). In mammals, cyhalothrin is metabolized as a result of ester cleavage to cyclopropanecarboxylic acid and 3-phenoxybenzoic acid, and eliminated as conjugates. Tissue levels decline after exposure stops and residues in the body are low (IPCS, 1990a).

Ecological Effects

Acute Exposure

Toxicity to Non-Target Terrestrial Organisms

Like other synthetic pyrethroids, lambda-cyhalothrin has been shown to be toxic to honey bees but has little effect on birds and domestic animals (EXTOXNET, 1996). In birds, the toxicity of lambda-cyhalothrin ranges from nontoxic to slightly toxic. Oral LD_{50} values in mallard duck are reported as greater than 3,950 mg/kg. Dietary LC_{50} values of 5,300 ppm are reported in bobwhite quail. Additionally, there is no evidence of lambda-cyhalothrin accumulation in bird tissues or in eggs (EXTOXNET, 1996). Lambda-cyhalothrin has shown mixed toxicity to other non-target terrestrial organisms. It is extremely toxic to honey bees, with a

contact LD_{50} of 0.9 µg/bee and an oral LD_{50} of 38 ng/bee (EXTOXNET, 1996), but has no adverse effect on earthworms (IPCS, 1990a).

Toxicity to Aquatic Organisms

Like other synthetic pyrethroids, lambda-cyhalothrin has been shown to be quite toxic under laboratory conditions to both cold and warm water fish. Acute 96-hr LC_{50} values range from 0.2 to 1.3 µg/L. It is also highly toxic to aquatic arthropods with 48-hr LC_{50} ranging from 0.008 to 0.4 µg/L (IPCS, 1990a; WHO, 2003). In the field, however, these effects are not likely to occur under the recommended use scenarios (WHO, 2003). No serious adverse effects have been observed due to the low rates of application and the lack of persistence in the environments (IPCS, 1990a). Accumulation studies have shown that although bioaccumulation is possible in fish, it is unlikely due to the rapid metabolism of lambda-cyhalothrin (EXTOXNET, 1996).

Chronic Exposure

Toxicity to Non-Target Terrestrial Organisms

No data were located on the chronic toxicity to non-target terrestrial organisms.

Toxicity to Aquatic Organisms

No data for chronic duration exposures of aquatic organisms were located; however, a subchronic study in Sheepshead minnow embryos and larvae showed no effect on hatchability or larval survival when exposed to up to 0.25 µg/L through 28 days post hatching. A significant effect on larval weight was observed at 0.38 µg/L. In an additional subchronic exposure study, survival, growth, and reproduction of *Daphnia magna* were seen at 40 ng/L but not at 2.5 ng/L (IPCS, 1990a).

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Profile for Malathion:

CAS Registry Number 121-75-5

Summary

Chemical History

Malathion is an organophosphate pesticide used in a wide variety of applications, including agricultural, veterinary, and public health uses. In pest eradication programs, malathion is used to eradicate mosquitoes, Mediterranean fruit flies, and boll weevil (ATSDR, 2003b). The primary target of malathion is the nervous system; it causes neurological effects by inhibiting cholinesterase in the blood and brain. Exposure to high levels can result in difficulty breathing, vomiting, blurred vision, increased salivation and perspiration, headaches, and dizziness (U.S. EPA, 2005c). Loss of consciousness and death may follow very high exposures to malathion (ATSDR, 2003b).

Description of Data Quality and Quantity

Several comprehensive reviews on the toxicity of malathion have been prepared or updated in recent years:

- EPA risk assessment for the Reregistration Eligibility Decision (RED) document (U.S. EPA, 2005c)
- IRIS summary review (U.S. EPA, 2005d)
- *Toxicological Profile for Malathion* (ATSDR, 2003b)
- *Specifications and Evaluations for Public Health Pesticides for Malathion* (WHO, 2003).

EPA and ATSDR have developed quantitative human health benchmarks (EPA's acute and chronic oral RfDs, short-, intermediate-, and long-term dermal and inhalation benchmarks and ATSDR's acute inhalation and intermediate oral and inhalation MRLs).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.026	mg/kg/day	Inhalation LOAEL for respiratory effects in rats of 25.8 mg/kg/day (0.1 mg/L) with UF of 100 and SF of 10 applied	U.S. EPA (2005c)
Acute	Oral	0.14	mg/kg/day	Acute RfD based on neurological effects in rats	U.S. EPA (2005c)
Intermediate	Oral	0.03	mg/kg/day	Adopt chronic oral RfD for intermediate duration	
Chronic	Oral	0.03	mg/kg/day	Oral RfD based on neurological effects in rats	U.S. EPA (2005c)
Acute, Intermediate, Chronic	Dermal	0.05 (child) 0.5 (adult)	mg/kg/day	Dermal NOAEL for neurological effects in rabbits with UF of 100 applied (for children, an additional SF of 10 was also applied)	U.S. EPA, 2005c

For inhalation exposure, a LOAEL of 0.1 mg/L (25.8 mg/kg/day, assuming absorption via inhalation route is equivalent to oral absorption) for histopathological lesions in the nasal cavity and larynx of rats was identified for malathion. Uncertainty factors of 10 each were applied to account for interspecies and intrahuman variability and a safety factor of 10 to account for the extrapolation from LOAEL to NOAEL

and the severity of effect (U.S. EPA, 2005c). This value is appropriate for short- (1–30 days) and intermediate-term (1–6 months) inhalation exposures; this value was also adopted for chronic (long-term, >6 months) exposures.

For oral exposure, an acute oral RfD of 0.14 mg/kg/day was derived based on the inhibition of red blood cell (RBC) cholinesterase in rats and uncertainty factors of 10 each to account for interspecies and intrahuman variability (U.S. EPA, 2005d). A chronic oral RfD of 0.03 mg/kg/day was derived based on the RBC cholinesterase inhibition in rats and uncertainty factors of 10 each to account for interspecies and intrahuman variability (U.S. EPA, 2005c).

For dermal exposures, a NOAEL of 50 mg/kg/day for plasma, RBC, and brain cholinesterase inhibition in rabbits exposed dermally was identified for malathion. Uncertainty factors of 10 each to account for interspecies and intrahuman variability were applied; a safety factor of 10 to account for susceptibility of young was applied to be protective of children (U.S. EPA, 2005d). This value is appropriate for short- (1–30 days), intermediate- (1–6 months), and long-term (>6 months) dermal exposures.

Background

CASRN:	121-75-7
Synonyms:	1, 2-Di (ethoxycarbonyl) ethyl, *O, O*-dimethyl, phosphorodithioate (ATSDR, 2003b), maldison, malathon, mercaptothion, mercaptotion, carbofos (WHO, 2003)
Chemical Group:	organophosphate
Registered Trade Names:	Cekumal, Fyfanon®, Malixol®, Maltox® (ATSDR, 2003b); Celthion, Cythion, Dielathion, El 4049, Emmaton, Exathios, Fyfanon and Hilthion, and Karbofos (EXTOXNET, 1996)

Usage

Malathion is a nonsystemic, broad-spectrum organophosphate insecticide used to control sucking and chewing pests in agricultural and horticultural applications (WHO, 2003). It is also used to control household insects, fleas, ectoparasites in animals, and head and body lice in humans (EXTOXNET, 1996). A major public health use of malathion is to eradicate mosquitoes and Mediterranean fruit flies, with ground application and aerial spraying being the most common methods of application (ATSDR, 2003b).

Formulations and Concentrations

There are several typical formulations for malathion, each formulation varying in the amount of active ingredient (ai) it contains. The typical formulations for malathion are (U.S. EPA, 2005c; ATSDR, 2003b)

- Technical grade (91–95 percent ai)
- Dust (1–10 percent ai)
- Emulsifiable concentrate (3–82 percent ai)
- Ready-to-use liquid (1.5–95 percent ai)
- Pressurized liquid (0.5–3 percent ai)
- Wettable powder (6–50 percent ai).

Malathion may also be used to formulate other pesticides (ATSDR, 2003b).

Degradation Products

In the United States, technical grade malathion is >90 percent pure and contains less than 5 percent impurities (reaction byproducts and degradation products). As many as 14 different impurities have been identified in technical grade malathion (ATSDR, 2003b), some of which are toxic themselves and potentiate the toxicity of malathion. Because of their toxicological properties, relevant impurities include malaoxon (CASRN 1634-78-2), isomalathion (CASRN 3344-12-5), MeOOSPS-triester (CASRN 2953-29-9), MeOOOPS-triester (CASRN 152-18-1), MeOSSPO-triester (CASRN 22608-53-3), and MeOOSPO-triester (CASRN 152-20-5). Both isomalathion and malaoxon are more toxic than malathion, and isomalathion is a potentiator of malathion (WHO, 2003). Degradation products of malathion include dimethyl phosphate, dimethyldithiophosphate, dimethylthiophosphate, isomalathion (a metabolite of malathion), malaoxon, and malathion dicarboxylic acid and are generally the result of impurities or exposure to extreme storage conditions (PAN, 2005).

In dustable powder form, malathion levels decrease when it is stored and it is converted into the more toxic metabolite isomalathion (WHO/FAO, nd). In the environment, malathion is usually broken down into other chemical compounds within a few weeks by water, sunlight and bacteria found in the soil and water (ATSDR, 2003b). At pH 5.0, malathion is reasonably stable to hydrolysis. It hydrolyzes rapidly at pH 7.0 and above or below pH 5.0 (WHO, 2003; ATSDR, 2003b). It is stable in an aqueous solution that is buffered at a pH of 5.26 (WHO/FAO, nd). In air, malathion is broken down by reacting with sunlight as well as other chemicals found naturally in the air (ATSDR, 2003b). Malathion is generally stable to photolysis (WHO, 2003).

Shelf Life

Malathion levels decline over time during storage. The extent of the decline depends on the type of formulation, as does the increase in isomalathion levels. Technical grade malathion stored at 20°C for 25–30 months lost 3–8 g/kg, while isomalathion levels increased 2.2-2.4 mg/kg. Levels of other impurities did not increase significantly. Malathion stored for 14 days at 54°C declined 2.6 percent as an emulsifiable concentrate, 2.8 percent as a emulsion (oil in water), and 5 percent as a dustable powder, while isomalathion levels increased 0.11 percent, 0.095 percent, and 1.35 percent, respectively (WHO, 2003).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Malathion is released directly into the air during aerial application to target areas such as crops or residential areas. It may also be released via volatilization from crop and ground surfaces. Aerial applications may also release malathion into the soil by way of spray droplets that reach the surface of the soil. This may include spraying and fogging applications. Malathion may also be released into the soil as a consequence of wet deposition applications or when improperly disposed of (ATSDR, 2003b).

In air, malathion may be transported from the site of application to other areas by wind and precipitation. In soils, malathion is moderately to highly mobile, indicating a potential to readily move from soil into groundwater. However, because malathion degrades rapidly in the environment, movement from soil to groundwater is not a significant concern (ATSDR, 2003b).

Malathion degrades through atmospheric photo-oxidation, hydrolysis, and biodegradation. (ATSDR, 2003b). In the atmosphere, malathion breaks down rapidly in sunlight, with a half-life of 1.5 days. In soil, malathion is of low persistence with an average half-life of 6 days. It degrades rapidly depending on the degree of soil binding, which is generally moderate (EXTOXNET, 1996). Malathion degrades more quickly in moist soil (ATSDR, 2003b). The persistence of malathion in vegetation depends largely on the lipid content of the plant. The degradation process is increased with moisture content (EXTOXNET, 1996).

Fate and Transport in Aquatic Systems

Malathion may be released into surface waters through direct applications, spills, runoff from sprayed areas, wet deposition from rain, manufacturing or processing facilities, and wastewater releases (ATSDR, 2003b). The water solubility of malathion is 148 mg/l at 25°C. At pH 5, it is reasonably stable to hydrolysis; however, as pH increases, malathion hydrolyzess more readily (WHO, 2003). Because it is highly soluble and binds moderately to soil, malathion may also pose a risk to groundwater or surface waters (EXTOXNET, 1996).

In water, malathion degrades relatively quickly due to the action of the water as well as bacteria in the water (ATSDR, 2003b). In water, malathion breaks down into mono- and dicarboxylic acids. However, degradation also depends on the temperature and pH of the water. In river water, malathion breaks down in 1 week, while it is stable in distilled water for 3 weeks. Degradation increases with water temperature, alkalinity, and salinity of the water. Because of its short half-life in water, malathion is not expected to bioaccumulate in aquatic organisms (EXTOXNET, 1996).

Human Health Effects

Acute Exposure

Effects/Symptoms

Similar to other organophosphates, malathion is a cholinesterase inhibitor and interferes with the normal functioning of the nervous system. Malathion exhibits low acute toxicity via ingestion, dermal, and inhalation exposures (ATSDR, 2003b). Human volunteers fed very low doses of malathion for 6 weeks showed no significant effects on blood cholinesterase activity (ATSDR, 2003b). However, acute exposure to high concentrations can cause numbness, headaches, sweating, abdominal cramps, blurred vision, difficulty breathing, respiratory distress, loss of consciousness, and occasionally death. Acute exposure data for humans are limited and come from case reports of accidental poisonings (ATSDR, 2003b).

Several factors affect the toxicity of malathion, including the product purity, route of exposure, gender, and the amount of protein in the diet. Animal studies have shown that malathion is only slightly toxic following acute oral and dermal exposures, with reported LD_{50} values in rats of 1,000–10,000 mg/kg and 400–4,000 mg/kg, respectively. Additionally, as protein levels in the diet decrease, malathion toxicity increases. Females have been shown to be more susceptible to malathion toxicity than males due to differences in metabolism, storage, and excretion (EXTOXNET, 1996). It is uncertain whether children are more susceptible to the toxic effects of malathion; however, animal studies have shown that very young animals are more susceptible to the effects of malathion than older ones when exposed to high levels (ATSDR, 2003b). Weanling male rats acutely exposed to malathion were twice as susceptible to malathion as adults (EXTOXNET, 1996).

Treatment

Exposure to malathion may be determined through laboratory tests of urine and blood that measure breakdown products of malathion in urine or cholinesterase levels in blood (ATSDR, 2003b).

Long-term deleterious effects may be avoided if people exposed to high amounts of malathion are given the appropriate treatment quickly after exposure (ATSDR, 2003b). Oral exposure to malathion should be treated with rapid gastric lavage unless the patient is vomiting. Dermal exposures should be treated by washing the affected area with soap and water. If the eyes have been exposed to malathion, flush them with saline or water. People exposed to malathion who exhibit respiratory inefficiency with peripheral symptoms should be treated via slow intravenous injection with 2–4 mg atropine sulfate and 1,000–2,000 mg pralidoxime chloride or 250 mg toxogonin (adult dose). Exposure to high levels of malathion that result in respiratory distress,

convulsions, and unconsciousness should be treated with atropine and a reactivator. Morphine, barbiturates, phenothiazine, tranquillizers, and central stimulants are all contraindicated (WHO/FAO, nd).

Chronic Exposure

Noncancer Endpoints

Most chronic human data come from studies of workers who are exposed to malathion via inhalation or dermally. Chronic exposure data in both humans and animals indicate that the main target of malathion toxicity is the nervous system (ATSDR, 2003b). A two-year rat study showed no adverse effects other than cholinesterase enzyme depression (EXTOXNET, 1996). Chronic animal studies have shown no reproductive or developmental toxicity at doses of malathion that are not maternally toxic. Malathion has been shown to be a contact sensitizer. Recent animal studies indicate that malathion can affect immunological parameters at doses that are lower than those that cause neurotoxicity (ATSDR, 2003b).

Cancer Endpoints

EPA has classified malathion as "suggestive evidence of carcinogenicity" (U.S. EPA, 2005c). While some studies indicate an increased incidence of some forms of cancer in people who are regularly exposed to malathion, such as those exposed occupationally, there is no conclusive evidence that malathion causes cancer in humans. In one study, rodents fed very high doses of malathion in their diet had increased incidences of liver tumors (ATSDR, 2003b; U.S. EPA, 2005c).

Toxicokinetics

Malathion is absorbed via inhalation, the gastrointestinal tract, and dermally (WHO/FAO, 1997). Dermal absorption is dependent on the site and dose applied (ATSDR, 2003b). Malathion is broken down in the liver into metabolites. One of its metabolites is malaoxon, from which malathion exhibits its toxic effects via cholinesterase inhibition (ATSDR, 2003b; U.S. EPA, 2005c; WHO/FAO, 1997). Neither malathion nor its metabolites tend to accumulate in the body and are mostly excreted within a few days (ATSDR, 2003b). Malathion is excreted mostly in the urine with a small amount being excreted in the feces. A very small amount may also be excreted in breastmilk. Metabolites excreted include the monoacid and diacid of malathion, demethyl malathion, dimethyl phosphate, and O,O-dimethylphosphorothioate. In feces, the majority of material excreted is malathion with a smaller amount being malaoxon (WHO/FAO, 1997)

Ecological Effects

Acute Exposure

Malathion is not expected to pose a hazard to birds and mammals from acute dietary exposure. Malathion exhibits low to moderate toxicity to birds (U.S. EPA, 2005e). Acute oral LD_{50} values in various bird species include blackbirds and starlings (over 100 mg/kg), pheasants (167 mg/kg), chickens (525 mg/kg), and mallards (1,485 mg/kg). Malathion is rapidly metabolized by birds, with 90 percent being excreted in the urine within 24 hours. The toxicity of malathion to reptiles has not been evaluated, but the avian toxicity thresholds have been used to estimate the hazard. Acute effects were reported in one study of the Carolina anole and another on developing snapping turtle embryos (U.S. EPA, 2005e). Malathion is extremely toxic to beneficial insects, including honeybees (U.S. EPA, 2005e; EXTOXNET, 1996).

Malathion also has a wide range of toxicity to species in the aquatic environment, from being quite toxic to walleye with a 96 hr LC_{50} of 0.06 mg/L to being slightly toxic in goldfish with a 96 hr LC_{50} of 10.7 mg/L (EXTOXNET, 1996). In invertebrates and amphibians in their aquatic stages, malathion is also found to be highly toxic. In aquatic invertebrates, EC_{50} values range from 1 μg/L to 1 mg/L. However, since malathion

has a very short half-life, there is little potential for bioconcentration in aquatic organisms (EXTOXNET, 1996). Malathion is also highly toxic to the larvae of terrestrial, non-target insects that have aquatic early life stages (U.S. EPA, 2005e).

Chronic Exposure

Although not persistent in the environment, birds may be chronically exposed because current labels do not restrict consecutive applications, intervals, or avoidance of nesting birds. Sublethal effects to birds may include reduced nesting behavior, disorientation, and loss of motor coordination. Studies have shown that chronic malathion exposure in the diet of terrestrial avian species causes moderate toxicity. Bobwhite quail exposed to 350 ppm for 10 weeks exhibited regressed ovaries, enlarged or flaccid gizzards, and a reduction in number of eggs that hatched. At higher exposures, a reduction in the number of eggs produced, viability of embryo, and an increase in cracked eggs was observed, while studies in waterfowl showed low toxicity (U.S. EPA, 2005e).

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Profile for Methoprene:

CAS Registry Number 40596-69-9

Summary

Chemical History

Methoprene is a larvicide and growth regulator that is used in agricultural, horticultural, and public health applications (HSDB, 2005; EXTOXNET, 1996). It is considered a biochemical pesticide because it acts by interfering with the life cycle of the insect instead through direct toxicity. It regulates growth by preventing insects from reaching maturity or reproducing (U.S. EPA, 2005, 2002, 2001, 1991a, 1991b; ATSDR, 2005; EXTOXNET, 1996; HSDB, 2005). Methoprene was first registered for use in the United States in 1975; there are currently 13 registered products. EPA has classified methoprene as toxicity class IV or slightly to almost nontoxic (EXTOXNET, 1996). In food production, methoprene is used on meat, milk, eggs, mushrooms, peanuts, rice, and cereals. As food additive, it prevents the breeding of hornflies in manure. In water, methoprene is used to control mosquito larvae as well as various flies, moths, beetles, and fleas (ATSDR, 2005; EXTOXNET, 1996; U.S. EPA, 2002, 2001, 1991a, 1991b). Methoprene is also used to on mammalian pets to control ectoparasites (U.S. EPA, 2005). It is available as a suspension, emulsifiable and soluble concentrate formulations, briquettes, pellets, sand granules, liquids aerosols, and bait (U.S. EPA, 2002; EXTOXNET, 1996).

Methoprene is selective, stable, and potent but not persistent in the environment or toxic to mammals. It presents no long-term hazard other than to the target species (U.S. EPA, 1991a, 1991b; WHO/FAO, n.d.). It has low potential for acute oral or inhalation toxicity. It is not a skin or eye irritant or skin sensitizer and is of low acute dermal toxicity. No adverse effects have been seen in humans or other non-target species (U.S. EPA, 2005, 2001, 1991a, 1991b). No chronic, oncogenetic, reproductive, developmental, or mutagenic effects have been seen in animals. In mammals it is rapidly and completely metabolized (U.S. EPA, 1991a). In mosquito control uses, there is little chance for human exposure because methoprene is applied directly to ditches, ponds, marshes, or flood areas that are not used for drinking water (U.S. EPA, 2002). Humans can be exposed to methoprene in small amounts through the food supply; through mixing, loading, or application of the pesticide; or while working with treated crops. Methoprene used in mosquito control does not pose a high risk of toxicity to wildlife or the environment. It is of low toxicity to birds and fish and nontoxic to bees; however, it is highly acutely toxic to aquatic invertebrates under laboratory conditions (U.S. EPA, 2005, 2002, 1991a, 1991b).

Description of Data Quality and Quantity

An extensive toxicity database has been compiled for methoprene, which includes acute toxicity batteries, irritation/sensitization studies, subchronic feeding studies, developmental and reproductive toxicity studies, mutagenicity studies, chronic feeding studies, lifetime carcinogenicity studies, and special studies on metabolism and fate and potential for endocrine disruption (U.S. EPA, 2001). Reviews on the toxicity of methoprene have been prepared:

- Registration Eligibility Document Isopropyl (2E, 4E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate (Referred to as Methoprene) (U.S. EPA, 1991a)
- Toxicologic Information About Insecticides Used for Eradicating Mosquitoes (West Nile Virus Control): Methoprene (ATSDR, 2005)
- Residues in Food – 1984. Toxicological Evaluations – Methoprene (WHO/FAO, 1984)

- Data Sheet on Pesticides No. 47. Methoprene (WHO/FAO, n.d.)
- Pesticide Information Profiles: Methoprene (EXTOXNET, 1996)
- The Pesticide Action Network (PAN) Pesticide Database (PAN, 2005).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	25	mg/kg/day	Inhalation NOAEL in rats with a UF of 100 applied	
Acute, Intermediate, Chronic	Oral	0.4	mg/kg/day	Chronic oral RfD based on liver effects in mice	U.S. EPA (1991a)
Acute, Intermediate, Chronic	Dermal	1	mg/kg/day	Dermal NOAEL of 100 mg/kg in rabbits with a UF of 100 applied	

For inhalation exposure, a NOAEL of 20 mg/L (21,000 mg/kg/day)[5] was identified in rats exposed to methoprene via inhalation for 4 hours per day, 5 days per week for 3 weeks (Olson and Willigan, 1972; ATSDR, 2005). The concentration was adjusted for intermittent exposure[6] (2,500 mg/kg/day) and an uncertainty factor of 100 was applied to account for interspecies and intrahuman variation, for an inhalation benchmark of 25 mg/kg/day. This value is appropriate for all exposure durations.

For oral exposure, a chronic oral RfD of 0.4 mg/kg/day was derived based on a NOAEL of 37.5 mg/kg/day for liver effects (pigmentation) in mice exposed to methoprene for 18 months (Wazeter and Goldenthal, 1975), with an uncertainty factor of 100 applied to account for interspecies and intrahuman variability (U.S. EPA, 1991a). The RfD was adopted to also represent acute and intermediate exposures.

For dermal exposure, a NOAEL of 100 mg/kg was identified in a 30-day rabbit study (Nakasawa et al., 1975). The LOAEL for the study was 300 mg/kg for erythema at the application site (ATSDR, 2005). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability. This value is appropriate for acute, intermediate, and chronic dermal exposures.

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5 Conversion between mg/m^3 and mg/kg/day assumes, for Wistar rats (species not specified, but Wistars represent the median body weight for laboratory rats), an average body weight of 0.187 kg and inhalation rate of 0.2 m^3/day (U.S. EPA, 1988).

6 Adjustment for intermittent exposure is the product of air concentration and exposure of 4/24 hours/day and 5/7 days/week.

Insecticide Background

CASRN:	40596-69-9
Synonyms:	isopropyl (E,E)-(RS)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate, ZR-515; ENT-70460, 1-Methylethyl (E,E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate, 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, 1-methylethyl ester, (E,E)- , 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, ispropyl ester, (E,E)-, Isopropyl (2E,4E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate, Isopropyl (2E,4E)-11methoxy-3,7,11-trimethyl-2-4 dodecadienoate, Isopropyl (2E,4E)-11methoxy-3,7,11-trimethyl-2-4 dodecadienoate (methoprene), Isopropyl (E,E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate, Methopreen, Methopren, Methoprene, Methoprene (ANSI), Methoprene Isopropyl (WHO/FAO, 1984; PAN, 2005)
Chemical Group:	Not available (EXTOXNET, 1996)
Registered Trade Names:	Altosid, Altosid Bruquets, Altosid CP10, Altosid SR 10, Altosid IGR, Altosand, Apex, Diacon, Dianex, Extinguish, Fleatrol, Kabat, Manta, Minex, Ovitrol, Pharoid, Precor (EXTOXNET, 1996; U.S. EPA, 2001; WHO/FAO, 1984, n.d; PAN, 2005; HSDB, 2005)

Usage

Methoprene is an insect growth regulator used indoors and outdoors to control a broad spectrum of insect pests in agricultural, horticultural, public health, and household applications. It is used on both food and nonfood crops, ornamentals, livestock, and mammalian pets (WHO/FAO, 1984; U.S. EPA, 2001, 2005; HSDB, 2005). Pest species it is used to control include mosquitoes, horn flies, beetles, tobacco moths, sciarid flies, fleas (eggs and larvae), fire ants, pharoah ants, midge flies, boll weevils, lice, leaf hoppers, plant hoppers, cucumber beetles, cigarette beetles, mites, Indian meal moths, and others. In public health applications, the most important uses are against flood water mosquitoes (U.S. EPA, 2001, 2005; WHO/FAO, n.d.). Slow-release formulations are applied to prevent the breeding of mosquitoes in places such as rice cultivations, storm drains, ponds, and water treatment works, among others (WHO/FAO, 1984). Because methoprene acts by disruption of insect development, it is not usually used for a quick kill in preharvest situations (WHO/FAO, 1984). Methoprene is used widely in the mushroom cultures to prevent the emergence of sciarid flies, it is mixed into feed supplements for cattle to control adult hornfly breeding in manure, and it is sprayed at food and tobacco handling and storage facilities (WHO/FAO, 1984; HSDB, 2005).

Formulations and Concentrations

Methoprene is available as technical grade product and in formulations including emulsifiable and soluble concentrates, suspension concentrates, granules, briquettes, aerosols, fogging solutions, baits, flowables, encapsulated and feed supplement formulations up to 10 percent ai (HSDB, 2005; EXTOXNET, 1996; WHO/FAO, 1984, n.d.). WHO indicated that the content of methoprene in the formulated products must be declared and shall not exceed the listed standards. Technical grade (RS)-methoprene must have no less than 920 g/kg (RS)-methoprene. The mean content of the highly active trans (E) isomer must be 900 g/kg while the maximum content of the cis (Z) isomer is 20 g/kg. For the (RS)-methoprene emulsifiable concentrate, the (RS)-methoprene content should be $\leq$ 25 g/kg + 15% of the declared content, > 25–100 g/kg + 10% of the declared content, 100–250 g/kg + 6% of the declared content (WHO, 2001).

Shelf Life

Methoprene is a stable compound (WHO/FAO, n.d.). It is stable in sterile aqueous solutions but biodegrades easily by common bacteria, sunlight, and ultraviolet light (WHO/FAO, 1984).

Degradation Products

Methoprene is rapidly and extensively degraded in the soil. The breakdown products include small amounts of nonpolar metabolites, including hydroxyl ester. However, more than 50 percent of the applied dose was converted to carbon dioxide (WHO/FAO, 1984). In humans, methoprene is degraded and excreted in the urine as hydroxyepter (isopropyl 11-hydroxy-3,7,11-trimethyl - 2,4-dodecadienoate), the hydroxyacid (11-methoxy-3,7,11-trimethyl-2,4-dodecadienoic acid), and several lesser metabolites, including 7-methoxycitronellic acid, 7-hydroxycitronellic acid, and 7-methoxycitronellal which are excreted as free compound or conjugates (WHO/FAO, n.d.). Degradation products in unsterile pond water include ZR-724, ZR-725, ZR-669, and recovered methoprene each of which was a 1:1 mixture of cis-2 and trans-2 isomers, although 94 percent of the applied dose was trans-2 methoprene (WHO/FAO, 1984).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Methoprene binds tightly to soil and it is only slightly soluble in water, making it almost immobile in most soil types (EXTOXNET, 1996; ATSDR, 2005). Field leaching studies in sand, sandy loam, silt loam and clay loam have shown that even after repeated washings with water, methoprene remains only in the top few inches of soil (EXTOXNET, 1996; WHO/FAO, 1984). In studies with radiolabeled methoprene, 87 percent of the applied dose was bound to the soil (WHO/FAO, 1984). These results indicate that methoprene does not leach from soil (U.S. EPA, 2001, 1991a, 1991b).

In soil, methoprene is of low persistence (EXTOXNET, 1996; U.S. EPA, 2001, 1991a, 1991b). It is rapidly and extensively broken down in soil (WHO/FAO, 1984). The reported field half-life is up to 10 days, while the half-life in sandy loam soil is about 10 days. The half-life of high application rates (1 pound/acre) of the formulated Altosid product is less than 10 days (EXTOXNET, 1996; ATSDR, 2005; WHO/FAO, n.d.). Methoprene is rapidly broken down by microbial degradation which is the major fate process to mostly carbon dioxide. It also undergoes rapid photodegradation (EXTOXNET, 1996; U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.).

Additionally, formulated Altosid does not persist in plants. Half-lives of less than 1 day in rice, 2 days in alfalfa, and 3–7 weeks in wheat were reported. Methoprene residues are not expected in plants that are grown in treated soil (EXTOXNET, 1996; ATSDR, 2005).

Fate and Transport in Aquatic Systems

Because methoprene binds tightly to soil and is practically insoluble in water, very little leaching into groundwater has been reported (EXTOXNET, 1996; ATSDR, 2005). Methoprene rapidly degrades in water. Half-lives in ponds have been reported at approximately 30 hours for application of 0.001 mg/L and 40 hours for application of 0.01 mg/L (EXTOXNET, 1996). Sunlight and temperature play major roles in the breakdown of methoprene in water (EXTOXNET, 1996; U.S. EPA, 2001; WHO/FAO, 1984). Half-lives of <1 day for sunlight conditions and > 4 weeks for darkness were reported (ATSDR, 2005). Biodegradation and photodegradation are the major fate processes (EXTOXNET, 1996). The potential for bioconcentration of methoprene in aquatic organisms is very high, as indicated by its bioconcentration factor of 3,400 (ATSDR, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of methoprene in humans because no obvious signs of poisoning have been reported in humans from either accidental or occupational exposures (EXTOXNET, 1996; WHO/FAO, n.d.). In human health screening studies, no significant effects were seen (U.S. EPA, 1991a, 1991b). From those data and animal data it is concluded that methoprene has very low acute oral and inhalation toxic potential in humans. It is also not a skin or eye irritant or a skin sensitizer in humans (U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.).

In animals, acute oral and inhalation exposures to methoprene are almost nontoxic while dermal exposures are only slightly toxic (EXTOXNET, 1996; ATSDR, 2005). Oral LD_{50} values of 2,323 – >34,600 mg/kg in rats, 2,285 mg/kg in mice, and 5,000–10,000 mg/kg in dogs were reported. In rats, 20 percent mortality was seen within 4 months following oral doses of 232 mg/kg/day, while no deaths were seen at 116 mg/kg/day. In rats, an inhalation LC_{50} value of >210,000 mg/m^3 was reported, which was the highest dose tested. Reported dermal LD_{50} values range from > 2,000–10,000 mg/kg in rabbits and are > 5,000 mg/kg in rats (ATSDR, 2005; HSDB, 2005; EXTOXNET, 1996; WHO/FAO, n.d.; NIHE, 2001).

In short-term studies, no inhalation or dermal effects were reported in rats, rabbits, or dogs (U.S. EPA, 2001; WHO/FAO, n.d.; ATSDR, 2005). In subchronic studies, some systemic effects (e.g., increased liver weights and other liver and kidney effects in rats) have been observed at high concentrations (U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.).

Methoprene is of low dermal toxicity. It does not cause skin or eye irritation in rabbits and it is not a skin sensitizer in guinea pigs (HSDB, 2005; EXTOXNET, 1996; ATSDR, 2005; U.S. EPA, 1991a, 1991b; WHO/FAO, n.d.; NIHE, 2001). No systemic effects were reported in rabbits dermally exposed in a 30-day study; erythema was reported at the application site (ATSDR, 2005; U.S. EPA, 2001). Additionally, hyperemia and edema of the skin was observed following repeated dermal applications (HSDB, 2005). Available data also suggest that methoprene is not genotoxic (NIHE, 2001).

Treatment

No laboratory tests have been identified as indicators of exposure to methoprene, and blood levels have not been established in humans (WHO, n.d.; HSDB, 2005). Because methoprene is of low acute toxicity, there are no clear signs or clinical symptom of toxicity in humans. If a person has been exposed to methoprene and shows signs of illness, treatment before being seen by a physician is supportive. Because no acute toxicity is expected even with ingestion of large doses, any illness seen following exposure is likely due to the solvent used in formulation (WHO/FAO, n.d.). Only following ingestion of large amounts of methoprene should gastrointestinal decontamination be employed. Recommended doses of activated charcoal include 25–100 g in adults and adolescents, 25–50 g in children, and 1 g/kg in infants less than one year old. Dermal exposure should be treated by decontamination of the skin by washing with soap and water. Treatment of ocular exposure consists of flushing the eyes with large amounts of saline or clean water. Medical attention should be sought if irritation continues (HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to methoprene, though it is not likely to cause long-term problems when used under normal conditions. No overt signs of toxicity have been reported

from long-term occupational exposures (EXTOXNET, 1996). Based on animal studies, methoprene is not likely to cause chronic toxicity in human. Animal data indicate that the organ mainly affected by chronic methoprene exposure is the liver. Increased liver weights were reported in a 90-day feeding study in rats. However, these effects were not replicated in 2-year feeding studies in rats or in mice given methoprene in the diet for 90 days (EXTOXNET, 1996; U.S. EPA, 2001; WHO/FAO, n.d.).

Methoprene does not appear to have reproductive, developmental, or neurotoxic effects in animals. No reproductive effects were observed in a 3-generation reproduction study in rats or a 90-day study in dogs (EXTOXNET, 1996; ATSDR, 2005; U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.; NIHE, 2001). No teratogenic effects were seen in rats, rabbits, or mice (WHO/FAO, n.d.; EXTOXNET, 1996; ATSDR, 2005; U.S. EPA, 1991a, 1991b). Methoprene does not show potential estrogenic, androgenic anabolic, or glucocorticoid effects (U.S. EPA, 2001; WHO/FAO, n.d.).

Cancer Endpoints

Existing data suggest that methoprene is not carcinogenic. Long-term feeding studies in rats and mice showed no increase in tumors (U.S. EPA, 1991a; EXTOXNET, 1996; NIHE, 2001). Additionally, methoprene does not show any mutagenic potential (EXTOXNET, 1996).

Toxicokinetics

Methoprene is absorbed via the gastrointestinal tract, inhalation of spray mist and through intact skin (WHO/FAO, n.d.). Oral absorption is rapid and extensive. It is distributed mainly to organs related to absorption, biotransformation, and excretion (NIHE, 2001). No evidence of accumulation in body tissues or fluids including fat, muscle, liver, lungs, blood, or bile was seen in a study using ^{14}C-labelled methoprene (WHO/FAO, 1984, n.d.). Methoprene is rapidly and completely metabolized and excreted in the urine, feces, and expired air of mammals (EXTOXNET, 1996; U.S. EPA, 2001; ATSDR, 2005; NIHE, 2001). In cattle, methoprene is excreted unchanged and in sufficient quantities in the feces to have the desired effect of killing larvae that breed in the waste (EXTOXNET, 1996). In mice intubated with radiolabeled methoprene, 63.6 percent and 12.3 percent of the radioactivity was excreted within 24 hours in the urine and feces, respectively (ATSDR, 2005).

The metabolism of methoprene occurs mainly by hepatocyte microsomal esterases to methoprene acid. After alpha oxidation, methoprene acid is susceptible to beta oxidation to acetate. It is then further broken down to carbon dioxide or intermediary metabolites by the Krebs' cycle. It is excreted from the body as carbon dioxide or in urine and feces. Poor intestinal absorption and rapid metabolism of absorbed methoprene may be indicated by the finding of high amounts of unmetabolized methoprene in the feces but not the urine or blood. Products of urinary excretion include the hydroxyepter (isopropyl 11-hydroxy-3,7,11-trimethyl - 2,4-dodecadienoate), the hydroxyacid (11-methoxy-3,7,11-trimethyl-2,4-dodecadienoic acid), and several lesser metabolites including 7-methoxycitronellic acid, 7-hydroxycitronellic acid, and 7-methoxycitronellal. Excretion of the primary urinary products is as free compounds or as conjugates. Methoprene is found in the eggs of laying hens and the milk of lactating cows (WHO/FAO, n.d.) however, no placental transfer was evident in mice (ATSDR, 2005). Approximately 8 percent of the radiolabel was excreted in the milk of lactating cows within 7 days while 19 percent was found in eggs of chickens after 14 days (NIHE, 2001). Most of the radiolabel in most species is excreted within 5 days (NIHE, 2001).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Methoprene is very unlikely to harm terrestrial organisms other than its targets. It has a very low toxicity in birds (U.S. EPA, 2001, 1991a, 1991b; EXTOXNET, 1996; WHO/FAO, n.d.). Reported oral LD_{50} values include 4,640 ppm in chickens for the formulation Altosid and 2,000 mg/kg for mallard ducks (EXTOXNET, 1996). Reported acute 5–8 day LC_{50} values for Altosid in Mallard ducks and Bobwhite quail were all >10,000 ppm (EXTOXNET, 1996). Similar effects were reported in feeding studies using the technical material (WHO/FAO, n.d.). No reproductive effects or embryotoxicity were seen in mallard ducks and bobwhite quail fed Altosid (U.S. EPA, 2001, 1991a, 1991b; EXTOXNET, 1996; WHO/FAO, n.d.). However, acute oral exposure in birds to higher levels resulted in slowness, reluctance to move, sitting, withdrawal, and incoordination. These effects appeared quickly and persisted for up to 2 days making the birds potentially more susceptible to predation (EXTOXNET, 1996). No toxicity was seen in honeybees or earthworms (EXTOXNET, 1996). The oral and dermal LD_{50} in bees is >1,000 µg/L/bee (HSDB, 2005). An unintended but beneficial effect has been observed in Japanese silk worms where exposure to methoprene extends the time period in which they make silk (WHO/FAO, n.d.).

Toxicity in Non-Targeted Aquatic Systems

Acute effects of methoprene have been reported in a wide variety of aquatic species. It is very highly toxic in aquatic insects, highly toxic in crustaceans, moderately toxic in zooplankton, and slightly toxic in molluscs and fish (PAN, 2005; EXTOXNET, 1996; U.S. EPA, 2001, 1991a, 1991b). In fish, accumulation, behavioral, biochemistry, growth, mortality, and population effects have been reported (PAN, 2005). In freshwater fish, methoprene is more toxic to warm-water fish and less toxic to cold-water fish (U.S. EPA, 1991a, 1991b). No death or toxicity was observed in mosquito fish treated for 10 weeks in ponds at 56–560 g/ha (WHO/FAO, n.d.). The reported 96-hour LC_{50}s in fish for the formulation Altosid range from 4.4 mg/L to > 100 mg/L in channel catfish and largemouth bass (EXTOXNET, 1996). For technical methoprene, reported LD_{50}s in fish range from 4,000 µg/L in Australian blue-eye to 124,950 µg/L in Mummichog (PAN, 2005).

Methoprene is highly acutely toxic to freshwater invertebrates such as crayfish and Daphnia manga (EXTOXNET, 1996; U.S. EPA 1991a, 1991b). Additionally, it can have high acute toxicity in estuarine and marine invertebrates such as grass shrimp and mud crabs; however, marine invertebrates are less likely to be exposed than estuarine invertebrates since methoprene is used as a mosquito larvicide. Additionally, the rapid degradation of methoprene in water mitigates the risks to estuarine organisms (U.S. EPA, 1991a, 1991b). In arthropods including crustacean, insecta, molluca, shrimp, damselfly, beetle, and tadpole, 24- and 48-hour LC_{50s} were greater than 900 ppb (U.S. EPA, 2001). The reported LC_{50} for freshwater shrimp is > 100 mg/L while it is > 0.1 mg/L for estuarine mud crab (EXTOXNET, 1996). Similar 5-day LC_{50} values for technical methoprene have been reported for crayfish, freshwater shrimp and white and pink shrimp (100 ppm) (WHO, n.d.). A 48-hour EC_{50} of 360 µg/L was reported for Daphnia (HSDB, 2005).

In amphibians, behavioral, developmental, growth, mortality, and population effects have been reported (PAN, 2005). The reported LC_{50} values for *R. catesbeiana* and *R. pipiens* larvae are greater than 10,000 ppb, and in adult *B. woodhousei,* the reported LC50 value is greater than the highest dose tested (>1,000 ppb) (U.S. EPA, 2001).

A slight potential for bioconcentration has been reported in bluegill sunfish and crayfish (EXTOXNET, 1996). Methoprene has an estimated bioconcentration factor of 3,400 which suggests that its potential for bioconcentration is very high (ATSDR, 2005).

Chronic Exposure

Methoprene is of minimal chronic risk to freshwater fish, invertebrates, and other estuarine species from use in mosquito products (U.S. EPA, 2001). The use of briquettes poses a potential risk for chronic exposures in estuarine organism since methoprene is released slowly over an extended period of time (U.S. EPA, 1991a, 1991b). However, laboratory and field studies using mosquito product formulations have shown that methoprene dose not reach levels that are toxic to nontarget aquatic species during chronic exposures (U.S. EPA, 2001)

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Profile for Permethrin:

CAS Registry Number 52645-53-1

Summary

Chemical History

Permethrin is a synthetic pyrethroid insecticide used in agricultural and human health applications. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (WHO/FAO, 1984; IPCS, 1990). For mosquito control, it is used in bed nets and other materials that are dipped in permethrin to protect the user (EXTOXNET, 1996; WHO/FAO, 1984). Permethrin is of low risk to humans when used at levels recommended for its designed purpose (ATSDR, 2003a). However, as a synthetic pyrethroid, permethrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels in nerve cells (Choi and Soderlund, 2006). Typical symptoms of acute exposure are irritation of skin and eyes, headaches, dizziness, nausea, vomiting, diarrhea, and excessive salivation and fatigue. Inhaled permethrin has been shown to cause cutaneous paresthesias or a burning, tingling, or stinging. However, these effects are generally reversible and disappear within a day of removal from exposure (ATSDR, 2003a). EPA has not classified synthetic pyrethroids, including permethrin, as endocrine disruptors.

Description of Data Quality and Quantity

Several comprehensive reviews on the toxicity of permethrin have been prepared or updated in recent years:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003a)
- An EPA risk assessment for the Reregistration Eligibility Decision (RED) document (U.S. EPA, 2005f)
- IRIS summary review (U.S. EPA, 2005g).

EPA and ATSDR have developed quantitative oral human health benchmarks (EPA's acute and chronic RfDs, short-, intermediate-, and long-term inhalation and dermal benchmarks and ATSDR's acute and intermediate oral MRLs). Other relevant references include

- Environmental Health Criteria 94: Permethrin (IPCS, 1990)
- Specifications for Permethrin (WHO, 1999a).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.11	mg/kg/day	Inhalation NOAEL of 0.042 mg/L (11 mg/kg/day) for neurological effects in rats with UF of 100 applied	U.S. EPA (2005f)
Acute, Intermediate, Chronic	Oral	0.25	mg/kg/day	Acute and chronic RfD based on clinical effects in rats	U.S. EPA (2005f)
Acute, Intermediate, Chronic	Dermal	5	mg/kg/day	Dermal NOAEL of 500 mg/kg/day in rats with a UF of 100 applied	U.S. EPA (2005f)
Cancer	Inhalation, Oral, Dermal	0.009567	per mg/kg/day	CSF for lung tumors in female mice	U.S. EPA (2005f)

For inhalation exposure, a NOAEL of 0.042 mg/L (11 mg/kg/day) was identified for neurological effects in rats exposed via inhalation and an uncertainty factor of 100 was applied. This value is appropriate for short- (1–30 days), intermediate- (1–6 months), and long-term (>6 months) inhalation exposures (U.S. EPA, 2005f).

For oral exposure, an acute and chronic oral RfD of 0.25 mg/kg/day was derived based on a NOAEL of 25 mg/kg/day for clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature observed in rats, with an uncertainty factor of 100 applied (U.S. EPA, 2005f). The acute and chronic RfD was adopted to also represent intermediate exposures.

For dermal exposure, a NOAEL of 500 mg/kg/day was identified in rats dermally exposed for 21 days and an uncertainty factor of 100 was applied. This value is appropriate for all exposure durations (U.S. EPA, 2005f).

To assess potential carcinogenic risks, a cancer slope factor (CSF) of 9.567×10^{-3} per mg/kg/day was derived based on lung tumors in female mice chronically exposed to permethrin in the diet (U.S. EPA, 2005f).

Insecticide Background

CASRN:	52645-53-1
Synonyms:	3-Phenoxyphenyl)methyl3-(2,2-dichloroehenyl)-2,2-dimethylcyclopropanecarboxylate (ATSDR, 2003a)
Chemical Group:	pyrethroid
Registered Trade Names:	Ambush, BW-21-Z, Cellutec, Dragnet, Ectiban, Eksmin, Exmin, FMC 33297, Indothrin, Kafil, Kestrel, NRDC 143, Pounce, PP 557, Pramex, Qamlin, and Torpedo (EXTOXNET, 1996), Acion, AI3, AMbushfog, BW-21-7, CO-Opex, Matadon, NIA 33297, Outflank, OMS-1821, Perthrine, Picket G, Perigen, PP557, R86557, Stockade, Stomoxin, S-3151, SBP-1513, Talcord, WL43479 (WHO/FAO, 1984)

Usage

Permethrin is used as a broad spectrum insecticide to combat pests on a variety of crops. It is also used to control ectoparasites in animals, biting flies, and cockroaches and is used in greenhouses, gardens, and for termite control (EXTOXNET, 1996). It belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies (ATSDR, 2003a). For mosquito protection, it is used in bed nets and other materials that are dipped into the permethrin to protect the user. Permethrin for agricultural use is restricted by EPA due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003a).

Formulations and Concentrations

Permethrin is available in technical grade, emulsifiable concentrates, dusts, smokes, ultra-low volume (UVL), and wettable powder formulations (EXTOXNET, 1996). Technical grade permethrin may be mixed with carriers or solvents resulting in the commercial formulations. These commercial formulations may also include ingredients that may potentiate the toxicity compared to technical grade permethrin. These ingredients must be identified on the label. WHO indicated that the content of permethrin in the formulated products must be declared and shall not exceed the listed standards. For impregnated mosquito netting, the permissible permethrin content is 20 +/- 3 mg/kg (WHO, 2002). Technical grade permethrin must have no less than 900 g/kg permethrin. The emulsifiable concentrate should contain > 25–100 g/kg +/- 10% of the declared content, 100–250 g/kg +/- 6% of the declared content, or > 250–500 g/kg +/- 5% of the declared content (WHO, 1999a). Permethrin that is used for bed nets comes in the emulsifiable concentrations ranging from 10 to 55 percent active ingredient. The 55 percent emulsifiable concentration is only for professional use (WHO, 1999a).

Shelf Life

Permethrin is stable for 2 years or longer at 50°C. It is most stable in acidic environments and optimal stability is at pH 4. Photochemical degradation occurs in laboratory studies but not in field data. Pyrethrins, in general, are stable for a long time in water-based aerosols (HSDB, 2005).

Degradation Products

Pyrethroid insecticides are often formulated with synergists that act to prevent the breakdown of enzymes and thus enhance the activity of the pyrethroid (ATSDR, 2003a). Permethrin needs to be stored in a dry, cool, well-ventilated location to prevent the risk of it breaking down prior to use. Permethrin's breakdown products include 3-phenoxybenzyl(1RS)-cis, trans-3-(2,2-dichloroviny)-2-2dimethylcyclopropanecarboxylate (PAN, 2005).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Permethrin is moderately stable in the environment (WHO/FAO, 1984). It binds tightly to soil making it almost immobile in most soil types. Studies have shown that permethrin is immobile in clay and loamy sands, while its degradation products have some mobility. As a result, it is not easily taken up by plants or leached into groundwater (ATSDR, 2003a).

In soil, permethrin is of low to moderate persistence (EXTOXNET, 1996). The reported half-life ranges from 30 to 38 days in soil (EXTOXNET, 1996) and < 2.5 days in a sediment and seawater solution. The U.S. Department of Agriculture (USDA) Pesticide Database lists the half-life of permethrin as 4–40 days in

aerobic soils. It is broken down largely by microorganisms in nonsterile soil and may also be broken down by sunlight at the surface of soil (ATSDR, 2003a).

Fate and Transport in Aquatic Systems

Permethrin is not expected to be released in large quantities into water because it is generally applied to crops and vegetation aerially or on the ground from sprayers. Nearby waters, however, might be affected by spray drift. Permethrin is prohibited from being applied for mosquito control within 100 feet of lakes, rivers, or streams due to its aquatic toxicity (ATSDR, 2003a). Because permethrin binds tightly to soil and is practically insoluble in water, very little leaching into groundwater has been reported (EXTOXNET, 1996). Due to its low vapor pressure and Henry's law constant, permethrin volatilizes slowly from water. When permethrin is released into water, it rapidly partitions to suspended solids and sediments, which further mitigates volatilization. Studies have shown that greater than 95 percent of permethrin applied directly onto lake sediment was absorbed.

Permethrin breaks down quickly in water. Studies have reported a half-life of < 2.5 days near estuarine areas (EXTOXNET, 1996). Additionally, permethrin undergoes photolysis in sunlit surface waters, with a reported half-life of 14 days in seawater exposed to light (ATSDR, 2003a). In water, a loss of toxicity was observed for permethrin that had aged for 48 hours in sunlight (EXTOXNET, 1996).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of permethrin in humans. Acute effects observed from occupational exposure include burning and itching of the skin of the periorbital area within a few hours of inhalation exposure to permethrin. Ingestion of permethrin causes nausea and vomiting. As a Type I pyrethroid, its primary target is the nervous system (U.S. EPA, 2005f). Typical effects seen following acute exposure to higher levels of permethrin are almost all related to the action of it on the nervous system, as pyrethroids prolong the open phase of the sodium channel during nerve cell excitation. Animal studies have indicated that effects may be caused by repetitive activity in sensory motor nerves (IPCS, 1990; WHO/FAO, 1984). These symptoms of permethrin exposure are transitory and disappear anywhere within a few hours to a few of days once the exposure is discontinued (EXTOXNET, 1996).

In animals, oral and inhalation exposures to permethrin are almost nontoxic. Reported LD_{50} values for technical permethrin range from 430 to 4,000 mg/kg in rats, while a 4-hour LC_{50} of 23.5 mg/L is reported in rats. Permethrin is slightly toxic through dermal contact, with dermal LD_{50}s of over 4,000 mg/kg in rats and over 2,000 mg/kg in rabbits. The toxicity depends on the ratio of cis and trans isomers, with cis being more toxic, and the solvent used (EXTOXNET, 1996; WHO/FAO, 1984). Reported dermal LD_{50} values include > 4,000 mg/kg (no solvent) in rabbits, > 2,500 mg/kg (no solvent) in rats and mice, and 750 mg/kg (in xylene) in rats (WHO/FAO, 1984). Dermal exposure to permethrin has caused mild irritation to both intact and abraded skin of rabbits (EXTOXNET, 1996).

Treatment

Permethrin and its metabolites can be detected in blood and urine; however the methods are not practical given how quickly these compounds are broken down in the body (ATSDR, 2003a; WHO/FAO, 1984). Levels of the degradation product 3-phenoxybenzyl in urine may be useful indicators of exposure (WHO/FAO, 1984).

There are no antidotes for permethrin exposure. Treatment depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following permethrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible (PAN, 2005; WHO/FAO, 1984). Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts of permethrin should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent and exposure to light should be avoided.

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to permethrin, though it is not likely to cause long-term problems when used under normal conditions (EXTOXNET, 1996). Chronic occupational exposure to permethrin caused skin and eye irritation in 33 percent of exposed Swedish workers. However, no complaints were reported in volunteers exposed to 0.5 mg/m^3 from an indoor application (WHO/FAO, 1984).

Data in animals indicate that oral exposure to permethrin is not highly toxic, but effects reported are largely neurological. Doses of 5 mg/kg/day for 90 days did not produce effects in dogs (EXTOXNET, 1996) while higher oral doses of 500 mg/kg and greater for 3 months caused transient clinical signs. Mice and rats chronically exposed to dietary levels up to 5,000 mg/kg (mice) and 2,500 mg/kg (rats) exhibited no consistent effects on growth or food consumption (WHO/FAO, 1984). Inhalation and dermal studies in animals indicate that permethrin is nontoxic or minimally toxic. No effects were observed in rats exposed to up to 500 mg/m^3, 6 hours per day, for 13 weeks. Additionally, rabbits dermally exposed to 1.0 g/kg/day on abraded skin for 21 days showed no effects other than moderate skin irritation (WHO/FAO, 1984). Based on the lack of reproductive effects in animals exposed to high oral does of permethrin, human reproductive toxicity is not expected. Additionally, permethrin shows no teratogenic or mutagenic activity (EXTOXNET, 1996; WHO/FAO, 1984).

Cancer Endpoints

EPA has classified permethrin as "likely to be carcinogenic to humans" by the oral route. A long-term, high dose dietary exposure study reported an increased incidence of benign lung and liver tumors in mice. This is supported by equivocal evidence in one strain of rats and structure-activity relationship information (U.S. EPA, 2005f).

Toxicokinetics

Permethrin is readily absorbed via the gastrointestinal tract, inhalation, and less so through intact skin (WHO/FAO, 1984). In mammals, permethrin is rapidly metabolized in the liver (EXTOXNET, 1996). The trans isomer is metabolized by hydrolysis and the cis isomer is not as easily hydrolyzed and is thus more toxic (WHO/FAO, 1984). The hydroysis and oxidation products of permethrin metabolism are quickly excreted in urine and feces with the trans isomers more rapidly excreted than the cis isomers. The primary excretion products of both isomers in most species studied include 4'-HO-3-PBA sulfate (in rats), 4'-HO-3-PBA (trans) and 6-HO-3-PBA (cis) sulfates (in mice), N-(3-phenoxybenzoyl) glutamate (in cows), and cyclopropane-

carboxylic acid glucuronides and 3-PBA glucuronides products in most of the species studied (WHO/FAO, 1984). Permethrin may persist in fatty tissues. The reported half-life in the brain and body fat is 4–5 days (EXTOXNET, 1996).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Permethrin, like other pyrethroids, is very unlikely to harm terrestrial organisms other than its targets, such as mosquitoes and other pests (EXTOXNET, 1996). Permethrin has a very low toxicity in birds (WHO/FAO, 1984; EXTOXNET, 1996). Oral LD_{50} values range from 9,900 mg/kg for the formulation Pramex in mallard ducks to over 15,500 mg/kg in Japanese quail (EXTOXNET, 1996), while the acute oral LD_{50} for the technical material was >11,275 mg/kg in mallard ducks and >32,000 mg/kg in starlings. Subacute LD_{50}s were >23,000 mg/kg for all bird species tested. No adverse effects or significant accumulation in tissues or eggs were seen in hens exposed to a spray mist of 3.77–11.94 mg/bird (WHO/FAO, 1984). As with other pyrethroid insecticides, permethrin is extremely toxic to honey bees (EXTOXNET, 1996).

Toxicity in Non-Targeted Aquatic Systems

Permethrin is very toxic to fish (EXTOXNET, 1996); however, because it is rapidly absorbed and degraded in the aquatic environment, the risk is of short duration (WHO/FAO, 1984). The high toxicity in fish is illustrated by the low exposures that cause lethality. The reported 48-hour LC_{50} for rainbow trout is 0.0054 mg/L, while in bluegill sunfish and salmon it is 0.0018 mg/L (EXTOXNET, 1996). The 96-hour LC_{50}s range from 0.1–0.5 µg/L in rainbow trout to 15 µg/L in mosquito fish (WHO/FAO, 1984). Permethrin has a low to moderate potential to accumulate in fish, with reported bioconcentration factors of over 700 times the concentrations in water for bluefish and catfish (EXTOXNET, 1996). A bioconcentration factor of 1,900 was reported in eastern oysters following a 28-day incubation (ATSDR, 2003a). Permethrin is also known to be toxic to some aquatic invertebrates, amphibians in larval form, aquatic insects, and crustaceans (WHO/FAO, 1984). A disruption in growth and development of tadpoles has been reported (EXTOXNET, 1996).

Chronic Exposure

Due to low rate of application and low persistence of permethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005)

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Profile for Piperonyl butoxide:

CAS Registry Number 122453-73-0

Summary of Insecticide

Chemical History

Piperonyl butoxide (PBO) is a pesticide synergist. It does not, by itself, have pesticidal properties. However, when added to insecticide mixtures (typically pyrethrin, pyrethroid, or carbamate insecticides) their potency is increased considerably. (Jones 1998)

PermaNet ® 3.0, has been designed to improving efficacy against pyrethroid-resistant mosquito populations. PermaNet® 3.0 is a mosaic net combining deltamethrin coated- polyester side panels and a deltamethrin plus PBO incorporated-polyethylene roof. PBO has been incorporated to the net as it showed to enhance the effects of deltamethrin against insects by inhibiting metabolic defence systems, mainly P450s.

(Corbel V et al. 2010).

Insecticide Background

Chemical name and class

The chemical name for PBO is 5-[2-(2-butoxyethoxy) ethoxymethyl] -6-propyl-1,3-benzodioxole and it is unclassified as a pesticide as it is a synergist, but it belongs to the chemical class of benzodioxoles.

Synonyms, trade names, and formulations

PBO is produced by many chemical companies. AgrEvo Environmental Health Inc. produces Butacide. Other brand names are Holide, Endura PB, Ultra PBO, Prentox, PBO-8, Incite. PBO is registered by USEPA in 36,882 products too numerous to mention (www.pesticideinfo.org).

As a synergist PBO is formulated with other insecticides, mainly pyrethroids. These are formulated as dusts, emulsifiable concentrates, fogger, paper coating, pressurized spray, solution, and wettable powers. In the context of this study PBO is impregnated into mosquito nets with a synthetic pyrethroid such as deltamethrin. For example, PermaNet 2.0 is a deltamethrin-coated LN manufactured by Vestergaard Frandsen (Switzerland). The net is made of knitted poly-filament polyester fibres and is treated with deltamethrin to a target concentration of 55 mg/m^2 (= 1.4 g/kg for a 100-denier net; 1.8 g/kg for a 75-denier net). The insecticide is bound in a resin coating that reduces the amount of insecticide lost during routine washing. There is also PermaNet 3.0 with a higher concentration. A denier is a unit of measure for the linear mass density of fibers. It is defined as the mass in grams per 9,000 meters. The denier is based on a natural standard: a single strand of silk is one denier. A 9,000 meter strand of silk weighs one gram. (WHOPES 2009)

Usage

PBO is used in combination with synthetic pyrethroids for public health pests and agricultural pests in the field, in structures, and directly onto domesticated animals. PBO is in many indoor household insecticides (dusts, sprays, foggers), as well as garden, lawn and ornamental plant pesticides. Many agricultural pesticide products contain PBOs. Public health and urban areas are protected as well including by mosquito abatement products, termite treatments, impregnated materials (animal ear tags, pest strips, mosquito netting), as well as aerosols for adult mosquito control. PBO acts as an enzyme and has no pesticidal properties but enhances the efficacy of the pesticide. PBO inhibits the ability of insects to metabolize certain insecticides. This allows products containing PBO to be equally effective with lower concentrations of insecticides. (Jones 1998)

Shelf Life

PBO is a stable chemical and will last three years if stored in a dark, cool storage room.

Degradation Products

A large number of metabolites has been developed from studies on metabolism in mammals and degradation in the environment.

PBO-alcohol (soil),

PBO-aldehyde (soil),

PBO-acid (soil)

Metabolite A (MA): 1,3-benzodioxole-5,6-dicarboxylic acid

MB: 5,6-dihydroxyphthalide (4,5-dihydroxy-2-hydroxymethylbenzoic acid)

MC: lactone of (6-hydroxymethyl-1,3-benzodioxol-5-yl)acetic acid

MD: (6-propyl-1,3-benzodioxole-5-yl)methoxyacetic acid

ME: 6-propyl-1,3-benzodioxole-5-carboxylic acid or 4,5-methylenedioxy-2-propylbenzoic acid

MF: (2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}ethoxy)acetic acid

MG: 4-{[2-(2-butoxyethoxy)ethoxy]methyl}-5-propyl-1,2-benzenediol

MZ: 2-oxa-5,6-methylenedioxyindane

M2: 4-{[2-(2-butoxyethoxy)ethoxy]methyl}-2-methoxy-5-propylphenol

M4: 2-(2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}ethoxy)ethanol

M5: 2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}ethanol

M7: 2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}acetic acid

M8: 4-{[2-(2-butoxyethoxy)ethoxy]methyl}-5-propyl-1,2-benzenediol glucuronide

M9: 4-{[2-(2-butoxyethoxy)ethoxy]methyl}-2-methoxy-5-propylphenol glucuronide

M10: 2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}ethanol glucuronide

M11: 2-[2-(4-hydroxy-5-methoxy-2-propylbenzyloxy)ethoxy]ethoxyacetic acid

M12: 2-(4-hydroxy-5-methoxy-2-propylbenzyloxy)ethoxyacetic acid

M13: 4-{2-[2-(hydroxyethoxy)ethoxy]methyl}-5-propyl-1,2-benzenediol

M14: 2-[2-(5-hydroxy-2-propyl-4-sulfooxybenzyloxy)ethoxy]ethoxyacetic acid

M16: 4,5-dihydroxy-2-propylbenzyloxyacetic acid phenolic glucuronide

M17: 2-[2(4-hydroxy-5-methoxy-2-propylbenzyloxy)ethoxy]ethanol glucuronide

HMDS: hydroxymethyldihydrosafrole

M20: Glucose conjugate of HMDS

M21: Glucose conjugate of 2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethanol

M22: Glucose conjugate of 4-{2-[z-(6-propyl-1,3-benzodioxol-5-ylmethoxy)ethoxy]ethoxy}butan-1-ol

M23:4,5-methylenedioxy-2-propylbenzaldehyde

M24: bis(3,4-methylenedioxy-6-propylbenzyl) ether

M25: 2'-[2-(2-butoxyethoxy)ethoxy(hydroxy)methyl]4',5'-methylenedioxypropiophenone

M26: 2'-[2-(2-butoxyethoxy)ethoxymethyl]4',5'methylenedioxypropiophenone

M27: 2-ethylcarbonyl-4,5-methylenedioxybenzaldehyde (HSDB, Jones, USEPA 2006)

Environmental Behavior

Fate and Transport in Terrestrial Systems

PBO degrades rapidly (8.4-hour half-life) in the environment as it is metabolized by soil microorganisms. Other tested routes of degradation, such as hydrolysis, aerobic and anaerobic aqueous metabolism, are very slow. The atmospheric half-life of PBO is 3.4 hours, based on the estimated reaction rate with hydroxyl radicals. Little volatilization from soil or water is expected, but PBO may enter the atmosphere as an aerosol when applied by spraying. (Jones, USEPA 2006)

PBO's production may result in its release to the environment through various waste streams; its use as a synergist for the pyrethrins and related insecticides will result in its direct release to the environment. If released to air, an estimated vapor pressure of $5.2x10^{-6}$ mm Hg at 25° C indicates PBO will exist in both the vapor and particulate phases in the atmosphere. Vapor-phase PBO will be degraded in the atmosphere by reaction with photo-chemically-produced hydroxyl radicals. Particulate-phase PBO will be removed from the atmosphere by wet or dry deposition. An estimated BCF of 27 suggests the potential for bio-concentration in aquatic organisms is low. If released to soil, PBO is expected to have moderate to low mobility based upon Koc values ranging from 399-830. Volatilization from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry's Law constant of $8.9x10^{-11}$ atm m^3/mole. PBO is not expected to volatilize from dry soil surfaces based upon its vapor pressure. A half-life in aerobic soils of 14 days suggests that biodegradation may be an important environmental fate process. (Jones, HSDB)

Fate and Transport in Aquatic Systems

PBO is moderately mobile in soil-water systems (K_{oc} = 399-830). If released into water, PBO is expected to adsorb to suspended solids and sediment based upon the Koc. Volatilization from water surfaces is not expected to be an important fate process based upon this compound's estimated Henry's Law constant. PBO is stable to hydrolysis at pH 5, 7 and 9 under sterile, dark conditions. The USEPA determined that PBO degrades somewhat rapidly in the environment, and therefore has a moderately low chance of contaminating water sources. PBO degrades rapidly (8.4-hour half-life) in the environment by photolysis in water. The major degradates PBO-alcohol, PBO-aldehyde, and PBO-acid are expected to be more soluble in water than the parent and therefore more mobile in soil-water systems. The toxicity of the degradates was considered to be equivalent to that of the parent in the absence of data. (Jones, USEPA 2006)

Human Health Effects

Acute Exposure

Clinical Symptoms

Ingesting PBO may cause vomiting and diarrhea. Hepatic changes and liver injury have been seen with large doses given to various animal species. Various anemias have been reported in animal studies from exposures. Animal studies have also shown elevated metabolic enzymes after ingestion. PBO inhibits mixed function

oxidase enzymes of the liver which metabolize pyrethrins and pyrethroids, with which they are combined. One case of pathological laughter has been reported with human exposure! Primary sources of data are from animals which include reports of hyper-excitability, unsteadiness, coma, seizures, and brain damage in large overdoses. PBO is minimally toxic. Acute oral or dermal exposure is unlikely to result in significant signs and symptoms of systemic toxicity or dermal irritation. This chemical is often combined with hydrocarbons or other insecticides that may require treatment. (HSDB)

Acute toxicity

The acute oral and dermal toxicity of PBO in mammals is low. Oral toxicity in the rat has an LD_{50} of 4570 (toxicity class III) for the technical grade but formulated products are rated even less toxic (IV). The LD_{50} for dermal exposure for the pure technical formulation for rabbits is 1880 mg/kg body weight which falls within toxicity level III (moderately toxic). Dermal tests on rats indicate that the compound may cause redness and swelling. Acute inhalation LC_{50} exposure in the rat for 4 h is >5.9 mg/L^3 of air which is toxicity level IV. (USEPA 2006)

Acute eye exposure of the technical material produces only a mild irritation (toxicity level IV) indicating PBO may cause eye irritation, but is not damaging. Exposure to the skin of a rabbit of the technical material in the rabbit is only minimally irritating (toxicity level IV). Dermal sensitization (technical) does cause sensitivity in the skin with guinea pigs. Skin irritation or significant percutaneous absorption is not expected following normal dermal exposure. (USEPA 2006)

Medical treatment for acute poisoning

PBO is of low toxicity on its own but is normally combined with pyrethroids making a more toxic formulation. Control any seizures first. Gastric decontamination is only indicated if there is a co-ingestant with significant toxicity such as a pyrethroid. Instructions say to consider gastric lavage after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect the patient's airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. (HSDB)

First aid is to administer charcoal as a slurry (240 ml water/30 g charcoal). Usual dose: 25-100 g in adults/adolescents, 25-50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old. Move the patient to fresh air after inhalation. Monitor for respiratory distress. If a cough or difficulty breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer oxygen and assist ventilation as required. Treat bronchospasm with inhaled beta2 agonist and oral or parenteral corticosteroids. (MSDS)

Irrigate exposed eyes with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persists, the patient should be seen in a health care facility. Irrigate each eye continuously with 0.9% saline (NS) during transport. From dermal exposure remove contaminated clothing and wash exposed area thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists. (HSDB)

Chronic Exposure

Non-cancer Endpoints

Occupational exposure to PBO may occur through inhalation of dust and dermal contact with this compound at workplaces where PBO is produced or used. Monitoring data indicate that the general population may be exposed to PBO via inhalation of dust, ingestion of food, and dermal contact with this compound or other insecticide products containing PBO. PBO targets the liver, but does not disrupt the

metabolism of other chemicals as it does in insects. It generally has a low toxicity in humans through any route of exposure. (USEPA 2006)

Sub-chronic oral toxicity from exposure over 90 days produced a NOAEL endpoint for rats of 15.5 mg/kg/day. The LOAEL for dogs was 52.8 mg/kg/day.

The standard 28-day inhalation toxicity test @ 4 h/day produced a LOAEL for rats of 3.91 mg/kg/day (0.015 mg/L^3). Chronic exposure for 1 year in dogs produced a NOAEL of 16 mg/kg/day. Chronic toxicity NOAEL for 2 years in rats and mice was similar at 30 mg/kg/day. Chronic maternal systemic toxicity administered throughout gestation in rats gave a LOAEL of 1065 mg/kg/day for the developmental endpoint. Reproductive toxicity over 2 generations produced a LOAEC in the rat as 469 mg/kg bodyweight/day. (USEPA 2006)

PBO is a suspected endocrine disruptor (www.pesticideinfo.org). Mutagenic risk was evaluated by in vitro mammalian cell mutation assays, chromosomal aberration and sister chromatid exchange in CHO cells, and unscheduled DNA synthesis. It is debatable whether the substance is oncogenic, mutagenic, or teratogenic in humans. The ADI for mammals is 0.2 mg/kg body weight /day. (USEPA 2006)

A 2011 study found a significant association between PBO measured in personal air collected during the third trimester of pregnancy, and delayed mental development at 36 months. Children who were more highly exposed in personal air samples (≥4.34 ng/m^3) scored 3.9 IQ points lower on the Mental Developmental Index than those with lower exposures similar to that observed in lead exposure. (Horton et al. 2011)

Cancer Endpoints

The EPA classifies PBO as a group C carcinogen, a possible human carcinogen (EPA). It is debatable whether the substance is oncogenic in humans. (www.pesticideinfo.org)

Toxicokinetics and Metabolism

Radioactive PBO was administered to male and female rats by gavage at a dose rate of 50 or 500 mg/kg body weight. In all cases, the radioactivity was rapidly excreted with 87-99% being found in the 0-48-hr excreta and the majority of the dose (64.1-85.0%) being eliminated in feces. The metabolism of PBO was complex with over 25 peaks of radioactivity being seen by radio-high-performance liquid chromatography (HPLC). Using HPLC/tandem mass spectrometry (MS/MS) and nuclear magnetic resonance (NMR), 12 urine metabolites were assigned structures together with four plus PBO in feces. Metabolism occurred at two sites: the methyl-enedioxy ring, which opened to form a catechol that could then undergo methylation, and the 2-(2-butoxyethoxy) ethoxy-methyl side-chain, which underwent sequential oxidation to a series of alcohols and acids. The identified metabolites accounted for approximately 60% of the administered dose. (HSDB).

Ecological Effects

Toxicity in Non-Targeted Terrestrial Organisms

PBO is only slightly toxic in mammals as evidence from rats. It has a low toxicity in birds with a 2250 mg a.i./kg with quail. The dietary LD_{50} quail is 5620 ppm. It is practically non-toxic to bees with a LD_{50} of 25 µg /bee. (USEPA 2006)

Toxicity in Non-Targeted Aquatic Systems

PBO is moderately toxic to fish, but it is highly toxic to other aquatic organisms and amphibians. The LC_{50} is 1.9 ppm in rainbow trout and 3.94 ppm in sheepshead minnow. PBO has a LC_{50} of 0.51 ppm for Daphnia water flea, 0.49 ppm for the mysid shrimp, and 0.21 ppm in western chorus frog tadpoles (EPA). The EC_{50}

for 5 d exposure of the alga *Chlorella fusca* is 44 ppm. An estimated BCF of 27 suggests the potential for bio-concentration in aquatic organisms is low. (USEPA 2006)

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Profile for Pirimiphos-Methyl:

CAS Registry Number 29232-93-7

Summary of Insecticide

Chemical History

Pirimiphos-methyl is a fast-acting, broad spectrum, noncumulating organophosphate insecticide and acaricide used in agricultural, horticultural, and public health applications (WHO/FAO, 1983, 1974). In public health applications, it is used to control disease vector insects, including mosquitoes, ants, beetles, bed-bugs, cockroaches, fleas, flies, lice, and mites (WHO/FAO, 1983, 1974). Pirimiphos-methyl has both contact and fumigant action (WHO/FAO, 1974). It is applied as a liquid concentrate, ready to use formula, and as treated articles (ear tags) (U.S. EPA, 1999b). It can be applied by closed system containers, low- and high-pressure hand wands, backpack sprayers, tagging equipment, and foggers (U.S. EPA, 2001). Pirimiphos-methyl acts like other organophosphates by inhibiting cholinesterase activity (U.S. EPA, 1999d). It is of low mammalian toxicity (WHO/FAO, 1983). WHO/FAO (1992) has classified it as slightly hazardous. Early symptoms of pirimiphos-methyl exposure include excessive sweating, headache, weakness, giddiness, nausea, vomiting, stomach pains, blurred vision, slurred speech, and muscle twitching. Symptoms of more severe poisoning may advance to convulsions, coma, loss of reflexes, and loss of sphincter control (WHO/FAO, 1983).

Description of Data Quality and Quantity

Comprehensive reviews on the toxicity of pirimiphos-methyl have been prepared:

- Interim Reregistration Eligibility Decision for Pirimiphos-methyl Case No. (2535) (U.S. EPA, 2001)
- IRIS summary review (U.S. EPA, 2006)
- Data Sheet on Pesticide No. 49 – Pirimiphos-methyl (WHO/FAO, 1983).

EPA has developed quantitative human health benchmarks that include an oral acute and chronic RfD and short- and intermediate-term inhalation and dermal benchmarks.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute	Inhalation	0.015	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 1000 applied; assume no portal of entry effects	U.S. EPA (2001)
Intermediate	Inhalation	0.0007	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 300 applied; assume no portal of entry effects	U.S. EPA (2001)
Chronic	Inhalation	0.0007	mg/kg/day	Adopt intermediate for chronic duration	U.S. EPA (2001)
Acute	Oral	0.015	mg/kg/day	Acute oral RfD based on a LOAEL of 15 mg/kg/day for neurological effects in rats and UF of 1,000 applied	U.S. EPA (2001)

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Intermediate	Oral	0.0002	mg/kg/day	Adopt chronic RfD for intermediate duration	U.S. EPA (2001)
Chronic	Oral	0.0002	mg/kg/day	Chronic oral RfD based on a LOAEL of 0.2 mg/kg/day for neurological effects in rats and UF of 1,000 applied	U.S. EPA (2001)
Acute	Dermal	0.015	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 1,000 applied; assume no first pass effects and 100% oral absorption	U.S. EPA (2001)
Intermediate	Dermal	0.0007	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 300 applied; assume no first pass effects and 100% oral absorption	U.S. EPA (2001)
Chronic	Dermal	0.0007	mg/kg/day	Adopt intermediate for chronic duration	

For oral exposure, an acute RfD of 0.015 mg/kg/day was derived based on a LOAEL of 15 mg/kg/day for brain, red blood cell, and plasma cholinesterase inhibition in rats (EPA MRID# 43594101, citation not provided). An uncertainty factor of 1,000 was applied for the use of a LOAEL and the degree of cholinesterase inhibition (10), and intra- and inter-species variability (100) (U.S. EPA, 2001).

A chronic oral RfD of 0.0002 mg/kg/day was derived based on an LOAEL of 0.2 mg/kg/day for plasma cholinesterase inhibition in a subchronic rat study (EPA MRID# 43608201, citation not provided). An uncertainty factor of 1,000 was applied for the use of a LOAEL and data gaps for long-term studies (10), and intra- and inter-species variability (100) (U.S. EPA, 2001). The chronic RfD was used to represent intermediate exposures.

For inhalation and dermal exposure, the oral toxicity endpoints (i.e., LOAELs) were selected for use, and both assume 100 percent absorption and no first pass or portal-of-entry effects (U.S. EPA, 2001). For acute inhalation and dermal benchmarks, an uncertainty factor of 1,000 was applied for the use of a LOAEL and the degree of cholinesterase inhibition (10), and intra- and inter-species variability (100). For intermediate inhalation and dermal benchmarks, an uncertainty factor of 300 was applied for the use of a LOAEL (3) and intra- and inter-species variability (100). The intermediate benchmark was used to represent chronic exposures.

Insecticide Background

CASRN:	29232-93-7
Synonyms:	O-(2-Diethylamino)-6-methyl-4-pyrimidinyl) O,O-dimethyl phosphorothioate, 2-diethylamino-6-methylpyrimidin-4-yl dimethyl phosphorothionate, pirimifosmethyl, methylpirimiphos, pyridimine phosphate, ENT 27699GC, PP511, CMS 1424 (U.S. EPA, 2001, 2006; WHO/FAO, 1983
Chemical Group:	organophosphate (U.S. EPA, 2001; WHO/FAO, 1983)

Registered Trade Names: Actellic 5E, Atelic, Atellic, Atellifog, Blex, Nu-Gro Insecticide, Nu-Gro 5E, Tomahawk Insecticide Ear Tags, LPM Insecticide Ear Tags, Silosan, Sybol (U.S. EPA, 2001, 2006; WHO/FAO, 1983)

Usage

Pirimiphos-methyl is a fast-acting, broad spectrum organophosphate insecticide and acaricide used to control a wide variety of sucking and chewing pests in agricultural and horticultural applications. It is used in horticultural applications; to clean fruits and vegetables before harvest; to control pests on stored products; and to eradicate nuisance and disease vector insects, including mosquitoes, ants, beetles, bed-bugs, cockroaches, fleas, flies, lice, and mites (WHO/FAO, 1983, 1974). The intended uses of existing products include greenhouse applications, treatment of stored grain and seeds (corn and sorghum) intended for both human and animal consumption, and direct animal applications including incorporation into cattle eartags and sprays (U.S. EPA, 1999c, n.d.). Pirimiphos-methyl is used to control a large number of different insects including, but not limited to, cigarette beetles; confused flour beetles; corn sap beetles; flat grain beetles; hairy fungus beetles; red flour beetles; sawtoothed beetles; granary weevils; maize weevils; merchant grain beetles; rice weevils; lesser grain borers; and angoumois grain moths, Indian meal moths, and almond moths on corn (seed and whole-grain), rice (whole-grain), wheat (whole-grain), and grain sorghum (seed and whole-grain); mealy bugs; mites (iris bulbs) horn flies and face flies (U.S. EPA, 2001). For malaria control, typical use includes the application of 1 or 2 g pirimiphos-methyl/m^3 of a 2–5 percent suspension to indoor walls and ceilings every 3 months. Ultra-low-volume (ULV) sprays and thermal fogs are additional application methods. To control DDT resistant fleas, a 2 percent dust is applied in rodent burrows. Pirimiphos-methyl is not recommended for use directly on humans or on processed foods (WHO/FAO, 1983; U.S. EPA, 1999c). Current registered uses in the United States include food and non-food uses. Food uses include use on sorghum, corn (gain and seed), nonlactating dairy cattle, beef/range/feeder cattle, and calves. Non-food uses include use on iris bulbs. No residential or public health uses are currently registered in the United States (U.S. EPA, 2001)

Formulations and Concentrations

There are several typical formulations for pirimiphos-methyl, each formulation varying in the amount of active ingredient (ai) it contains. The typical formulations for pirimiphos-methyl include (U.S. EPA, 1999c, 2001; WHO/FAO, 1983) the following:

- U.S. registered formulations: emulsifiable liquid concentrate (57 percent ai), treated ear tags (14 percent and 20 percent ai)
- For agricultural and horticultural uses: emulsifiable concentrate (250–500 g ai/L), ULV concentrate (500 g ai/L), encapsulated formulas (250–400 g ai/kg), dusts (10 and 20 g ai/kg), wettable powders (250 and 400 g ai/kg), fog (100 g ai/L), aerosol (20 g ai/L with pyrethroids), solvent free formulation (900 g ai/kg), smoke generator formulation
- For public health uses: emulsifiable concentrate (250 and 500 g ai/L), ULV concentrate (500 g ai/L), encapsulated formulation (200 g ai/L), dusts (10 and 20 g ai/kg), wettable powder (250 and 400 g ai/kg), fog (100 g ai/L), aerosol (20 g ai/L with pyrethroids), solvent-free formulation (900 g ai/kg), smoke generator formulation
- For household uses: emulsifiable concentrate (80 g ai/L), dusts and aerosols (with pyrethroids) for use in the home and garden.

Degradation Products

Stored pirimiphos-methyl products are broken down by hydrolysis of the phosphorus-ester side chain, which results primarily in the parent hydroxyl-pyrimidine (WHO/FAO, 1974). The main hydrolysis degradates at pH 5, 7, and 9 were 2 (diethylamino)-4-hydroxy-6-methyl pyrimidine and O-2-diethylamino-6-methylpyrimidin-4-yl o-methyl-phosphorothioate (U.S. EPA, 2001). In soil, the major metabolite is the parent hydroxypyrimidine (IV) together with smaller amounts of the related compounds (V) and (VI). Compound (IV) is the major degradation product in water with only trace quantities of the P=0 analogue (III) detected (WHO/FAO, 1974).

In humans, pirimiphos-methyl is broken down into the degradation products desethyl pirimiphos-methyl and pirimiphos-methyloxon, which are also active and have transient stability (WHO/FAO, 1983). When pirimiphos-methyl is broken down in rats and dogs, the major urinary metabolite (30 percent of administered dose) was 2-ethylamino-4-hydroxy-6-methylpyrimidine. Other metabolites included 4-0(2-diethylamino-6-methylpyrimidinyl-ß-D-glucosiduronic acid (11 percent of dose in dogs), an unidentified phosphorus-containing product likely to be a dealkylated derivative of either pirimiphos-methyl or its oxygen analogue (12 percent of dose in rats), and 2-amino-4-hydroxy-6-methyl pyrimidine (8 percent of dose in rats and 5 percent of dose in dogs) (WHO/FAO, 1992).

Shelf Life

Under normal storage conditions at room temperature, pirimiphos-methyl is stable for up to 6 months. However, it decomposes in sunlight (WHO/FAO, 1983).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Pirimiphos-methyl has limited mobility and persistence in soil (WHO/FAO, 1974). For a variety of soil types, pirimiphos-methyl has a half-life of less than one month (WHO/FAO, 1974). It hydrolyzes rapidly in acidic soils and is stable in neutral and alkaline environments with a half-life of 7.3 days at pH 5, 79 days at pH 7, and 54–62 days at pH 9 (U.S. EPA, 2001). Pirimiphos-methyl decomposes in sunlight (WHO/FAO, 1983).

Fate and Transport in Aquatic Systems

Pirimiphos-methyl is not expected to have a significant impact on water resources due to the lack of significant outdoor uses (U.S. EPA, 2001). It degrades in water mainly by hydrolysis, which is attenuated by sunlight. In sunlight, 50 percent degradation occurs within one day. Volatilization also occurs from still water; however, it is not as significant as hydrolysis (WHO/FAO, 1974).

Human Health Effects

Acute Exposure

Effects/Symptoms

Similar to other organophosphates, pirimiphos-methyl is a cholinesterase inhibitor and interferes with the normal functioning of the nervous system. It causes dose-related reversible decreases in plasma, red blood cell, and brain cholinesterase at very low doses by ingestion, dermal, and inhalation exposures. It is of relatively low acute oral, dermal, and inhalation toxicity (U.S. EPA, 1999b). In two human studies, volunteers were fed a dose of 0.25 mg/kg/day for up to 56 days. Marginal plasma cholinesterase depression was observed after both dosing periods (U.S. EPA, 1998b, 2006). However, these studies have many deficiencies and should be used as supplemental data. When compared to animal data, they provide some evidence that

humans may be more sensitive than animals as is indicated by the lower effect level for cholinesterase inhibition in humans (U.S. EPA, 1999b). No human poisonings from mishaps with pirimiphos-methyl have been reported (WHO/FAO, 1983).

Animal studies have shown that pirimiphos-methyl is only slightly toxic following acute oral and dermal exposures, with reported LD_{50} values in rats of >2,400 mg/kg (U.S. EPA, 1999a). Other reported oral LD_{50}s are as follows: rabbit (male) 1,154–2,300 mg/kg, mouse (male) 1,020–1,360 mg/kg, guinea pig (female) 1,000–2,000 mg/kg, dog (male) > 1,500 mg/kg, and cat (female) 575–1,150 mg/kg. The reported dermal LD_{50} is > 4,500 mg/kg in female rats (WHO/FAO, 1983), >4,050 mg/kg in female rabbits, and 2,200–4,050 mg/kg in male rabbits (U.S. EPA, 2001, 1999a, 1998a). The reported acute inhalation LC_{50} is > 4.7 mg/L for rats (U.S. EPA, 2001, 1999a, 1998a). Among mammals, no one species appears to be more susceptible. However, the hen is appears to be highly susceptible with a reported LD_{50} of 79–80 mg/kg (WHO/FAO, 1983). Clinical signs of exposure include neurotoxicity, excessive salivation, abnormal gait, ataxia, and leg paralysis. Dermal exposure also decreased plasma cholinesterase levels (WHO/FAO, 1983). Eye and skin irritation have been observed in rabbits (U.S. EPA 1999d, 1998b); however, pirimiphos-methyl has not been shown to be a dermal sensitizer in guinea pigs or rats (U.S. EPA, 1998b; WHO/FAO, 1983).

Treatment

Exposure to pirimiphos-methyl may be determined through laboratory tests of urine and blood that measure breakdown products of pirimiphos-methyl in urine or cholinesterase levels in blood. Blood levels of cholinesterase, especially in plasma, are the most useful in diagnosis of poisoning. However, neither urinary or blood tests are specific for pirimiphos-methyl exposure. Early symptoms of pirimiphos-methyl exposure include excessive sweating, headache, weakness, giddiness, nausea, vomiting, stomach pains, blurred vision, slurred speech, and muscle twitching. Symptoms of more severe poisoning may advance to convulsions, coma, loss of reflexes, and loss of sphincter control. Following dermal exposures, the person should stop working and any contaminated clothing should be removed. Exposed areas of skin should be washed with soap and water and flushed with large quantities of water. For oral exposures, vomiting should not be induced unless a potential lethal dose has been ingested and the person is conscious. Care should be taken as the vomitus may contain toxic amounts of the chemical. Once under medical care, potential lethal doses should be treated by rapid gastric lavage unless the patient is already vomiting. Any ocular exposure should be treated by washing with isotonic saline. If no respiratory insufficiency is noted, peripheral symptoms should be treated with 2–4 mg of atropine sulfate and 1,000–2,000 mg pralidoxime chloride or 250 mg toxogonin (adult dose) by slow intravenous injection. If severe respiratory difficulties, convulsions, and unconsciousness are present, atropine and a reactivator should be given immediately. The airway should be maintained. Morphine, barbiturates, phenothiazine, tranquillizers, and central nervous system stimulants are all contraindicated (WHO/FAO, 1983).

Chronic Exposure

Noncancer Endpoints

Workers in two WHO-supervised health spray program did not show any signs of pesticide poisoning; however, at the end of one of the programs, plasma cholinesterase activity was 70–75 percent of the mean of pre-exposure values. The people living in the spray areas exhibited no signs of poisoning and no effect on cholinesterase activity. Volunteers exposed to 0.25 mg/kg/day for up to 56 days exhibited no toxic effects on liver function or blood tests and an acceptable daily intake (ADI) of 0.01 mg/kg was established (WHO/FAO, 1983).

Chronic exposure data in animals indicates that a main target of pirimiphos-methyl toxicity is the nervous system. Rats repeatedly exposed to high doses of pirimiphos-methyl showed a cumulative inhibitory effect on

cholinesterase (WHO/FAO, 1983). In 90-day and 2-year dietary studies in rats, plasma cholinesterase and some erythrocyte and brain cholinesterase inhibition was reported. In a 2-year dog study and an 80-week mouse study, similar effects were observed (WHO/FAO, 1983).

In developmental and reproductive toxicity studies in rats and rabbits, maternal/parental NOELs were less than or the same as offspring NOELs. No increased sensitivity was noted in fetuses or pups. There is no evidence that pirimiphos-methyl is teratogenic in rat or rabbit feeding studies (U.S. EPA, 1998b, 2006; WHO/FAO, 1983). In several mammalian studies, no mutagenic potential was observed (U.S. EPA, 1998b; WHO/FAO, 1983).

Cancer Endpoints

EPA determined that the carcinogenic potential of pirimiphos-methyl could not be determined because a reliable rat carcinogenicity study is lacking (U.S. EPA, 1998b). In an 80-week mouse feeding study, a 78-week mouse feeding study, a 80-week mouse oral study, a 2-year rat feeding study, a 78-week rat feeding study, and a 2-year oral dog study, no evidence of carcinogenic potential was identified (WHO/FAO, 1983; U.S. EPA, 1998b, 2006). Additionally, mammalian mutagenicity studies do not provide any evidence that supports a carcinogenic potential for pirimiphos-methyl (WHO/FAO, 1983).

Toxicokinetics

Pirimiphos-methyl can be absorbed via the gastrointestinal tract, the skin, or, less commonly, by inhalation of fogs, smokes, or spray mists. It is rapidly metabolized and excreted. Pirimiphos-methyl is broken down into desethyl pirimiphos-methyl and pirimiphos-methyloxon, which are also active and have transient stability. In rats dosed with radiolabeled pirimiphos-methyl, 70 percent was excreted within 24 hours and 100 percent was excreted within 5–6 days. Excretion was mainly in the urine (85 percent) and to a lesser extent, feces (15 percent). Pirimiphos methyl and its metabolites do not accumulate in the liver, kidneys, or fatty tissues of rats and domestic animals following oral exposure (WHO/FAO, 1983).

Ecological Effects

Acute Exposure

Pirimiphos-methyl is not expected to pose a hazard to birds and mammals from acute exposure, because of lack of exposure. In the laboratory, pirimiphos-methyl exhibits relatively high toxicity to birds (WHO/FAO, 1983). Acute oral LD_{50} values in various bird species include chickens (79–80 mg/kg), Japanese quail (140 mg/kg), and green finches (200–400 mg/kg). Dietary LD_{50}s of 630 mg/kg for mallard ducks and 206 mg/kg for bobwhite quail chicks were identified. No lasting adverse effect on hens; chicks; or egg production, quality, or hatchability was seen in studies of chickens fed 4–40 ppm in their diet (WHO/FAO, 1983).

When used for its registered purposes, pirimiphos-methyl is not expected to result in significant exposures of aquatic organisms (U.S. EPA, 2001). Additionally, any risk would be mitigated by its strong tendency to decompose in water and to undergo photo-oxidation (WHO/FAO, 1983). In static tests, the reported 48-hour LC_{50} was 1.4 mg/L in carp and 0.25 mg/L in rainbow trout. The 24-hour LC_{50} for carp was 1.6 mg/L. In flow-through tests, the reported 48-hour LC_{50} was 4.1 mg/L in fathead minnow and 0.53 mg/L in rainbow trout, while the 24-hour LC_{50} was 5.6 mg/L in fathead minnow and 0.78 mg/L in rainbow trout (WHO/FAO, 1983).

Chronic Exposure

Due to low risk of both terrestrial and aquatic acute ecological effects of pirimiphos-methyl, serious adverse effects are not anticipated from chronic exposures. Subchronic 90-day exposure of birds to oral doses of up to 10 mg/kg did not result in clinical or histopathological findings (WHO/FAO, 1983).

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Profile for Propoxur:

CAS Registry Number 114-26-1

Summary of Insecticide

Chemical History

Propoxur is a broad spectrum, nonsystemic carbamate insecticide that was first introduced in 1959. It is used by homeowners and pest control operators in both agricultural and nonagricultural applications to kill a variety of chewing and sucking pests, mosquitoes, ants, flies, cockroaches, hornets, crickets, and lawn and turf insects (U.S. EPA, 1997a, 2000; EXTOXNET, 1996). Propoxur (Baygon) was first registered in the United States for pesticide use in 1963 and currently there are two registered technical products, several manufacturing use only products, and 173 registered products containing propoxur (U.S. EPA, 1997b).

Propoxur exhibits its toxic effects through reversible cholinesterase inhibition (U.S. EPA, 2000). It has moderate toxicity in mammals (WHO/FAO, 1976), high toxicity in birds, and moderate toxicity in fish (EXTOXNET, 1996; U.S. EPA, 1997b). Short-term exposures may cause effects on the nervous system, liver, and kidneys (IPCS, 1994). In humans, symptoms of acute oral poisoning include red blood cell cholinesterase inhibition with mild transient cholinergic symptoms including nausea, vomiting, sweating, blurred vision, and tachycardia. Long-term inhalation exposures in humans results in cholinesterase inhibition, headaches, nausea, and vomiting (U.S. EPA, 2000). Propoxur pesticides are available as emulsifiable concentrates, wettable powders, dusts and powders, baits, aerosols, fumigants, granular baits, containerized baits, pest strips, shelf paper, pet flea collars, and oil sprays (EXTOXNET, 1996; U.S. EPA, 1997a). Applications methods include aerosol can and injection tube; concentrated liquid using a compressed air sprayer or hand or power sprayer; wettable powder using a ready-to-use sprayer liquid, a power or had pressurized sprayer, or a low pressure sprayer for oil soluble liquid (U.S. EPA, 1997b).

Description of Data Quality and Quantity

Extensive review data for propoxur are limited. Relevant resources include

- Propoxur: Registration Eligibility Decision (RED) Document (U.S. EPA, 1997b)
- IRIS summary review (U.S. EPA, 2006)
- Pesticide Information Profile for Propoxur (EXTOXNET, 1996)
- Data Sheet on Pesticides. No. 25: Propoxur (WHO/FAO, 1976)
- International Safety Cards: Propoxur (IPCS, 1994).

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks) for propoxur.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.004	mg/kg/day	Inhalation NOEL (2.2 mg/m3) for neurological effects in rats, adjusted for intermittent exposure and UF of 100 applied	U.S. EPA (1997b)
Acute, Intermediate, Chronic	Oral	0.005	mg/kg/day	Chronic RfD based on LOEL in humans with UF of 30 applied	U.S. EPA (1997b)
Acute, Intermediate, Chronic	Dermal	10	mg/kg/day	Dermal NOAEL for toxicity in rabbits with UF of 100 applied	U.S. EPA (1997b)
Cancer	Inhalation, Oral, Dermal	0.0037	per mg/kg/day	Cancer slope factor based on male rat bladder tumors	U.S. EPA (1997b)

For inhalation exposure, a NOEL of 2.2 mg/m^3 (2.4 mg/kg/day)[7] was identified in rats exposed to propoxur (Pauluhn, 1992, 1994) via inhalation for 6.3 hours per day, 5 days per week for 2 years. Significant plasma, red blood cell, and brain cholinesterase inhibition were observed at higher concentrations (U.S. EPA, 1997b). The concentration was adjusted for intermittent exposure[8] (0.4 mg/kg/day) and an uncertainty factor of 100 was applied to account for interspecies and intrahuman variation, for an inhalation benchmark of 0.004 mg/kg/day. This value is appropriate for all exposure durations. However, the vapor pressure of propoxur is extremely low and significant human exposure via inhalation is not expected (U.S. EPA, 1997b).

For oral exposure, the chronic oral RfD of 0.005 mg/kg/day was calculated based on a LOEL of 0.15 mg/kg for a 40 percent red blood cell cholinesterase inhibition reported in a human exposure study (Vandekar et al., 1971) with an uncertainty factor of 30 applied to account for intrahuman variability (10) and the use of a LOEL (3) (U.S. EPA, 1997b). This value is appropriate for all exposure durations.

For dermal exposure, a NOEL of 1,000 mg/kg/day for lack of toxic effects in a subchronic rabbit study (Diesing and Flucke, 1989) is appropriate for all exposure durations (U.S. EPA, 1997b); an uncertainty factor of 100 was applied to account for interspecies and intrahuman variability. This value is appropriate for all exposure durations. However, studies indicate a very low absorption potential (<20 percent in humans) and/or hazard by the dermal exposure route (U.S. EPA, 1997b).

EPA classified propoxur as a Group B2 chemical, probable human carcinogen. EPA calculated a unit risk of 3.7×10^{-3} per mg/kg/day based on bladder tumors in male rats (U.S. EPA, 1997b).

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[7] Conversion between mg/m^3 and mg/kg/day assumes, for Wistar rats, an average body weight of 0.187 kg and inhalation rate of 0.2 m^3/day (U.S. EPA, 1988).

[8] Adjustment for intermittent exposure is the product of air concentration and exposure of 6.3/24 hours/day and 5/7 days/week.

Insecticide Background

CAS #:	114-26-1
Synonyms:	o-isopropoxyphenyl methylcarbamate (IUPAC); 2-(1-methylethoxy) phenyl methylcarbamate (CA) (WHO, 2005; U.S. EPA 1997b) 2-Isopropoxyphenyl methylcarbamate Phenol, 2-(1-methylethoxy)-,methylcarbamate, Phenol, o-isopropoxy-, methylcarbamate, Propoxur [Phenol, 2-(1-methylethoxy) -, methylcarbamate 2-(1-Methylethoxy)phenyl methylcarbamate PHC (PAN, 2005; IPCS, 1994)
Chemical Group:	carbamate (EXTOXNET, 1996; U.S. EPA 1997b)
Registered Trade Names:	Trade and other names for propoxur include: Arprocarb, Bay, Bay 9010, Bay 5122, Bay 9010, Baygon, Bayer 39007, Bifex, Blattanex, Blattosep, Brifur, Bolfo, BO Q 5812315, Chemagro 9010, Compound 39007 , Dalf dust , DMS 33, ENT 25671, Invisi-Gard, OMS 33, PHC (JMAF), Pillargon, Prentox Carbamate, Propogon, Proprotox, Propyon, Rhoden, Sendra, Sendran, Suncide, Tendex, Tugon, Fliegenkugel, UN Carbamate, Unden, and Undene (WHO, 2005; PAN, 2005; EXTOXNET, 1996; IPCS, 1994; WHO/FAO, 1976; IPCS, 1973)

Usage

Propoxur is a residual carbamate insecticide that has a variety of indoor uses, including the control of mosquitoes, ants, cockroaches, crickets, flies, bees, hornets, wasps, ticks, yellow jackets, bedbugs, fleas, woodlice, and spiders (U.S. EPA, 1997b; WHO, 2005; WHO/FAO, 1976). Indoor food applications include only crack and crevice treatment in food areas (U.S. EPA, 1997b). There are limited outdoor applications consisting mostly of perimeter and spot treatments of nests and lawn and turf insects (U.S. EPA, 1997b, 2000). Crop applications include sugar cane, cocoa, grapes, other fruit, maize, rice vegetables, cotton, lucerne, forestry, and ornamentals (WHO, 2005). Propoxur is used in the control of malaria and in pet flea collars (U.S. EPA, 2000). In public health and agricultural applications, propoxur is applied as a dust or by spraying (WHO, 2005). It is available in commercial products as a single active ingredient or combined with other pesticides (U.S. EPA, 1997b).

Formulations and Concentrations

Common formulations of pesticides containing propoxur include technical grade propoxur, emulisfiable concentrates, wettable powders, baits, aerosols, fumigants, granules, and oil sprays (EXTOXNET, 1996). Typical formulations and percent propoxur content include ready-to-use liquid (0.5–1 percent), pressurized aerosol liquid (0.25–2 percent), oil-soluble liquid/liquid concentrate (8–19.6 percent propoxur), pastes (2 percent), wettable powders (70 percent), solid baits (0.25–2 percent), pet flea collars (impregnated plastic) (0.4–10 percent), impregnated shelf papers (1 percent), and insecticidal tapes (10 percent) (U.S. EPA, 1997b). Common formulations used for agricultural, horticultural, and forestry applications include wettable powders (50 percent), dusts (1–2 percent), granules, oils, emulsifiable concentrates (200 g/L; 20 percent w/w), pressurized sprays, smokes, baits (various concentrations) (WHO/FAO, 1976; IPCS, 1973).

WHO (2005) indicated that the propoxur content in various preparations should be declared and contain the following:

- Technical grade propoxur: not less than 980 g/kg
- Wettable Powder: 500 g/kg ± 5% of the declared content.

Shelf Life

Propoxur is reported to be stable under normal storage and use conditions (IPCS, 1973) but unstable in highly alkaline media. The half-life propoxur is reported as 40 minutes at pH 10 at 20°C (WHO/FAO, 1976). WHO (2005) reported that following storage at 54 ± 2°C for 14 days, 97 percent or greater of the active ingredient must be present in wettable powder formulations.

Degradation Products

In vivo, propoxur is biotransformed by depropylation to 2-hydroxyphenol-N-methylcarbamate and by hydrolysis to the phenol. The glucuronides detected in urine are accounted for by ring hydroxylation and isopropoxy hydroxylation followed by conjugation. Major metabolites in rats include 5-hydroxy-2-isopropoxyphenyl n-methylcarbamate, 2-hydroxyphenyl n-methylcarbamate, o-isopropoxyphenol, o-isopropoxyphenyl, and n-hydroxymethylcarbamate. In mice, the major metabolies include o-isopropoxyphenyl n-hydroxymethylcarbamate. In bean plants, the major metabolites include 4-hydroxy-2-isopropoxyphenyl n-methylcarbamate, 2-hydroxytphenyl n-methylcarbamate, and o-isopropoxyphenyl n-hydroxymethlycarbamate (HSDB, 2005). Limited human data are available. Many propoxur metabolites were found in the urine of a person attempting suicide by ingestion of a large quantity of the emulsifiable concentrate formulation. These were present both as free compound or conjugated with glucuronide or sulfate. As in other species, biotransformation was from depropoxylation, hydrolysis of the ester bond and ring hydroxylation (IPCS, 1989).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Propoxur is expected to be moderately to very highly mobile and moderately persistent in soil (HSDB, 2005; U.S. EPA, 1997a, 1997b; EXTOXNET, 1996). With a K_{oc} ranging from <1 to 103, high to very high mobility is expected if propoxur is released in soil (HSDB, 2005); however, the mobility depends on the soil type and previous exposures to propoxur. Biodegradation in soil is more rapid in previously exposed soils. In many soil types, propoxur is highly mobile due to its low affinity for soil binding (EXTOXNET, 1996; U.S. EPA, 1997a, 1997b). It evaporates from soil, with the amount increasing with the moisture content of the soil, and the half-life is 6–8 weeks, depending on the soil type (IPCS, 1973). Data from studies of the persistence of propoxur in several soil types suggest that it moves rapidly through all soil profiles below the 12 inch sampling depth. Its fate and transport characteristics are similar to those chemicals that are known to leach into groundwater (U.S. EPA, 1997b).

Hydrolysis appears to be the primary mode of degradation (U.S. EPA, 1997b). At neutral pH, propoxur is hydrolically stable but degrades rapidly at alkaline pH values (U.S. EPA, 1997b). Half-life values of a propoxur in aqueous solutions at 20°C are reported to range from 1 minute at pH 12.8 to 40 minutes at pH 10.8 (IPCS, 1973). Half-life values of 16 days at pH 8, 1.6 days at pH 9, and 0.17 days at pH 10 are reported (U.S. EPA, 1997b). Volatilization is not expected to be a major fate process from moist soil surfaces (HSDB, 2005). The major fate process in moist soils is biodegradation. Under aerobic conditions, biodegradation half-lives of 80 days in silt loam soil and 120 days in sandy loam soil are reported (HSDB, 2005). On inert surfaces, however, volatilization is the main fate process. On a glass surface, 50 percent of a propoxur residue was still present 1.8 hours after application (IPCS, 1973). Propoxur in soil shows no or little susceptibility to

photolysis (U.S. EPA, 1997b; IPCS, 1973). Half-lives of several months were reported for the degradation of propoxur under aerobic and anaerobic conditions (U.S. EPA, 1997b).

Fate and Transport in Aquatic Systems

Propoxur is highly soluble in water and there is a high likelihood of groundwater penetration because it does not adsorb strongly to soil particles (HSDB, 2005; EXTOXNET, 1996; U.S. EPA, 1997a). It is relatively stable in water at pH 7 or less but hydrolyzes rapidly at pHs greater than 7 (IPCS, 1973). In a 1 percent aqueous solution at pH 7, propoxur hydrolyzes at a rate of 1.5 percent per day (EXTOXNET, 1996). Reported field half-lives for propoxur are 14–50 days (EXTOXNET, 1996). The hydrolysis half-life of propoxur is reported to be 1 year at pH 4, 93 days at pH 7, and 30 hours at pH 9 (HSDB, 2005). Volatilization from water is not expected to be a major fate process. However, propoxur is susceptible to photolysis in water (U.S. EPA, 1997b). The half-life of propoxur irradiated with light more than 290 nm is reported as 88 hours (HSDB, 2005). Because propoxur degrades rapidly in water, bioconcentration in fish is unlikely (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Propoxur causes its toxic effects by reversible inhibition of cholinesterase. Short-term exposures may cause effects on the nervous system, liver, and kidneys (IPCS, 1994). In humans, symptoms of acute oral poisoning include red blood cell cholinesterase inhibition with mild transient cholinergic symptoms including nausea, vomiting, sweating, blurred vision, and tachycardia (U.S. EPA, 2000). Limited data exist on the human health effects of acute exposure to propoxur. In volunteers, a single oral dose was reported to cause stomach discomfort, sweating, and redness of the face. However transient erythrocyte cholinesterase activity inhibition (up to 27 percent) was observed at a higher level and was associated with vomiting, sweating, and blurred vision (WHO/FAO, 1976). When used to control for malaria, spray operators experienced occasional short-lasting symptoms including nausea, headache, sweating, and weakness from which they quickly recovered (WHO/FAO, 1976; EXTOXNET, 1996). Additionally, some mild reactions were reported by residents where it was applied (WHO/FAO, 1976).

In animals, propoxur is acutely toxic via the oral, inhalation, and dermal routes (U.S. EPA 1997b, 2000; EXTOXNET 1996). Acute inhalation and dermal exposures are moderate to highly toxic while oral exposures are highly to be extremely toxic (U.S. EPA, 1997a, 2000). Propoxur is highly toxic to animals via ingestion. In rats, the oral LD_{50} for propoxur ranges from 68 mg/kg in females to 116 mg/kg in males (EXTOXNET, 1996; WHO/FAO, 1976; U.S. EPA, 1997b). In other species, reported oral LD_{50} values include approximately 100 mg/kg in mice and 40 mg/kg in guinea pigs (EXTOXNET, 1996). Reported dietary levels causing no toxic effects in animals include 300mg/kg/day for mice, 10 mg/kg/day for rats, and 5 mg/kg/day for dogs (IPCS, 1989). Via the dermal route, the reported LD_{50} values in various species include greater than 2,400 mg/kg in rats (EXTOXNET, 1996; WHO/FAO, 1976) and 500 mg/kg to > 2000 mg/kg in rabbits (EXTOXNET, 1996; U.S. EPA, 1997b). Via inhalation, the reported LC_{50} values include a 4-hour LC_{50} of >0.5 mg/L in rats (U.S. EPA, 1997b) and a 1-hour LC_{50} of > 1.44 mg/L (EXTOXNET, 1996).

Similar to its effects in humans, acute exposure to propoxur in animals causes symptoms typical of cholinesterase inhibition (EXTOXNET, 1996; U.S. EPA, 1997b). Cholinesterase depression, muscle spasms, and salivation have been reported within 10 minutes of oral administration in rats (U.S. EPA, 1997b). In rats fed propoxur in their diet for 16 weeks, whole blood cholinesterase was inhibited at dietary levels over 500 ppm while plasma, whole blood, and brain cholinesterase were inhibited at dietary levels greater than 1,000

ppm at study termination. Signs of cholinesterase inhibition were also observed in both rats and mice within 15 minutes of exposure to different concentrations of propoxur aerosol (WHO/FAO, 1976). Brain pattern and learning ability changes can occur at lower concentrations than those that cause cholinesterase inhibition and/or organ weight changes (EXTOXNET, 1996).

Although propoxur is a mild eye irritant in rabbits, it is not a skin irritant in rabbits or a dermal sensitizer in guinea pigs (U.S. EPA, 1997b). Acute exposure to propoxur is not considered to be teratogenic in rats (WHO/FAO, 1976).

Treatment

Exposure to propoxur may be determined through laboratory tests that determine cholinesterase levels in blood with erythrocyte cholinesterase being a more informative indicator than either plasma or whole blood. However, the enzyme will only be inhibited for a few hours following exposure. Additionally, phenol metabolites may be determined in urine (WHO/FAO, 1976; U.S. EPA, 2000). However, neither of these tests are reliable indicators of total exposure because they are not specific for propoxur (U.S. EPA, 2000).

Propoxur poisoning should be treated by first removing any contaminated clothing, and washing affected skin with soap and water and flushing the area with large amounts of water (WHO/FAO, 1976; IPCS, 1994). If propoxur gets in the eyes, they should be rinsed immediately with isotonic saline or water. Contact lenses should be removed, if possible. Oral exposure to propoxur should be treated by administration of activated charcoal (HSDB, 2005; IPCS, 1994). Rapid gastric lavage with 5 percent sodium bicarbonate is indicated if the patient is not already vomiting. Medical attention should be sought (WHO/FAO, 1976; HSDB, 2005). Inhalation exposures should be treated by removal to fresh air, placing in a half-upright position, monitoring for respiratory distress, and seeking medical attention (HSDB, 2005; IPCS, 1994). Because propoxur is quickly metabolized and symptoms are of a short duration, atropine treatment is not usually necessary by the time the patient reaches medical help (WHO/FAO, 1976). However, adults showing signs of propoxur toxicity should be treated with 1–2 mg atropine sulfate given intramuscularly or intravenously as needed. Oxygen may be necessary for unconscious patients or those in respiratory distress. Pralidoxime is usually not necessary unless the poisoning is severe. Barbiturate and central stimulants are contraindicated (HSDB, 2005; WHO/FAO, 1976).

Chronic Exposure

Noncancer Endpoints

Limited data are available on the effects of chronic exposure to propoxur in humans. Chronic effects are expected to be similar to acute effects (EXTOXNET, 1996). Cholinesterase inhibition, headaches, vomiting, and nausea were reported in humans following chronic inhalation exposure (U.S. EPA, 2000). When used to control for malaria, spray operators experienced occasional short lasting symptoms including nausea, headache, seating, and weakness from which they quickly recovered (WHO/FAO, 1976). No data are available on human reproductive or developmental effects (U.S. EPA, 2000).

In animals, propoxur is quickly detoxified and does not accumulate in body tissues over time. Daily doses approximating the LD_{50} have been tolerated by rats for long periods of time when the dose was given over the course of the day (EXTOXNET, 1996; WHO/FAO, 1976). Chronic oral exposure to propoxur in animals has been reported to cause cholinesterase inhibition, decreased body weight, liver and bladder effects, and a small increase in neuropathy (U.S. EPA, 1997b, 2000; WHO/FAO, 1976). Significant plasma, red blood cell, and brain cholinesterase inhibition was observed in male and female rats exposed to propoxur in air over a 2-year period (U.S. EPA, 1997b).

The nervous system and liver are the main organs affected by propoxur in both humans and animals (EXTOXNET, 1996). Increased liver weights were observed in rats fed propoxur in feed for 2 years (WHO/FAO, 1976). Reproductive and developmental effects have not been reported in rabbits orally exposed to propoxur. However, some fetotoxicity, decreased litter size, central nervous system impairment in offspring, and decreased fetal weights have been reported in rats orally exposed to propoxur (U.S. EPA, 1997b, 2000; WHO/FAO 1976). The data indicate that reproductive effects in humans are not expected at typical exposure levels and teratogenic effects will occur only at high levels (EXTOXNET, 1996). The available data indicate that propoxur is not mutagenic (EXTOXNET, 1996; U.S. EPA, 1997a).

Cancer Endpoints

EPA's OPP has classified propoxur as Group B2, probable human carcinogen, with a unit risk of 3.7×10^{-3} per mg/kg/day (U.S. EPA, 1997a, 1997b). No information is available on the carcinogenicity of propoxur in humans (U.S. EPA, 2000). A significant increase in bladder papillomas and/or carcinomas was reported in male rats while a significant increase in hepatocellular adenomas and combined adenoma/carcinoma was reported in male mice (U.S. EPA, 1997b, 2000). High dose exposure to propoxur is also associated with an increase in tumors of the uterus (U.S. EPA, 2000).

Toxicokinetics

Like most carbamates, propoxur can be absorbed through the oral, inhalation, and dermal pathways (HSDB, 2005; IPCS, 1994; WHO/FAO, 1976). It is readily absorbed by the lungs (HSDB, 2005) and gastrointestinal tract (IPCS, 1994) but to a lesser extent through the skin (WHO/FAO, 1976). Dermal rat studies indicate that absorption decreases with dose in a nonlinear way. Absorption of a dermal dose of 6.91 $\mu g/cm^2$ was 7.88, 10.2, 17.9, 23.2 and 32.5 percent for durations of 0.5, 1, 2, 4, 8, and 32 hours, respectively, which was a higher rate of absorption than in human studies of 8 and 24 hour exposures. Human studies indicate that the rate of 19.6 percent absorption most closely approximates the rate expected in the field (U.S. EPA, 1997b). Approximately 16 percent of the dose of radiolabeled propoxur applied to the forearms of volunteers was available for percutaneous absorption (HSDB, 2005). Additionally, the rate of dermal absorption is affected by the solvent used (U.S. EPA, 1997b).

Propoxur and its metabolites are distributed by the lymph system. Metabolism studies in rats exposed to radiolabeled propoxur have shown radioactivity in all organs (especially the intestines) except bones at 1 hour. High concentrations of radioactivity were still present in the gastrointestinal tract, bladder, and mucous membranes of the pharyngeal system after 24 hours. Some radioactivity was still present in the liver, kidneys, and mucous membranes of the pharyngeal region at 48 and 72 hours (U.S. EPA, 1997b). Peak concentrations were seen in the blood (at 15 minutes), brain (1 hour), liver (4 hours), and kidneys (6 hours) after oral exposure to 50 mg/kg propoxur, with the highest concentrations seen in the kidneys and the lowest concentration in the brain (HSDB, 2005). Ingested propoxur is rapidly absorbed, broken down, and excreted in the urine (EXTOXNET, 1996; U.S. EPA 1997b). The major routes of metabolism in rats are depropylation to 2-hydroxyphenyl-N-Methylcarbamate and hydrolysis to isopropoxyl phenyl. Peak circulating and tissue concentrations of isopropxyl phenol were achieved 30–60 minutes after a single oral dose in rats (HSDB, 2005). Because of its rapid metabolism and excretion, propoxur does not accumulate in mammalian tissues (EXTOXNET, 1996). The main route of excretion for propoxur is probably the urine (WHO/FAO, 1976) accounting for 60–95 percent of the dose (HSDB, 2005). In humans, 38 percent of a single oral dose of Baygon was excreted in the urine within the first 24 hours. Of that, most was excreted by the first 8–10 hours (EXTOXNET, 1996). In dermal studies in humans, total excretion was 19.6 percent of the total dermal dose (U.S. EPA, 1997b). Lesser amounts of propoxur are excreted as carbon dioxide (20–26 percent) and in feces (4 percent) (HSDB, 2005).

Ecological Effects

Acute Exposure

Acute exposure to technical grade propoxur is very highly toxic to many bird species (EXTOXNET, 1996; U.S. EPA, 1997b). Remarkable variation in the results of dietary studies of the toxicity of propoxur has been reported. Oral LD_{50} values for 97 percent ai in a 2 percent bait product range from 4.2 mg ai/kg body weight in mourning doves to 120 mg ai/kg body weight in sharp-tailed grouse (U.S. EPA, 1997b; EXTOXNET, 1996). An unexplained phenomenon where, in some instances, birds of a given species are able to metabolize propoxur has been reported. U.S. EPA (1997b) indicated more confidences in the LD_{50} values for Mallard ducks (9.44 mg ai/kg) and Bobwhite quail (1,005 mg ai/kg formulated product). In the diet, subacute 5-day LC_{50} values range from 206 ppm in Northern bobwhite quail exposed to an unknown concentration to greater than 5,000 ppm in Mallard ducks exposed to 98.8 percent ai and Japanese quail exposed to an unknown concentration (U.S. EPA, 1997b). The reported oral LD_{50} in mule deer is 100–350 mg/kg (EXTOXNET, 1996). Additionally, propoxur has been found to be highly toxic to honeybees (EXTOXNET, 1996).

Propoxur is expected to pose a minimal risk to aquatic organisms because of its limited outdoor bait use (U.S. EPA, 1997b). However, when exposures occur, they pose a slight to moderate acute risks to fish and other aquatic species (EXTOXNET, 1996). In freshwater fish, propoxur is moderately toxic with LC_{50} values ranging from >1–10 ppm (U.S. EPA, 1997b). The reported 96-hour LC_{50} values range from 3.7 ppm in rainbow trout exposed to 98.8 percent ai to 25 ppm in fathead minnow exposed to 88 percent ai (U.S. EPA, 1997b; EXTOXNET, 1996). The 96-hour LC_{50} for bluegill sunfish was reported as of 6.6 mg/L (EXTOXNET, 1996).

Propoxur is more toxic in freshwater and estuarine invertebrates. Acute exposure to technical grade propoxur is very highly toxic to freshwater and estuarine invertebrates with EC/LC_{50} values of 0.011 ppm in daphnids, 0.034 ppm in amphipods, 0.18 ppm in stonefly, and 0.041 ppm in pink shrimp (U.S. EPA, 1997b). An oral LD_{50} of 595 mg/kg was reported for propoxur in bullfrogs (EXTOXNET, 1996).

Chronic Exposure

Very little data exist for chronic exposure to propoxur in non-target terrestrial organisms. In birds, no reproductive effects were seen in Northern bobwhite quail fed diets containing greater than 320 ppm (98 percent ai) of propoxur for a number of weeks. No effects on brain cholinesterase were seen at concentrations up to 80 ppm. In Mallard ducks, no reproductive or brain cholinesterase effects were seen in birds fed diets containing 80 ppm (98 percent ai) for 23 weeks. However, reduced egg production and embryo survival were noted at 320 ppm (U.S. EPA, 1997b). Little or no data exist for chronic exposure to propoxur in marine/estuarine organisms. However, no significant accumulation of propoxur is expected in aquatic organisms (EXTOXNET, 1996).

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Profile for Pyriproxyfen:

CAS Registry Number 122453-73-0

Summary of Insecticide

Chemical History

Pyriproxyfen is a pyridine-based pesticide which is found to be effective against a variety of arthropods. It was introduced to the US in 1996 to protect cotton crops against whitefly. It has also found use protecting other crops and can also be used as a treatment for cat fleas. Pyriproxyfen is a juvenile hormone analog and a relatively stable aromatic compound. It functions as an insecticide by overloading the hormonal system of the target insect, ultimately affecting egg production, brood care and other social interactions, and inhibiting growth. It is active at very low dosages from 25-100 grams active ingredient per hectare (g a.i./ha). Pyriproxyfen is a potent insecticide and works especially well against public health insects like houseflies, mosquito larvae and ants. It gives 95% inhibition of emergence for mosquito larvae and its effects on mosquito larvae lasted for two months after application. Pyriproxyfen is an insect growth regulator that affects the physiology of morphogenesis, reproduction and embryogenesis of insects. It has low mammalian toxicity and environmental impact. The morphogenetic effect of pyriproxyfen is primarily seen during larval-pupal transformation. Therefore death occurs at the pupal stage and adult mosquitoes fail to emerge. (Sullivan)

Pyriproxyfen is a broad-spectrum insect growth regulator with insecticidal activity against public health insect pests. It is a WHOPES-recommended insecticide for the control of mosquito larvae. In agriculture and horticulture, pyriproxyfen has registered uses for the control of scale, whitefly, bollworm, leafhoppers, aphids and cutworms. Pyriproxyfen degrades rapidly in soil under aerobic conditions, with a half-life of 6.4–36 days. It disappeared from aerobic lake water sediment systems with half-lives of 16 and 21 days. Pyriproxyfen appeared to be degraded much more slowly in anaerobic lake water–sediment systems. (WHO 2006)

Pyriproxyfen is a juvenile hormone analogue, preventing larvae from developing into adulthood and thus rendering them unable to reproduce. Pyriproxyfen has a unique mode of action affecting the morphogenesis, reproduction and embryogenesis of insects. The morphogenetic effect of pyriproxyfen is primarily seen during larval-pupal transformation. Therefore death occurs at the pupal stage and adult mosquitoes fail to emerge. (Sullivan)

Insecticide Background

Chemical name and class

The CAS name for pyriproxyfen is 2-[1-methyl-2-(4-phenoxyphenoxy) ethoxy] pyridine and it belongs to the class of juvenile hormone mimics.

Synonyms, trade names, and formulations

Sumitomo Chemical Ltd. developed Sumilarv 0.5% G which is the most popular insecticide to control mosquito larvae. In the US pyriproxyfen is often marketed under the trade name Nylar. In Europe pyriproxyfen is known under the brand names Cyclio (Virbac) and Exil Flea Free TwinSpot (Emax). It is commonly formulated as an emulsifiable concentrate, granule, or water dispersible granules.

Common brand names are Adeal, Admiral, Atominal, Epingle. Juvinal, Knack, Lano, Nemesis (Farm Chemicals Handbook). There are 433 products registered by EPA with the bulk being for fleas, ticks and lice on pets.(www.pesticideinfo.org)

For example Archer insect growth regulator of Syngenta Crop Protection is for home and garden use against ticks, fleas, dermestid beetles, carpet beetle, hide beetle, carrion beetle, darkling beetles, gnats, midges, mosquitoes, house fly, stable fly, ants, cockroaches, and crickets. Distance Insect Growth Regulator sold by Valent USA. Corporation is labeled for ornamentals against shoreflies, fungus gnats, scales (crawlers), whiteflies, aphids, mealybugs, and spotted tentiform leafminer.

Esteem 25WP Insect Growth Regulator is another Valent product used on fruits and vegetables against leafrollers, leafminers, thrips, scales, whiteflies, citrus blackfly, aphids, pear psylla, fruitworms, peach twig borer, tomato pinworm, armyworms, cabbage looper, navel orangeworm, tobacco hornworm, oriental fruit worm, and codling moth. Etofenprox IGR Fogger is for mosquitoes etc. in urban areas as well as pillbugs, sowbugs, spiders, earwigs, fleas, silverfish, flies, fruit flies, wasps, ants, cockroaches, and crickets and is sold by Mclaughlin Gormley King Co.

Usage

Pyriproxyfen provides control of public health insect pests (flies, midges, mosquitoes). It is used on pets for control of fleas. It is applied to breeding sites such as swamps and livestock sheds. Pyriproxyfen can inhibit emergence of *Aedes aegypti* at very low dose rates. The LC_{50} has been shown to be 0.012 ppb. However in order to achieve complete inhibition of adult emergence and prolong the duration of control the actual field dose rates are higher than this, with label rates of 0.01 - 0.05 ppm of active ingredient (10 - 50 ppb). Using 0.5% pyriproxyfen equates to 2 g -10 g product per m^3 water. (Invest & Lucas)

Currently, pyriproxifen is one of several insecticides used in bait formulations for the control of the red imported fire ant. For managing fire ant, pyriproxyfen is formulated as bait on small particles such as corncob grits. Pyriproxyfen is also effective in controlling other insect pests, such as aphids, scales, whiteflies and psyllids and is in ant bait against pests of fruits and field crops and vegetables. (www.pesticideinfo.org)
Shelf Life

Pyriproxyfen is stable under recommended storage and handling conditions and would be expected to last for three years if properly stored. (MSDS)

Degradation Products

Examination of urine, feces, liver, kidney, bile, and blood metabolites yielded >20 identified metabolites. The major biotransformation reactions of pyriproxyfen include: (i) oxidation of the 4' - position of the terminal phenyl group; (ii) oxidation at the 5' - position of pyridine; and (iii) cleavage of the ether linkage and conjugation of the resultant phenols with sulfuric acid.

Core composites were analyzed for pyriproxyfen and two metabolites, 4-(4'-hydroxyphenoxy) phenyl-2-(2-pyridyloxy)-propyl ether (*a.k.a.* 4'-OH-Pyr) and 2-(2-pyridyloxy) propionic acid (PYPAC).

Six other metabolites were found from degradation in soil, plants, and water.

1. 4-(4-hydroxyphenoxy) phenyl (RS)-2-(2-pyridyloxy) propyl ether (soil)
2. (RS)-2-(2-pyridyloxy) propionic acid (soil)
3. 4-hydroxyphenyl (RS)-2-(2-pyridyloxy) propyl ether (water)
4. (RS)-2-hydroxypropyl 4-phenoxyphenyl ether (plant)
5. 2-hydroxypyridin (plant)
6. (RS)-2-(2-pyridyloxy)propyl alcohol (plant) (Sullivan, WHO 2006, 2007)

Environmental Behavior

Fate and Transport in Terrestrial Systems

The rate constant for the vapor-phase reaction of pyriproxyfen with photo-chemically-produced hydroxyl radicals has been estimated as 52 x 10^{-12} cm^3/molecule-sec at 25° C using a structure estimation method. This corresponds to an atmospheric half-life of about 7.4 hours at an atmospheric concentration of 5 x 10^5 hydroxyl radicals per cm^3. Pyriproxyfen is not expected to undergo hydrolysis in the environment due to the lack of hydrolysable functional groups. If released to soil, pyriproxyfen is expected to have no mobility based upon an estimated Koc of 405,000. Volatilization from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry's Law constant of 6.3x10^{-10} atm^3 m/mole. (Sullivan, WHO 2006, 2007)

Field studies evaluated the mobility and persistence of pyriproxyfen when applied to bare ground showed that both the parent compound and its major degradation metabolites, 4'-OH-Pyr PYPAC, were found to be stable in soil for up to a year. The greatest pyriproxyfen concentrations were found in the 0-6 inch soil layer. No pyriproxyfen residues were found above the level of quantitation below 12 inches. The half-life of pyriproxyfen in the 0-6 inch soil-layer was 36 days. No 4'-OH-Pyr or PYPAC residues were found below 2 inches or greater than 120 days. The metabolism of ^{14}C-pyriproxyfen in a sandy loam soil under aerobic conditions suggests that it degrades rapidly via biological catalysis, having a half-life of 6.4 to 9.0 days and serving as a carbon source for soil microorganisms. In a field study designed to show the efficacy of pyriproxyfen for controlling mosquitoes in dairy waste lagoons, the compound was shown to readily adsorb to organic matter; the test chemical concentration in the lagoon water samples slowly declined over a 64-day period, with a half-life of 7.5 days calculated. In leaching trials with four different soil types, over 50% of the active ingredient applied remained in the upper 6 cm of a 30-cm soil column; there was no indication of rapid potential for downward migration. (Sullivan, WHO 2006, 2007)

Pyriproxyfen degrades rapidly in soil under aerobic conditions, with half-lives of the parent and its two major metabolites, PYPAC and 4'-OH-Pyr, in soil and in water:

Half-life (d)	Pyriproxyfen	PYPAC 4'	-OH-Pyr
Aerobic soil metabolism	12.4	8.2	0.7
Aerobic aquatic metabolism:	23.1	15.8	0.7
Anaerobic aquatic metabolism:	346.5	41.25	4.80

Fate and Transport in Aquatic Systems

If released into water, pyriproxyfen is expected to adsorb to suspended solids and sediment based upon the estimated Koc. Volatilization from water surfaces is not expected to be an important fate process based upon this compound's estimated Henry's Law constant. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyze under environmental conditions. Pyriproxyfen has low water solubility but does not readily adsorb onto soil surfaces. Measured residue concentrations have been reported to decline by 50% in 24 hours in treated ponds. Pyriproxyfen remains biological activity for up to two months after an initial application. Its persistence in water in the absence of organic matter declines with increasing temperature and sunlight exposure. (Sullivan, WHO 2007)

The aerobic aquatic metabolic half-life of pyriproxyfen was determined to be from 16.2 to 20.8 days. Metabolism in aerobic aquatic media proceeds through oxidative cleavage of the ester linkages. Pyriproxyfen degraded quickly under aerobic aquatic conditions (lake sediment and water) to two major metabolites (PYPAC and 4'-OH-Pyr), several minor intermediate metabolites, bound residues, and CO_2. Pyriproxyfen is hydrologically stable under the conditions tested. Its persistence in water in the absence of organic matter declined as temperature and sunlight exposure increased. (Sullivan)

Human Health Effects

Acute Exposure

Clinical Symptoms

No data is available for this low toxicity insecticide.

Acute toxicity

The acute toxicity of pyriproxyfen is relatively low; transient, minimal signs of toxicity were observed only in animals in high oral dosages. Pyriproxyfen can cause brief and/or minor eye irritation. The expected adverse health effects resulting from an exposure may include redness and possible swelling. It can cause brief and minor irritation to skin. Pyriproxyfen is slightly toxic when absorbed through the skin but is not expected to cause allergenic skin reactions. It is minimally toxic when ingested. Based on an evaluation of the ingredients and/or similar products this product may be minimally toxic when inhaled. Exposure to high concentrations in the air may cause respiratory irritation. Signs and symptoms may include, but may not be limited to, nasal discharge, sore throat, coughing and difficulty in breathing. (Sullivan, WHO 2006, 2007)

Oral toxicity of the technical product if swallowed is in the safest toxicity classification (IV) having an LD_{50} > 5000 mg/kg in rats, thus is not expected to be very harmful. Similar toxicities were reported for mice (LD_{50} > 5000) and dogs (LD_{50} > 5000). Oral toxicity of the formulated product for the rat is surprisingly more toxic but lies in the next safest class (III) with a LD_{50} > 2000 mg/kg. The greater level of hazard would be due to the solvents in the formulated product. (Sullivan, WHO 2006, 2007)

Dermal toxicity was also measured in test animals with results all in toxicity class III: Rat, mice and rabbits all having LD_{50} > 2000 mg/kg. Therefore contact with skin is not expected to be very hazardous. Inhalation was moderately toxic (III) with a LC_{50} in rats of 4 h > 1.3 mg/L^3 of air. Pyriproxyfen is not irritating to the skin in the rabbit (toxicity level IV) and is only minimally irritating to eyes IV in rabbits. It is not sensitizing to the Guinea pig (level IV). (Sullivan, WHO 2006, 2007)

Medical treatment for acute poisoning

Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if needed. Administer oxygen by non-rebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary. Monitor for shock and treat if necessary. Anticipate seizures and treat if necessary. For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport. Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Cover skin burns with dry sterile dressings after decontamination. (HSDB)

In case of contact, immediately flush eyes with copious amounts of water for at least 15 minutes. In case of contact, immediately wash skin with soap and copious amounts of water. If inhaled, remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen. If swallowed, wash out mouth with water provided person is conscious. Call a physician. Wash contaminated clothing before reuse. (HSDB)

If swallowed do not induce vomiting and wash mouth with water. Give water to drink. If on skin remove contaminated clothing and wash skin thoroughly with soap and water. Launder contaminated clothing before reuse. Seek medical advice if irritation persists. If in eyes hold eyes open and flood with water for 15 minutes and seek medical advice. If inhaled move to fresh air. If any signs or symptoms occur or persist seek medical advice. Note to physician to apply basic aid and decontamination procedures (Sumitomo Chemical Company MSDS)

Chronic Exposure

Non-cancer Endpoints

In a sub-chronic oral exposure toxicity study with intake for 90 days, the NOAEL endpoints were derived for the rat (23 mg/kg/day), mouse (150-173 mg/kg/day), and dog (100 mg/kg/day). In the same sub-chronic oral toxicity tests the LOAEL for 90 days for the mouse was 901 mg/kg/day. In a study exposing animals 21 days in a dermal toxicity test for the rat gave a NOAEL of 1000 mg/kg. In the standard 28-day inhalation toxicity test @ 4 h/day exposure for the rat, the NOAEL was 0.482 mg/L^3 and 1.0 mg/L^3 for the LOAEL. Chronic toxicity of feeding of dogs for 1 year gave a NOAEL of 10 mg/kg/day. Chronic feeding determined that pyriproxyfen is a possible liver toxicant as well as a possible blood toxicant. Studies showed pyriproxyfen was non-mutagenic by Ames test, TK assay, cytogenetic assay, unscheduled DNA synthesis, micronucleus test. It was also non-teratogenic and non-genotoxic (reproductive). Pyriproxyfen is a suspected endocrine disruptor. Chronic maternal systemic toxicity tests (administered throughout gestation) administered in the rat gave a NOAEL of 100 mg/kg/day and a LOAEL of 300 mg/kg/day. Similarly the developmental NOAEL for the rat was 1000 mg/kg/day. Reproductive toxicity over 2 generations in the rat gave a LOAEL of 453 mg/kg body weight and a NOAEL of 476 mg/kg body weight. (Sullivan, WHO 2006, 2007)

In short- and long-term studies of the effects of pyriproxyfen in mice, rats and dogs, the liver (increases in liver weight and changes in plasma lipid concentrations, particularly cholesterol) was the main toxicological target. Repeated high exposure produced changes in the liver, kidney, and red blood cells but did not produce cancer in test animals. Overall this product is not expected to be a chronic hazard when used according to label directions. No developmental toxicity was produced in animals even at dosages that were toxic to the pregnant animal. It did not produce reproductive toxicity to test animals. Individuals that have pre-existing diseases of the liver, kidney, and red blood cells may have increased susceptibility to the toxicity of excessive exposures. Intake of pyriproxyfen from all sources is generally low and below the ADI. (Sullivan, WHO 2006, 2007)

Cancer Endpoints

Occupational exposure to pyriproxyfen may occur by dermal contact with this compound at workplaces where pyriproxyfen is produced or used. Studies by WHO concluded that pyriproxyfen was not carcinogenic. EPA has established the Reference Dose (RfD) for pyriproxyfen at 0.35 mg/kg/day. This RfD is based on a NOAEL of 35.1 mg/kg/day and an uncertainty factor (UF) of 100. The NOAEL was established from the combined chronic feeding/oncogenicity study in rats where the LOAEL was 3,000 ppm, based on a 16.9% decrease in body weight gain in females when compared to controls. (Sullivan, WHO 2006, 2007)

Toxicokinetics and Metabolism

The metabolic fate of pyriproxyfen was examined in rats and mice given single oral doses of (pyridyl-2,6-14C)- or (phenoxyphenyl-14C) pyriproxyfen at doses of 2 and 1000 mg/kg. The carbon-14 was excreted almost completely into urine and feces within 7 days after dosing and fecal excretion of carbon-14 predominated in both animals. Excretion of carbon-14 into feces and urine was, respectively, 84-97% and 4-

12% of the dose in rats and 64-91% and 9-38% in mice. Major metabolic reactions of pyriproxyfen were (1) hydroxylation at the 4-position of the terminal phenyl ring, (2) hydroxylation at the 2-position of the terminal phenyl ring, (3) hydroxylation at the 5-position of the pyridyl ring, (4) dephenylation, (5) cleavage of ether linkages, and (6) conjugation of the resultant phenols with sulfate or glucuronate. Although there was generally no marked difference in the metabolic profile of pyriproxyfen between the two species, significant sex-related differences were found in metabolic reactions 1, 3, and 6 in the rat but not in the mouse. (HSDB)

Ecological Effects

Pyriproxyfen is moderately toxic to birds having an acute LD_{50} > 2000 mg/kg for both mallard ducks and bobwhite quail. The dietary LD_{50} was 5200 ppm for quail and 2000 ppm for mallards which is safe. Against non-target terrestrial organisms, pyriproxyfen produced mixed results. Severe deformities at molt developed with several predatory bugs *Podisus maculiventris*, but was harmless to another predatory bug *Orius insidious*. However the larvae of *Rodolia cardinalis* ladybeetles successfully developed into adults after applications of pyriproxyfen. Pyriproxyfen is, however, practically non-toxic to bees. Bumblebee colonies were found to develop normally after feeding on pyriproxyfen-sucrose solution. The LD_{50} for honey bee adults (acute contact 48- and 96-hour exposure) is > 100 µg/bee. (Sullivan, WHO 2006, 2007)

The acute LC50 earthworm exposed over 14 d was >500 ppm indicating low toxicity. Pyriproxyfen has a low environmental impact and is suitable for the control of mosquito larvae but like any IGR may have some impact on other arthropods or crustacea. Usually the impact is low and populations rapidly recover but care should be taken to avoid application to natural rivers or lakes. When evaluated through the WHOPES it was concluded that pyriproxyfen will not adversely affect a vast majority of aquatic invertebrates and fish when applied at rates usually <50 ppb in mosquito control programs.'Pyriproxyfen is moderately to highly toxic (HT) to fish. Rainbow trout produced a LC50 (96h) > 0.325 mg/L (HT), while that for blue gill was 0.27 mg/L and carp at 0.45 , both highly toxic. Sheepshead minnow had an endpoint of 1.02 ppm/L which was moderately toxic. Pyriproxyfen was highly toxic to *Daphnia* with an EC_{50} (48h) of 0.40 mg/L and was very highly toxic to mysid shrimp with an EC_{50} (48h) of 0.065 µg/L. It was also highly toxic to *Selenastrum capricornutum* algae showing an EC_{50} (72 hour) of 0.064 mg/L. The duckweed aquatic plant showed a moderately toxic reaction as an EC_{50} (7 day) of 0.18 ppm. Oyster shell deposition was retarded from exposure over 96 h having an EC_{50} >92 µg/L. (Sullivan, WHO 2006, 2007)

Chronic exposures showed crustaceans and arthropods to be sensitive to pyriproxyfen. Two species of water fleas (*Daphnia magna* and *Daphnia pulex*) living in treated water, produced fewer progeny. This effect is, however, reversible. At field rates (6-28 g/ha) pyriproxyfen did not exhibit any marked effect on mayflies, dragonflies, ostracods, cladocerans, copepods, and water beetles. When pyriproxyfen was applied at doubled concentration, minor suppression of the reproductive capacity of cladocerans and copepods was observed. In a study of the efficacy of pyriproxyfen against mosquito larvae, non-target aquatic organisms that coexist in mosquito breeding habitats, exhibited no significant adverse effects resulting from a 0.01 ppm treatment in aquariums. Pyriproxyfen produced LC50 values of 0.098 ppm against the estuarine shrimp *Leander tenuicornis*, about 12 times the estimated field concentration. An estimated BCF of 3,700 suggests the potential for bioconcentration in aquatic organisms is very high based on an estimated log Kow of 5.6. (Sullivan, WHO 2006, 2007)

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Profile for Spinosad (spinosyn A & D):

spinosyn A: 131929-60-7

spinosyn D: 131929-63-0

Summary of Insecticide

Chemical History

In 1982, a vacationing scientist in the Caribbean took a soil sample from a drum that was used to make rum. From this sample, a new species of bacteria was identified in 1986: *Sacchrapolyspora spinosa*. The bacteria was later fermented in a lab and yielded a number of metabolites of *S. spinosa*. Together, they comprise spinosad. Spinosad has a mode of action as a stomach poison and contact insecticide. It activates the central nervous system of insects through interaction with the nicotinic acetylcholine receptors. Immediately after application, insect pests exhibit irreversible tremors, prostrate trembling, paralysis, and death. (Clarke, Kollman)

Spinosad is a mixture of tetracyclic macrolide neurotoxins, spinosyn A and D metabolites, produced during the fermentation. As such, it may be considered as a bioinsecticide. Spinosad is highly toxic to Lepidoptera, Diptera and some Coleoptera and has a unique mode of action involving the postsynaptic nicotinic acetylcholine and GABA receptors. The compound has been developed by Dow Agroscience (http://www.dowagro. com) as an agricultural insecticide for control of field crop, orchard and turf pests. Spinosad has a very low mammalian toxicity and a favorable environmental profile with low persistence and low toxicity to a number of predatory insects. As a result, the United States Environmental Protection Agency has classified spinosad as a reduced risk material. (Thompson, et al. 2000)

The U.S. Environmental Protection Agency (USEPA) has classified it as a "reduced-risk" compound. Because it is a naturally-derived, low- impact pesticide, spinosad labels carry the signal word "Caution", the lowest human hazard signal word assigned by the USEPA. (Kollman).

According to the EPA, the advantages of Reduced Risk pesticides include:

» Low impact on human health

» Lower toxicity to non-target organisms (birds, fish, plants)

» Low potential for groundwater contamination

» Low use rates

» Low pest resistance potential

» Compatibility with Integrated Pest Management (IPM) practices

In 2002, Clarke acquired the public health development rights to spinosad and has developed the mosquito larvicidal materials that it sells in its Natular brands. Spinosad is considered as a replacement for organophosphate treatment of domestic water supplies in Mesoamerica. For this, a slow-release formulation would be required for extended control in household water tanks, similar to the pellet and briquette formulations employed for slow release of Bti (*Bacillus thuringiensis* natural insecticide). Compared to Bti, spinosad also appears to provide longer lasting protection against reproduction of urban vectors such as *Aedes aegypti*. (Thompson et al. 2000)

Spinosad is available in suspension, gel/paste/cream, flowable concentrate, solution/liquid (ready-to-use), aqueous concentrate, and granular/flake formulations with the signal word "Caution" on the product labels.(Kollman)

It breaks down quickly and does not bioaccumulate in the environment. The active ingredient in Natula works like no other larvicide. Spinosad alters the function of mosquito larva's nicotinic acetylcholine receptors in a unique action that causes continuous nervous impulses. This constant involuntary nervous stimulus causes paralysis and death. The action results primarily by ingestion, as well as by contact with the active. Because of its unique mode of action, spinosad is classified as a Group 5 insecticide by the Insecticide Resistance Action Committee. It's the only active ingredient classified in Group 5 used for mosquito control. Because this class is unique and distinct from all other public health larvicides, this makes the Natular portfolio truly one of a kind. It also makes an excellent option for resistance management. Its novel mode of action and distinct class grouping makes Natular ideal for rotational use since it shows no cross-resistance with existing products used for mosquito control.

Spinosad begins to work immediately upon contact and ingestion; its first visible effects are seen within hours of application. Optimal control is reached within 24-72 hours, sustained at very uniform levels for the labeled control period. (Clarke)

Spinosad is a biologically derived insecticide produced via fermentation culture of the actinomycete *Saccharopolyspora spinosa*, a bacterial organism isolated from soil. It is composed of a mixture of two members of the chemical class of 12-membered macrocyclic lactones in a unique tetracyclic ring. Each component, designated spinosyn A and spinosyn D, is an unsaturated tetracyclic ester with two sugar derivatives (forosamine and rhamnose sugars) attached through ether linkages (Figure 1). Spinosyn A and D are identical in structure except for an additional methyl group on the core macrolide of spinosyn D. Commercial formulations contain a spinosyn A to spinosad D ratio of approximately 85:15. (Kollman)

Insecticide Background

Chemical name and class

In both A and D forms are most common in an 85:15 ratio. The chemical names are:

- SpinosynA is 2R,3aS, 5aR,5bS,9S,13S, 14R,16aS,16bR) –2-(6-deoxy-2,3,4-tri-O-methyl-_-Lmannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-_-Derythro-pyranosyloxy)-9-ethyl-2,3,3a,5a,6,7,9,10,11,12,13 ,14,15,16a,16bhexadecahydro-14-methyl-1H-8-oxacyclo-dodeca[b]as-indacene-7,15-dione; and

- Spinosyn D is (2R,3aS,5aR,5bS,9S,13S, 14R,16aS,16bR) –2-(6-deoxy-2,3,4-tri-O-methyl-_-Lmannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-_-Derythropyranosyloxy)-9-ethyl 2,3,3a,5a,6,7,9,10, 11,12,13,14,15,16a,16 bhexadecahydro-4,14-dimethyl-1H-8-oxacyclododeca[b]as-indacene-7,15-dione

Spinosad belongs to a new class of insecticides called spinosyns (Sparks 1998)

Synonyms, trade names, and formulations

Spinosad is manufactured by Dow AgroSciences under trade names of SpinTor, Success, Tracer, Naturalyte, Laser. There are 79 products registered with EPA within the trade names: Bonide, Bug-n-sluggo insect, slug and snail bait by W. Neudorff GMBH kg, Conserve fire ant bait, Spinosad 0.5% SC, Success, Entrust, Tracer and Gf-120 fruit fly bait by Dow, Natular 1 EC of Clarke mosquito control products Inc. Bonide spinosad ready-to-use by Bonide products. (www.pesticideinfo.org). Other trade names are Audienz, Biospin, Boomerang, Caribstar, Conserve insect control, Entrust insect control, Flipper, GF-120, Naturalyte Fruit Fly Bait, Laser, MS Superspin, Mozkill, Musdo Gold, SpY. Entrust is approved for use on USDA certified organic produce. (Clarke, Dow 2008)

The main formulation types available are suspension concentrates (SC) at 120 to 480 g spinosad/l, wettable powders (WP), water dispersible granules (WG), and granules for direct application (GR). Spinosad may be

co-formulated with other insecticide active ingredients. The suspension concentrate is commonly 20%. Clarke has the rights to produce spinosad against public health pests and has concentrated on mosquitoes. They have developed a slow release Tablet 75% and an Extended Release Tablet under the trade name Naturalyte. Laser is an aqueous suspension emulsion in oil (low volume) containing spinosad at 125 g/L and Tracer is an aqueous suspension concentrate containing spinosad at 480 g/L. (Clarke)

Usage

Spinosad is an insecticide used for the control of caterpillars, thrips, beetle and fly pests in a range of fruit and vegetable crops, ornamentals, turf, and stored grains. Spinosad has contact activity on all life stages of insects, including eggs, larvae and adults. Eggs must be sprayed directly but larvae and adults can be effectively dosed through contact with treated surfaces. Spinosad is most effective when ingested. (Clarke)

Foliar applications are not highly systemic, although trans-laminar activity is evident in certain vegetable crops and ornamental plants. Spinosad acts by altering the function of nicotinic- and GABA-gated ion channels of insect nervous systems but it does not interact with known binding sites for other nicotinic- or GABA-agonistic insecticides. It is used in agriculture, horticulture, forestry, and public health against a wide range of insects including thrips, Mediterranean fruit fly, olive fruit fly, codling moth, caterpillars, leaf miners, Colorado beetle and potato worm (Dow AgroSciences 2001, Sparks et al. 1998)

Shelf Life

Most pesticides have a shelf life of two years. Store tightly sealed and upright in its original labeled container, in a dry locked place out of reach of children. Avoid exposure to extreme temperatures. Avoid strong oxidizers. Eliminate all sources of ignition, such as flames and sparks. (Dow AgroSciences 2008)

Degradation Products

Degradation,irrespective of the mechanism, gives rise to intermediates in which the macrolide ring system is hydroxylated and/or the amino sugar is de-methylated (eg to form spinosyn B) several minor metabolites, including spinosyn B, spinosyn K, and N-demethylspinosyn D (NRAAVC)

Environmental Behavior

Fate and Transport in Terrestrial Systems

Spinosad degrades readily in the soil environment and is non-persistent. The primary mechanisms of degradation are sunlight photolysis and microbial breakdown. Under field conditions, spinosad breaks down rapidly in the soil with observed half-lives of less than one day, degrading into carbon dioxide and water by the soil microbial community. It is moderately to strongly absorbed by soil particles and is considered to be " relatively immobile to immobile" with regard to leaching. The routes of spinosad dissipation and transformation in the environment include photodegradation and biotransformation on plant surfaces, abiotic hydrolysis, aqueous photolysis, photodegradation on soil, and biotransformation via soil microorganisms. Volatilization from plant or soil is not a mechanism of transport of spinosad in the environment. Aqueous photolysis is rapid in natural sunlight, and is the primary route of degradation in aquatic systems exposed to sunlight. (NRAAVC)

In the soil environment, spinosad adsorbs strongly to soil particles and is unlikely to leach to great depths. It is photodegraded quickly on soil exposed to sunlight, but the degradation rate is decreased at longer exposure times. Spinosad is quickly metabolized by soil microorganisms under aerobic condition. Under anaerobic conditions, the degradation rate is slower. The majority of the spinosad applied rapidly photodegraded in the water column prior to adsorption to soil. Spinosad, therefore, is nonvolatile and would not volatilize from soil

or plant surfaces or drift from application sites. Volatilization is not a mechanism of transport of spinosad in the environment. (Kollman)

In laboratory studies, degradation of Spinosad appears restricted to aqueous and soil photolysis, and aerobic metabolism. There is some potential for Spinosad to be persistent in anaerobic sediment where degradation due to photolysis would be limited. Its movement off-site is probably limited to movement with substrate (eg soil). Field dissipation studies, however, in which spinosyn A was applied to bare soil indicated no movement of Spinosad from the top layer of soil and with rapid degradation, (half-lives <1 d). The mineralization half-life (assuming loss of label was due to production of CO_2), however, was 7 months. An aquatic microcosm test indicated that Spinosad residues could have a half-life of 3-5 d in relatively clear water. In aquatic sediment, however, it persisted and all samples had spinosyn levels of 15-20% of the applied dose, ie 24 h to 35 d after application, in agreement with the laboratory study result. (Kollman)

Soil microbes degrade spinosad into other spinosyns that can persist in the soil for several months and remain biologically active. Repeated applications could lead to some build-up of spinosyns in soil. A 10-month field study in California and Mississippi showed that no degradation products were found in soil below 24 inches (Kollman).

Fate and Transport in Aquatic Systems

When spinosad is applied to water in natural systems without light, very little breakdown (hydrolysis) occurs. In the absence of sunlight, the half-lives of spinosyn A and D are at least 200 days. But spinosad degrades rapidly in sunlight. A water column half-life of less than one day has been observed in artificial pond systems in outdoor conditions.Spinosyn A is more water-soluble than the other component of spinosad, spinosyn D, and therefore was the subject of soil mobility studies. However, spinosyn A and its soil metabolites bind to soil and have low soil mobility. (Kollman)

Human Health Effects

Acute Exposure

Clinical Symptoms

No data was seen although an alarming report of a number poisonings has occurred in the US among fifteen of the most common active ingredients for acute pesticide poisoning cases in the agricultural industry from 1998-2005. One person died from exposure to spinosad with ten with severe symptoms and 85 with moderate levels of poisoning. This is difficult to explain as spinosad is so safe that it can be used on produce sold in organic farms. (Calvert GM et al. 2008)

Acute toxicity

Mammalian toxicity of spinosad is extremely low rodents. Spinosad is of low acute oral toxicity having a LD_{50} of > 5000 mg/kg for rats which is in toxicity class IV and likewise for mice is > 5000 mg/kg. It also has low dermal acute toxicity (LD_{50}; >5000 mg/kg in rabbits and an inhalational toxicity value of (LC_{50} > 5180 mg/m^3 in rats). It was non- irritating to the skin of rabbits, induced slight eye irritation in rabbits in one study, but was found non irritating in a second study, and was not a skin sensitizer in guinea pigs.. Spinosad is slowly and poorly absorbed through the skin. Dermal exposures in the rat for 24 and 120 hours resulted in only 1 and 2% absorption, respectively. (HSDB, NRAAVC, WHO 2009)

Tracer Naturalyte Insect Control, which contains spinosad at 480 g/L, was of low acute oral and inhalational toxicity in rats LC_{50} value: > 5000 mg/m^3), low acute dermal toxicity in rabbits (LD_{50} value: > 2000 mg/kg) toxicity class III. It was a slight skin and eye irritant in rabbits, and was not a skin sensitizer in Guinea pigs. Because of its unique mode of action, spinosad is highly selective to insects. In mammals, spinosad is not

readily absorbed through the skin; any minute amounts that are absorbed or ingested are rapidly metabolized to inactive by-products, which are excreted. As a result, it has very low acute toxicity. (HSDB, NRAAVC, WHO 2009)

Medical treatment for acute poisoning

Spinosad is not a highly toxic material and would only cause health problems if exposure is high. Control any seizures first. Significant esophageal or gastrointestinal tract irritation or burns may occur following ingestion. The possible benefit of early removal of some ingested material by cautious gastric lavage must be weighed against potential complications of bleeding or perforation. Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Control any seizures first. Activated charcoal binds most toxic agents and can decrease their systemic absorption if administered soon after ingestion. Immediate dilution with milk or water may be of benefit in caustic or irritant chemical ingestions. If inhaled, move patient to fresh air. Monitor for respiratory distress. If cough or difficulty breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Irrigate exposed eyes with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility. (HSDB)

Skin Contact: Remove contaminated clothing and wash affected areas of skin with soap and water. Launder contaminated clothing before reuse.

Eye: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. Call a poison control center or doctor for treatment advice.

Inhalation: Remove affected person to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

Ingestion: Call a physician or Poison Control Center immediately. Do not induce vomiting. Vomiting may cause aspiration resulting in chemical pneumonia. Do not give anything by mouth to an unconscious person. (HSDB)

Note to Physician: Product contains petroleum distillate. Gastric lavage is indicated if material was taken internally. Vomiting may cause aspiration pneumonia. (Clarke)

Establish a patent airway and use suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if needed. Administer oxygen by non-rebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary. Monitor for shock and treat if necessary. Anticipate seizures and treat if necessary. For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport. Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Cover skin burns with dry sterile dressings after decontamination. (Bronstein & Currance)

Chronic Exposure

Noncancer Endpoints

The standardized tests for chronic exposure were given for spinosad. Using subchronic dosages applied orally over 90 days produced NOAEL endpoints for the rat at: 8.2 mg/kg/day, mouse at 7.5 mg/kg/day, and dog at 4.9 mg/kg/day. Similar tests produced LOAEL values resulted for the rat: 40.9 mg/kg/day, mouse at 22.5 mg/kg/day, and dog at 9.7 mg/kg/day. (HSDB, NRAAVC, WHO 2009)

Determining chronic acute values for 21-day dermal exposure resulted in a NOAEL endpoint in the rabbit of 1000 mg/kg. From 28-day inhalation toxicity @ 4 h/day the NOAEL for the rat: was 9.5 mg/m^3. Chronic toxicity for 1 year in the dog produced a NOAEL of 2.7 mg/kg/day and a LOAEL of 8.2 mg/kg/day. Longer term exposures of chronic toxicity were carried out for the rat with a NOAEL of 2.4 mg/kg/day and a LOAEL of 11.4 mg/kg/day over 2 years. Similarly with the mouse over 1.5 years the NOAEL was 11.4 mg/kg/day and corresponding LOAEL of 32.7 mg/kg/day. (HSDB, NRAAVC, WHO 2009)

Chronic maternal systemic toxicity administered throughout gestation produced a maternal NOAEL 50 mg/kg/day for the rat and 10 mg/kg/day for the rabbit. Correspondingly developmental exposures were under taken with the same two animals producing a NOAEL of 200 mg/kg/day for the rat and 50 mg/kg/day for the rabbit. Repeated dietary exposure to high levels of spinosad in mice, rats, and dogs resulted in marked reductions in bodyweight and/or death, and clinical signs of toxicity. Pathological examinations revealed that spinosad induced similar lesions in a wide range of tissues, and that these lesions were reported in all species studied. The major lesions were cellular vacuolation, inflammatory changes, necrosis, regenerative/degenerative changes, increased blood formation, and skeletal myopathy. Changes in haematological and clinical chemistry parameters were generally consistent with the type and extent of cellular injury or organ dysfunction reported. In chronic dietary studies in mice, rats and dogs there was no evidence to suggest that spinosad is carcinogenic. Although in a 12-month rat neurotoxicity study there was some damage to individual nerve fibers in both sexes following dietary exposure to spinosad at 49 mg/kg/day, in other specific neurotoxicity studies conducted in rats there was no evidence to suggest that spinosad has potential to induce neurotoxicity. (HSDB, NRAAVC, WHO 2009)

In a number of genotoxicity studies conducted with spinosad (Ames test, TK assay, cytogenetic assay, unscheduled DNA synthesis, micronucleus test) there was no evidence to suggest that spinosad damages genetic material as being mutagenic. Spinosad did not cause embryotoxicity, fetotoxicity, or teratogenicity in either rats or rabbits at dose levels that affected maternal animals. (Clarke). Spinosad is a suspected endocrine disruptor (www.pesticideinfo.org)

In order to calculate the acceptable daily intake (ADI) for humans, a safety factor is applied to the NOEL in the most sensitive species. The magnitude of the safety factor is selected to account for uncertainties in extrapolation of animal data to humans; variation within the human population; the quality of the experimental data, and the nature of the potential hazards. Using a safety factor of 100, an ADI of 0.02 mg/kg/day was established. (NRAAVC, WHO 2009)

Cancer Endpoints

In long term studies, no evidence of carcinogenicity has been observed. (HSDB)

In studies with repeated doses, no acute toxicological alerts were observed that might indicate the need for establishing an acute reference dose (acute RfD).(WHO 2009).

Toxicokinetics and Metabolism

Spinosad is widely distributed to the tissues following absorption, however only low levels were detected in the rat 7 days following exposure. Spinosad is extensively metabolized in animals. Spinosad, which is absorbed via the oral or dermal routes of exposure, has been found to be rapidly metabolized and eliminated in mammalian systems via the feces, urine, and bile in the first 24 hours. Within 48 hours of dosing, approximately 60-80% of spinosad or its metabolites was eliminated. Depletion of spinosad residues from tissues occurs rapidly following cessation of exposure.(HSDB)

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Northern bobwhite quail and mallard ducks were used in oral dose acute toxicity studies. The LD_{50}s determined for these species were both > 2000 mg/kg body weight, indicating that spinosad is practically non-toxic to birds when orally dosed. Ten day old Northern Bobwhite quails and Mallard ducks were used in acute dietary toxicity studies. The LC50s determined for these species were >5156 and 5253 ppm in the feed, respectively. These results indicate that Spinosad is practically non-toxic to birds when ingested with food. (Thompson et al 2000)

Results of reproductive studies on the mallard duck and northern bobwhite quail indicate a NOEC of 550 ppm for both species, based on clinical observations, gross necropsy results or reproductive effects, although clear concentration-effects curves were observed in the mallard test for egg-laying, hatchlings and 14 d old survivors, indicating the potential for effects at concentrations below the NOEC. (NRAAVC).

Spinosad is highly toxic to bees in laboratory tests. Field testing has demonstrated that once liquid spray residues have been allowed to dry for up to 3 hours that spinosad is not harmful to foraging honeybees and bumblebees. Spinosad has been used extensively in more than 85 countries with over 250 registered crop uses since its first launch in agriculture without any reported adverse effects on bees. (Clarke).

Toxicity in Non-Targeted Aquatic Systems

Spinosad shows moderate toxicity to fish and slight to moderate toxicity to aquatic invertebrates. Acute LC_{50}s over 48 h exposure for carp (*Cyprinus carpio*), sheepshead minnow (*Cyprinodon variegatus* - marine species), bluegill sunfish (*Lepomis macrochirus*), and trout (*O*ncorhynchus mykiss) were 5.0, 7.9, 5.9 and 30 mg/L, respectively. Therefore, spinosad has slight to moderate acute toxicity.

A feature of the chronic fish tests is the slow rate at which maximum mortality was reached, though it should be noted that concentrations were well above those that maybe encountered in the field and where extended exposure is highly unlikely.In 48 hour exposures the water flea (*Daphnia magna*) and the grass shrimp (*Palaemonetes pugio*) gave identical values of 7.9 ppm each (*Daphnia*) which are moderately toxic. The Eastern oyster (*Crassostrea virginica*) was exposed in a 96 h static-renewal and 96 h flow-through test giving an endpoint of 0.3 ppm (high toxicity). (Dow 2001).

The advantages of spinosad use for larval mosquito control are clear in terms of the minimal risks to human health. However, the impact of this compound on aquatic non-target organisms is poorly understood. Spinosad is toxic to a number of aquatic invertebrates including water fleas, chironomids, shrimp, and mollusks. In demographic studies on *Daphnia pulex*, continuous exposure to spinosad resulted in population extinction at >0.01 ppm. However, spinosad was at least five times less toxic than the organophosphate diazinon during continuous exposure studies. Whereas toxicity to fish is classed as slight or moderate with 96 h acute LC_{50} values between 5 and 30 ppm., depending on species (Thompson et al 2000)

Spinosyn A did not bioaccumulate in fish. The ecotoxicity profile of spinosad suggests that it is practically non-toxic in mammals and birds, and moderately toxic to fish, in acute studies. It is very slightly to slightly toxic to fish in chronic studies. No treatment-related mortality of oysters occurred, although a clear dose-response effect on new shell growth was evident. The acute toxicity of spinosad to oyster is rated as very high. The acute toxicity of spinosad to water flea is rated as moderately toxic in a static test, while there is a marked difference in the static-renewal test which indicates only very slight to slight toxicity. The difference may be due to the formation of a more toxic metabolite or degradation product over the longer period of the static test. Aquatic plant toxicity test results indicated that spinosad is practically non-toxic to green algae,

slightly toxic to the duckweed (based on growth and growth inhibition of both the plant and fronds), moderately toxic to blue-green algae, and highly toxic to freshwater and marine diatoms. (HSDB, NRAAVC, WHO 2009)

Spinosad has been tested in intermediate-term (90-day) and lifetime (1-2 years) feeding studies involving rats, mice, and dogs. Spinosad has not been found to cause tumors in laboratory animals or to have any potential to cause neurotoxicity. In addition, spinosad did not cause embryotoxicity, fetotoxicity, or teratogenicity in either rats or rabbits at dose levels that affected maternal animals. The primary effects of spinosad observed at high dosages include vacuolation, inflammation, and degeneration of selected tissues. These effects are similar to those caused by other cationic amphiphilic compounds including several pharmaceuticals. Based on no-observable effect levels (NOEL's) of 2.4 mg/kg/day (rats), 11.4 mg/kg/day (mice), and 2.68 mg/kg/day (dogs), the acceptable daily intake (ADI) for spinosad has been established as 0.02 mg/kg/day by U.S. EPA and other regulatory authorities. This ADI is based on application of standard safety factors to the observed NOEL's. U.S. EPA has determined no need for the use of additional uncertainty factors to account for special sensitivities of the young or unborn. (WHO 2009)

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Profile for Temephos:

CAS Registry Number 3383-96-8

Summary

Chemical History

Temephos is a nonsystemic organophosphate insecticide used in the United States since 1965 for public health reasons (U.S. EPA, 1999b, 2000) to control mosquito, midge, and black fly larvae (EXTOXNET, 1996). It is also used occasionally to treat potable water. Temephos has a low toxicity in mammals, moderate toxicity in birds, and high toxicity in some aquatic organism (HSDB, 2005). All food tolerances for temephos have been revoked (U.S. EPA, 2000). Temephos is available in emulsifiable concentrates (up to 50 percent), wettable powder (50 percent), and granular forms (up to 5 percent) (EXTOXNET, 1996). Because temephos is used primarily as a larvicide to treat bodies of water, the potential for incidental dermal or soil/dust exposure during this usage is minimal (HSDB, 2005). Occupationally exposed workers are the only population with potential elevated risk for temephos exposure due to its limited use pattern and lack of residential, dietary, and drinking water exposures (U.S. EPA, 1999b, 2000; ATSDR, 2005). Although human populations could potentially be exposed to very low levels from potable water that has been treated continually with temephos, little concern exits due to its low toxicity and solubility (ATSDR, 2005).

Description of Data Quality and Quantity

Because temephos is a new larvicide and has a limited use pattern, extensive review data do not exist. Relevant resources include

- Toxicologic Information About Insecticides Used For Eradicating Mosquitoes (West Nile Virus Control): Temephos (ATSDR, 2005)
- Reregistration Eligibility Decision (RED) Document (U.S. EPA, 2000)
- Pesticide Information Profile for Temephos (EXTOXNET, 1996)
- Specifications and Evaluations for Public Health Pesticides for Temephos (WHO, 1999).

EPA has developed quantitative human health benchmarks (intermediate and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks) for temephos.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.003	mg/kg/day	Oral NOEL for neurological effects in rats with UF of 100 applied; assume 100% absorption	U.S. EPA (2000)
Acute	Oral	0.2	mg/kg/day	Adopt intermediate RfD for acute duration	
Intermediate	Oral	0.2	mg/kg/day	Intermediate RfD based on NOAEL in rats with UF of 100 applied	U.S. EPA (1997)
Chronic	Oral	0.02	mg/kg/day	Chronic RfD based on NOAEL in rats with UF of 1000 applied	U.S. EPA (1997)
Acute, Intermediate, Chronic	Dermal	0.003	mg/kg/day	Oral NOEL for neurological effects in rats with UF of 100 applied; assume 38% absorption	U.S. EPA (2000)

For inhalation and dermal exposure, a NOEL of 0.3 mg/kg/day was identified for neurological effects (inhibition of red blood cell [RBC] cholinesterase) in rats fed temephos for 90 days and an uncertainty factor of 100 was applied. This value is appropriate for inhalation and dermal exposures and all exposure durations (U.S. EPA, 2000).

For oral exposure, intermediate and chronic oral RfDs of 0.02 and 0.2 mg/kg/day, respectively, were based on a NOAEL of 200 ppm in rats exposed to 200 ppm in the diet, with uncertainty factors of 100 and 1,000, respectively, applied (U.S. EPA, 1997). The intermediate-duration RfD was adopted to represent acute exposures.

Insecticide Background

CAS #:	3383-96-8
Synonyms:	Phosphorothioic acid, O,O'-(thiodi-4,1-phenylene) bis (O,O'-dimethyl) phosphorothioate; Phosphoric acid, O,O'-(thiodi,1,4-phenylene) O,O,O',O'-tetramethyl ester (U.S. EPA, 2000)
Chemical Group:	organophosphate (EXTOXNET, 1996)
Registered Trade Names:	Compounds containing temephos: Abat, Abate, Abathion, Acibate, Biothion, Bithion, Difennthos, Ecopro, Nimitox, and Swebate (EXTOXNET, 1996)

Usage

Temephos is an organophosphate insecticide that is used to control mosquito larvae. It is used in standing water, shallow ponds, swamps, marshes, intertidal zones, tire piles, and highly polluted waters. There are no registered residential uses for temephos (U.S. EPA, 1999b, 2000). Temephos may also be found in mixed insecticidal formulations such as trichlorfon (EXTOXNET, 1996). U.S. EPA (2000) has reported the use rates for temephos. Granular temephos may be applied at a maximum of 0.5 lbs/ai (active ingredient) per acre. The typical application of temephos in granular form ranges from 0.1–3 lbs/ai/acre. To treat tire piles,

the granular application rate is 0.05 lbs/ai/100 ft^2. As an emulsifiable concentrate, temephos may be applied at a maximum of 1.5 fl. oz/acre (0.0469 lbs/ai/acre). The typical application of temephos in the emulsifiable form is 0.5–1.0 fl. oz/acre (0.0156–0.0313 lbs/ai/acre) (U.S. EPA, 1999b, 2000).

Formulations and Concentrations

Temephos is available in emulsifiable concentrates (up to 50 percent), wettable powder (50 percent), and granular forms (up to 5 percent) (EXTOXNET, 1996; U.S. EPA, 1999b, 2000). It is most commonly applied from airplanes and helicopters. Other application methods include backpack power blowers and right-of-way sprayers, horn blowers, belly grinders, and spoons (U.S. EPA, 1999b, 2000). WHO (1999) indicated that the temephos content in the various preparations should be declared and contain the following:

- Technical grade temephos: no less than 800 g/kg
- Emulsifiable concentrate: 250–500 g/kg +/- 10% of the declared content or above 500 g/kg +/- 25 g/kg
- Emulsifiable concentrate for simulium control: 200 g/kg +/- 10 g/kg
- Sand granules:10 g/kg +/- 25% of the declared content.

Shelf Life

Temephos is reported to be stable indefinitely at room temperature (HSDB, 2005); however, no supporting data on its shelf-life could be located.

Degradation Products

In water, temephos degrades slowly, forming degradation products from the sulfide group and the phosphate group through oxidation and hydrolysis, respectively. Hydrolysis occurs in basic or highly acidic water, and temephos is stable in water at pH 5-7. Hydrolysis degradation products include 4,4-thiodiphenol. Photolysis of temephos in methanol through sunlight exposures produces sulfone. A similar reaction may also occur in waters exposed to sunlight. Biodegradation does not occur (HSDB, 2005). Temephos breaks down when heated or burned. Toxic fumes such as phosphorous oxides and sulfur oxides are produced during this process. Temephos reacts strongly with acids and bases (IPCS, 2005).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Based on temephos' very low water solubility and its high affinity for soil, the estimated half-life in soil is around 30 days (EXTOXNET, 1996). The affinity of temephos to soil also suggests that temephos is not extremely mobile in the soil (U.S. EPA, 1999b, 2000). Its very low vapor pressure suggests that it will not significantly volatilize from soil or sediments under most conditions. However, the breakdown products of temephos (temephos sulfoxide, temephos sulfone, temephos sulfide, and sulfone phenols) are more likely to migrate to and remain in water since they do not bind as strongly to soil. In field studies of sediments, temephos was shown to absorb rapidly to organic media and degrade rapidly to low or undetectable concentrations (U.S. EPA, 1999b, 2000). The breakdown of temephos in plants is very slow (EXTOXNET, 1996).

Fate and Transport in Aquatic Systems

Temephos is applied to aquatic environments where mosquitoes breed. It has a low water solubility and a low persistence in water. Several studies found that temephos rapidly degrades in natural waters (ATSDR, 2005;

U.S. EPA, 1999b, 2000; EXTOXNET, 1996). Microorganisms and exposure to sunlight are the main ways that temephos degrades and dissipates in water, however, in their absence, temephos does not dissipate significantly (U.S. EPA, 1999b, 2000; EXTOXNET, 1996). In water, temephos would take a very long time to volatilize, as indicated by its very low Henry's law constant, suggesting that it would instead partition to sediment or soil. Hydrolysis is expected within a few days in highly basic or acidic conditions, but temephos is expected to persist longer at pH 5–7 (ATSDR, 2005). Temephos is not likely to reach ground water that would be used for drinking water due to its relatively short half-life in natural waters and the lack of mobility in soil. Because temephos binds to fatty substances, it can bioconcentrate in fish (U.S. EPA, 2000).

Human Health Effects

Acute Exposure

Effects/Symptoms

Temephos causes its toxic effects by the inhibition of cholinesterase. Typical acute toxicity signs are eye irritation, blurred vision, dizziness, nausea, diarrhea, salivation, headaches, loss of muscle coordination, tremors, and difficulty breathing (EXTOXNET, 1996; U.S. EPA, 1999a, 2000; NIOSH, 2004). Compared to other organophosphates, temephos is of low to moderate toxicity (U.S. EPA, 2000). It is moderately toxic through acute dermal and oral exposures and has low toxicity through inhalation exposure (U.S. EPA, 2000). Few studies exist on the human health effects of acute exposure to temephos, presumably due to its low toxicity in humans (ATSDR, 2005). Human volunteers who ingested 256 mg/day for 5 days or 64 mg/day for 4 weeks exhibited no plasma or erythrocyte cholinesterase inhibition (ATSDR, 2005).

In animals, the target organs of acute temephos exposure are the nervous system and liver (EXTOXNET, 1996). Oral LD_{50} values in various animal species include 400–1,300 mg/kg in rats, 400-4,700 mg/kg in mice (EXTOXNET, 1996), and 5,000 mg/kg in cats and dogs (2 percent powder formulation) (EXTOXNET, 1996). In rabbits, a dermal LD_{50} of 1,850 mg/kg in males or 970 mg/kg in females is reported. Similar to its effects in humans, acute high dose exposure to temephos causes neurological effects in animals due to cholinesterase inhibition (U.S. EPA, 1999a, 2000). Effects of cholinesterase inhibition are generally at exposures of 10 mg/kg/day, with liver and other effects seen at higher exposures. However, a few studies have seen cholinesterase effects as low as 1 mg/kg/day (ATSDR, 2005). Although temephos causes slight eye irritation in animals, no skin irritation or dermal sensitization were observed (U.S. EPA, 1999a, 2000). Acute exposures to temephos are not considered to be reproductive or developmentally toxic (U.S. EPA, 1999a, 2000).

Treatment

Exposure to temephos may be determined through laboratory tests to determine cholinesterase levels in blood (WHO/FAO, 1978). Oral exposure to temephos should be treated by rinsing out the mouth and seeking immediate medical attention. For dermal exposures, any contaminated clothing should be removed and the exposed area should be rinsed and then washed with soap and water. Medical attention should be sought. If temephos gets in the eyes, they should be rinsed immediately with copious amounts of water for several minutes. Contact lenses should be removed if possible and medical attention should be sought. Inhalation exposures require removal to fresh air and rest. Artificial respiration should be performed if the person stops breathing, and medical attention should then be sought immediately (IPCS, 2005; NIOSH, 2004).

Chronic Exposure

Noncancer Endpoints

The effects of chronic exposure to temephos in humans have not been well described in the literature, although it is not expected to be toxic at the levels applied to control for mosquitoes. No effects on cholinesterase (plasma or erythrocyte) levels were also seen in residents of a community exposed to < 1 ppm temephos in their water supply for 19 months. Application of 2 percent temephos powder to human subjects and their bedding was deemed safe and effective (ATSDR, 2005).

Chronic-duration exposure studies in animals have shown that temephos can inhibit cholinesterase levels, with symptoms of poisoning occurring at higher levels. A slight decrease in blood and brain cholinesterase activity was seen in dogs chronically exposed to 3–4 mg/kg/day, while severe effects were seen at 14 mg/kg/day. Decreased liver weights were seen in rats fed small doses of temephos for more than 2 years, and rabbits had minor pathological liver changes at 10 mg/kg/day. Temephos is not expected to cause reproductive, teratogenic or mutagenic effects (EXTOXNET, 1996).

Cancer Endpoints

EPA has not classified temephos as a carcinogen (U.S. EPA, 2000). No data exist on the carcinogenic effect of temephos in humans. The existing data suggest that temephos is not carcinogenic. No tumors were reported in rats fed diets containing up to 15 mg/kg/day for 2 years (U.S. EPA, 1999a, 2000).

Toxicokinetics

Temephos can be absorbed through the oral, dermal, and inhalation pathways, with dermal exposure being the most likely and typical (EXTOXNET, 1996). However, in rats, only 38 percent of dermally applied temephos was absorbed (U.S. EPA, 2000). Oral studies in rats have shown that peak bloodstream concentration after a single oral dose of temephos was reached between 5 and 8 hours post-administration, with a half-life of 10 hours. In mammals, most temephos leaves the body unchanged in urine and feces, with only some breakdown products detected (sulfate ester and glucoside conjugates of phenolic hydrolysis) (ATSDR, 2005; EXTOXNET, 1996; WHO/FAO, 1978).

Ecological Effects

Acute Exposure

Temephos is not expected to have a direct effect on terrestrial animals, because it is applied to water so exposures are expected to be low (U.S. EPA, 1999b, 2000). However, it is toxic to nontarget terrestrial organisms such as birds. In birds, temephos may be highly toxic to some species while only moderately toxic to others. The LD_{50}s temephos ranges from 18.9 to 240 mg/kg in California quail and chucker partridge, respectively. However, no significant changes in reproduction were observed in mallard ducks fed diets that contained moderate amounts of temephos (EXTOXNET, 1996). Temephos has been found to be extremely toxic to bees. The direct contact LC_{50} is 1.55 µg/bee (EXTOXNET, 1996).

Temephos is used in shallow water as a larvicide. It has shown a range of toxicity in the aquatic environment depending on its formulation with the emulsifiable concentrate and wettable powders being the most toxic (EXTOXNET, 1996). In fish, temephos has been shown to be slightly to moderately toxic to a variety of species. The most sensitive were the rainbow trout, with an LD_{50} range of 0.16 to 3.49 mg/L. The 96-hour LD_{50} values for the emulsifiable concentrate in various other fish species range from 0.35 mg/L in coho salmon to 6.7 mg/L in Atlantic salmon. The 96-hour LD_{50} values for technical grade temephos in various fish species range from > 10 mg/L in channel catfish to 21.8 mg/L in bluegill sunfish (U.S. EPA, 1999b, 2000).

Temephos is a hydrophobic chemical, so it is more likely to bind to fatty substances; as a result, temephos has the potential to bioconcentrate (U.S. EPA, 1999b, 2000). Some data indicate that there was some bioaccumulation in fish after 20 days of exposure, but temephos was no longer detected 14 days after exposure ended (U.S. EPA, 1999b, 2000).

In aquatic invertebrates, temephos is highly to very highly toxic. This is not surprising because it is an insecticide used to control aquatic larval stages of mosquitoes and other pests. One laboratory study using a 5 percent granular temephos formulation indicated that the emulsifiable concentrate is much more toxic to marine/estuarine aquatic invertebrates than granular formulations (U.S. EPA, 1999b, 2000). The 96-hour LC_{50} values for some freshwater invertebrates include 0.08 mg/kg for Gamma lacustris and 0.01–0.03 mg/kg for stoneflies. One commercial temephos formulation (Abate4E; 46 percent emulsifiable concentrate) is very toxic to saltwater invertebrates, including pink shrimp and oysters. The LC_{50} values for those species are 0.0005 and 0.019 mg/L, respectively. This formulation is not toxic to bull frogs (EXTOXNET, 1996).

Chronic Exposure

Very little data exist for chronic exposure to temephos in nonterrestrial target organisms. Currently, no data exist for potential chronic effects in waterfowl or birds exposed via food. The data that do exist indicate there is little impact (U.S. EPA, 1999b, 2000).

Little data exist for chronic exposure to temephos in marine/estuarine organisms. However, because temephos may be replied repeatedly to water, the chronic exposure of fish is of potential concern. Studies have shown that no chronic effects were seen in fish following 10 applications of a commercial temephos formulation (granular Abate® 2G). Another study showed growth retardation in fish following the application of the liquid Abate® 4E formulation (U.S. EPA, 1999b).

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ANNEX F: INDOOR RESIDUAL SPRAYING PARAMETERS SURVEY RESPONSES

Table F-1

Summary of Survey Parameters Used in the Human Health Risk Assessment

		Burkina Faso			**Madagascar**			**Uganda**			**Unspecified Countries**			**AVERAGES**		
parameter	unit	low	mid	high	low	mid	high	low	mid	high	low	mid	high	low	mid	high
E_prep	tank/d	1	3.6	5.2	3	4	8	5		8	5		7	3.5	5.0	7.1
S_cycle	1/yr		1		1	1	2		2			1		1.0	1.25	2.0
EF_spray	day		30		30	30	42				36		60	33	36	44
T_vol	L	10	10	10	8	10	10							9	10	10
E_spray	house/d		10		6	10	15	10		11	10		15	9	11	14
AT_spray	day		35		35	35	49				42		70	39	42	51
EF_bath	bath/mo		30		1	15	30	16		20		30		9	23	25
T_bath	min/bath	5	10	20	5	20	40	5		10				5	13	23

E_prep: number of tanks prepared each day for IRS

S_cycle: number of spray cycles per year

EF_spray: the number of days in a spraying cycle when spraying takes place

T_vol: the volume of a backpack sprayer tank

E_spray: the number of houses sprayed per day

AT_spray: the total number of days from beginning to close of a spray cycle

EF_bath: the number of bathing events per month

T_bath: the length of a bathing event

IRS Exposure Parameters Survey (Burkina Faso)

USAID is updating the Malaria Vector Program Programmatic Environmental Assessment (PEA), and this exposure scenario information will be used to assess human health risks. The information you provide will help identify how a worker or resident is exposed to pesticides during the following activities:

- Mixing of pesticides
- Spraying of pesticides
- Activities of residents in the home after spraying

From your experience with working on the IRS program, please provide a "best estimate" and, if possible, a range of values for the following questions.

	Questions	**Units**	**Best Estimate Value**	**Range of Likely Values**
Worker / Mixing and Spraying	How many tanks does each sprayer prepares per day?	tanks / day	3.6	Low: 1.0 High:5.2
	What is the volume of the tank used for spraying?	L	10	Low:10 High:10
	What is the average number of homes each sprayer sprays per day?	homes / day	10	Low:17,5 High:0.7
	How long does it take the sprayer to spray a home?	Min/home	3.3	Low: High:
	How many spray cycles are there per year?	cycles / year	1	Low: High:
	How many weeks do the sprayers work per spray cycle?	weeks / cycle	5	Low: High:
	How many days do the sprayers work per week?	day / week	6	Low: High:
	What is the surface area sprayed in a home?	square meters	610	Low: High:
Resident	Based on your knowledge, what is the average time a resident spends in their home per day (this may vary based on season and age, please give an average for an entire year)?	hours /day	10	Low: High:
	Based on your knowledge, how often does a typical person in the target community take a bath?	baths / month	30	Low: High:
	Based on your knowledge, how long does a bath take for a typical person?	minutes / bath	10	Low:5 High:20
	Based on your knowledge, how much water does a household use per day (for drinking, cooking, etc.)		20	
	On average, how many times has each home been sprayed since the start of the IRS program?	min	3.3	

For each pesticide used in the program, is the concentrated product a wettable powder (WP), an emulsifiable concentrate (EC), or in another form?

IRS Pesticide	Concentrated Form (write WP, EC, or state the concentrated form)
alpha-cypermethrin	
bendiocarb	WP
bifenthrin	
cyfluthrin	
DDT	
deltamethrin	
etofenprox	
fenitrothion	
lambda-cyhalothrin	
malathion	
pirimiphos-methyl	
propoxur	

Additional Questions:

Are pesticides normally mixed prior to use in an enclosed space or outdoors (this relates to possible exposures from spilling)? Usually the pesticide is mixed outdoors before entering the space to be sprayed.

How are pesticides prepared for spraying (mixed in the spraying tank, mixed in another container and transferred to the tank, other)? Mixed in the spraying tank.

What are the sprayed surfaces in a house predominately made of (mud brick, concrete brick, wood planks, etc)? The homes that are being sprayed are made out of mud brick.

IRS Exposure Parameters (Madagascar)

USAID is updating the Malaria Vector Program Programmatic Environmental Assessment (PEA), and this exposure scenario information will be used to assess human health risks. The information you provide will help identify how a worker or resident is exposed to pesticides during the following activities:

- Mixing of pesticides
- Spraying of pesticides
- Activities of residents in the home after spraying

From your experience with working on the IRS program, please provide a "best estimate" and, if possible, a range of values for the following questions.

	Questions	Units	Best Estimate Value	Range of Likely Values
Worker / Mixing and Spraying	How many tanks does each sprayer prepare per day?	tanks / day	4	Low: 3 High: 8
	What is the volume of the tank used for spraying?	L	10	Low: 8 High: 10
	What is the average number of homes each sprayer sprays per day?	homes / day	10	Low: 6 High: 15
	How long does it take the sprayer to spray a home?	Min/home	10	Low: 5 High: 20
	How many spray cycles are there per year?	cycles / year	1	Low: 1 High:2
	How many weeks do the sprayers work per spray cycle?	weeks / cycle	5	Low: 5 High: 7
	How many days do the sprayers work per week?	day / week	6	Low: 6 High: 6
	What is the surface area sprayed in a home?	square meters	60	Low: 30 High: 250
Resident	Based on your knowledge, what is the average time a resident spends in their home per day (this may vary based on season and age, please give an average for an entire year)?	hours /day	12 (out of 24)	Low: 8 High: 17
	Based on your knowledge, how often does a typical person in the target community take a bath?	baths / month	15	Low: 1 High: 30
	Based on your knowledge, how long does a bath take for a typical person?	minutes / bath	20	Low: 5 High: 40
	Based on your knowledge, how much water does a household use per day (for drinking, cooking, etc.)		30L	Low: 10 High: 50
	On average, how many times has each home been sprayed since the start of the IRS program?		4	Low: 1 High: 4

For each pesticide used in the program, is the concentrated product a wettable powder (WP), an emulsifiable concentrate (EC), or in another form?

IRS Pesticide	Concentrated Form (write WP, EC, or state the concentrated form)
alpha-cypermethrin	WP5
bendiocarb	WP80
bifenthrin	
cyfluthrin	
DDT	
deltamethrin	WG250
etofenprox	
fenitrothion	
lambda-cyhalothrin	
malathion	
pirimiphos-methyl	
propoxur	

Additional Questions:

Are pesticides normally mixed prior to use in an enclosed space or outdoors (this relates to possible exposures from spilling)?

They are normally mixed prior to use in an enclosed space

How are pesticides prepared for spraying (mixed in the spraying tank, mixed in another container and transferred to the tank, other)? mixed in another container and transferred to the tank

What are the sprayed surfaces in a house predominately made of (mud brick, concrete brick, wood planks, etc)?

The homes that are being sprayed in the Central Highlands of Madagascar are made out of mud brick.

In some villages of the South of Madagascar the homes are made of wood planks.

IRS Exposure Parameters (Uganda)

USAID is updating the Malaria Vector Program Programmatic Environmental Assessment (PEA), and this exposure scenario information will be used to assess human health risks. The information you provide will help identify the duration and frequency a worker or resident is exposed during the following IRS activities:

- Mixing
- Spraying
- Sprayers washing the spray equipment/boots/visors/helmet/gloves/tarpaulins
- Washers washing PPE
- Residing in the home after spraying:
  - Contact with sprayed wall
  - Inhalation (fumes or contaminated dust)

From your experience with working on the IRS program, please provide a "best estimate" range for the following questions.

For each Country IRS program			
		Questions	Please provide a range for the following
Worker / Sprayer	Exposure frequency	How many tanks each sprayer prepares per day?	#tanks 5-8
		How is the pesticide prepared (mixed with water in tank, outside of tank, other)?	This will vary with the formulation and packaging type. Mostly inside (water soluble/WP formulations with small volumes/EC etc.) But if high volume WP formulation need to mix out side
		What is the average number of homes each sprayer sprays per day?	# homes In Uganda 10-11, but this depends on many factors like house size, house distribution, accessibility etc.
		How long does it take the sprayer to spray a home?	#minutes If house is properly prepared 10-15 minutes max. For house with 80 square meters sprayable area. (Properly prepared means that if all the belongings have been removed, if not the sprayer has to remove the items.
	Exposure duration	How many spray cycles are there per year?	# spray cycles 2 cycles in Uganda

		How many weeks do the sprayers work per spray cycle?	# weeks Maximum 5 weeks
		How many days a week do the sprayers work per week?	# days 6
		How many hours does each sprayer work per day?	# hours 8-9
		What is the total time a sprayer is actually spraying a home per day?	# hours Actual spry time 3-4 hours
		How many houses does the each sprayer spray per day	#houses 11
Resident	Exposure duration	Based on your experience, what is the average time a resident spends in their home per day (this will probably vary due to rainy season, other situations, please give an average for each scenario)?	# hours Basically from dusk to dawn, then women 4-5 hours day time, small kids 6-7 hours day time, school children 4-5 hours day time.
	Contaminated water exposure	Based on your knowledge, how often does a typical adult in the target community take a bath? And how long do the bath?	# baths per week # minutes 4-5 body wash with limited quantity of water for 5-10 minutes
	Contaminated water ingestion	Based on your knowledge, how much water does a household use per day (for drinking, cooking, etc.)	# gallons 20 liters for everything, but variable, water quantity is an issue here
		What is the average of size of the home (square meters)?	Meters 20-25 square meters in Northern Uganda
		What is the total area of walls sprayed per house (square meters) ?	Meters 75
		What are the houses predominately made of (mud brick, concrete brick, clay brick, etc)?	Mud wall/ thatched roof
		How many rooms are sprayed per home?	# rooms Highly variable, in northern Uganda majority are 1 room
	Exposure frequency	On average, how many times has each home been sprayed since the start of the IRS program?	4-6 times

IRS Exposure Parameters (Multiple Countries)

USAID is updating the Malaria Vector Program Programmatic Environmental Assessment (PEA), and this exposure scenario information will be used to assess human health risks. The information you provide will help identify the duration and frequency a worker or resident is exposed during the following IRS activities:

- Mixing
- Spraying
- Sprayers washing the spray equipment/boots/visors/helmet/gloves/tarpaulins
- Washers washing PPE
- Residing in the home after spraying:
  - Contact with sprayed wall
  - Inhalation (fumes or contaminated dust)

From your experience with working on the IRS program, please provide a "best estimate" range for the following questions.

For each Country IRS program			
		Questions	Please provide a range for the following
Worker / Sprayer	Exposure frequency	How many tanks each sprayer prepares per day?	Between 5-7 and this correspond to the number of sachets sprayed by day
		How is the pesticide prepared (mixed with water in tank, outside of tank, other)?	Inside the pumps/tank
		What is the average number of homes each sprayer sprays per day?	10-15 structures /day This depend on the size of the structures
		How long does it take the sprayer to spray a home?	In IRS evaluate the number of structure and not number of home. The time spent on a structure depends on his size. A small structure like in Senegal were I am now (15-20 Min) but a big structure with many room, you can evaluate 10 min by room and account time for helping preparation of the structure that can take

			20-30 min when IEC is not well executed
	Exposure duration	How many spray cycles are there per year?	One
		How many weeks do the sprayers work per spray cycle?	6-10 weeks
		How many days a week do the sprayers work per week?	6 days
		How many hours does each sprayer work per day?	5-6 hours/day
		What is the total time a sprayer is actually spraying a home per day?	15-20 min
		How many houses does the each sprayer spray per day?	10-15 depending on the size of structures
Resident	Exposure duration	Based on your experience, what is the average time a resident spends in their home per day (this will probably vary due to rainy season, other situations, please give an average for each scenario)?	Effectively, it depends on the country and the period. In general, African people pass more time outside the house in general under a tree.
	Contaminated water exposure	Based on your knowledge, how often does a typical adult in the target community take a bath? And how long do the bath?	One each day
	Contaminated water ingestion	Based on your knowledge, how much water does a household use per day (for drinking, cooking, etc.)	20-30 liters/day. Again this depend on the country. In desert it is very difficult to get water and the quantity is less
		What is the average of size of the home (square meters)?	Each country in Madagascar , house are very big in Haute Terre Central 150-200 m2, In Senegal, in rural area (Casa), structure are 20-30 m2 In Tanzania , 100-150 m2
		What is the total area of walls sprayed per house (square meters) ?	It depend on the type of structure. If it is a house with room, the number and the size varied. 60-200 m

		What are the houses predominately made of (mud brick, concrete brick, clay brick, etc)?	In Rural is mud in most of country and in concrete in towns
		How many rooms are sprayed per home?	It varied with country in Senegal each casa I one room , in Madagascar , more than 4 rooms
	Exposure frequency	On average, how many times has each home been sprayed since the start of the IRS program?	Some country are at their 4Th round and others at 5th Round (anzania, Madagascar, Senegal, etc.)

ANNEX G: EXPOSURE AND RISK CALCULATIONS

IRS, ITN Retreatment and Larviciding; Preparation of Pesticide

Table G-1. Worker's Subchronic Inhalation Exposure

$$Dose(mg/kg-day) = \frac{Unit\ exposure * IVM\ \ concentration * Tank\ \ volume * Exposure\ rate * Exposurefrequency * Spraycycles * Exposure\ duration}{PPE * Body\ Weight * Averaging\ \ time}$$

Parameter	Explanation	Value[1]	Units	Source
Unit exposure	Assumes open mixing/loading	0.096 (WP): IRS	mg_i / kg_i	SOPs (U.S. EPA, 1997a; Appdx B, wettable powder / all liquids); 2007 PEA (USAID, 2007)
		0.0026 (EC): IRS, larvicide		
		0.0037 (G): larvicide		
IVM concentration	Pesticide concentration in tank	See Table G-2	kg_i / L	2007 PEA (USAID, 2007)
Tank volume	Volume of sprayer tank (assumes one sprayer tank used)	10	L/tank	*Manual for IRS* (WHO, 2002); 2007 PEA (USAID, 2007) (*larvicide spray assumed equivalent to IRS*)
Exposure rate	Number of tanks prepared per day	3.5 / 5.0 / 7.1	tanks/day	See Annex F (*larvicide spray assumed equivalent to IRS*)
Exposure frequency	Number of day per spray cycle	33 / 36 / 44	day/cycle	See Annex F (*larvicide spray*

Parameter	Explanation	Value[1]	Units	Source
				assumed equivalent to IRS)
Spray cycles[2]	Number of spray cycles per year	1.0 / 1.25 / 2.0	cycle/yr	See Annex F (*larvicide spray assumed equivalent to IRS*)
PPE	Exposure reduction factor for use of PPE	20	unitless	N95 respirator
Body weight	Adult female mean	60	kg	WHO (2004); 2007 PEA (USAID, 2007)
Averaging time	For non-cancer endpoints, assumes sub-chronic exposure	39 / 42 / 51	day	See Annex F (*larvicide spray assumed equivalent to IRS*)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

[1] Low end / average / high end values are based on survey responses (see Annex F)
[2] For cancer risk calculations, only a single IRS spray cycle per year is assumed for the long-lasting pesticide DDT.
WP: wettable powder, EC: emulsifiable concentrate, G: granular

IVM Concentration for Indoor Residual Spraying (IRS)

Table G-2. Insecticide IVM Concentration

$$Insecticide\ \ IVM\ concentration(IRS) = \frac{Application * House_surface\ area * Houses\ per\ day * (1E+06)}{Tank\ volume * Exposurerate}$$

Parameter	Explanation	Value	Units	Source
Insecticide IVM concentration (IRS)	Mass of ai (kg) per unit volume	Calculated	mg_i /L	2007 PEA (USAID, 2007; Table G-5)
1E+06	Conversion factor for kg to mg	----	mg/kg	NA
Application	Amount of insecticide to be sprayed onto walls	See Table G-15	kg_i /m^2	Najera and Zaim (2002)
House_surface area	Total area of the walls of a house on which the insecticide is sprayed	3.58E+01	m^2/house	World Bank (1996); (USAID, 2007)
Houses per day	Number of houses sprayed per day; assumes 3 houses per hour and working 4 hours per day	9 / 11 / 14	houses/day	See Annex F
Tank volume	Volume of sprayer tank	10	L/tank	*Manual for IRS* (WHO, 2002); 2007 PEA (USAID, 2007)
Exposure rate	Number of tanks prepared per day	3.5 / 5.0 / 7.1	tanks/day	See Annex F

IRS, ITN Retreatment and Larviciding; Preparation of Pesticide

Table G-3. Worker's Subchronic Dermal Exposure

$$Dose(mg/kg-day) = \frac{Unit\ exposure * IVM\ concentration * Tank\ volume * Exposure\ rate * Exposure frequency * Spraycycles * Exposure\ duration}{PPE * Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value[1]	Units	Source
Unit exposure	Assumes open mixing/loading	9.7 (WP): IRS	mg_i / kg_i	SOPs (U.S. EPA, 1997a; Appdx B, wettable powder / all liquids / granular)
		6.4 (EC): IRS, larvicide		
		0.066 (G): larvicide		
IVM concentration	Pesticide concentration in tank	See Table G-4	kg_i / L	2007 PEA (USAID, 2007)
Tank volume	Volume of sprayer tank (assumes one sprayer tank used)	10	L/tank	*Manual for IRS* (WHO, 2002); 2007 PEA (USAID, 2007) (*larvicide spray assumed equivalent to IRS*)
Exposure rate	Number of tanks prepared per day	3.5 / 5.0 / 7.1	tanks/day	See Annex F (*larvicide spray assumed equivalent to IRS*)
Exposure frequency	Number of day per spray cycle	33 / 36 / 44	day/cycle	See Annex F (*larvicide spray assumed equivalent to IRS*)
Spray cycles[2]	Number of spray cycles per year	1.0 / 1.25 / 2.0	cycle/yr	See Annex F (*larvicide spray assumed equivalent to IRS*)
PPE	Exposure reduction factor for use of PPE	33 (EC:splash or spill) [3]	unitless	SOPs (U.S. EPA, 1997a; Appendix B)
		50 (WP or G: dusts) [4]		
Body weight	Adult female mean	60	kg	WHO (2004); 2007 PEA

Parameter	Explanation	Value[1]	Units	Source
				(USAID, 2007)
Averaging time	For non-cancer endpoints, assumes sub-chronic exposure	39 / 42 / 51	day	See Annex F (*larvicide spray assumed equivalent to IRS*)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

[1] Low end / average / high end values are based on IRS survey responses (see Annex F)
[2] For cancer risk calculations, only a single IRS spray cycle per year is assumed for the long-lasting pesticide DDT.
[3] All Liquids, mixing and loading: dermal exposure is 2.9 mg/lb_i. Rubber/PVC glove effectiveness assumed to be ~100%, and hand exposure contributes 2.8 mg/lb_i. Therefore, exposure reduction from wearing impermeable gloves is 0.1 mg/lb_i /2.9 mg/lb_i = 0.03%.
[4] Granular, open mixing loading: head and neck (0.0007 mg/lb_i) / all surfaces (0.03 mg/lb_i)) = 0.02 fractional exposure. WP, open mixing loading: head and neck (0.08 mg/lb_i) / all surfaces (4.4 mg/lb_i)) = 0.02 fractional exposure.
WP: wettable powder, EC: emulsifiable concentrate, G: granular

IVM Concentration for Larviciding

Table G-4. Insecticide IVM Concentration

$$Insecticide\ \ IVM\ concentration(larviciding) = \frac{Application * Water_surface\ area}{Tank\ volume * Exposure\ rate}$$

Parameter	Explanation	Value[1]	Units	Source
Larvicide IVM concentration	Mass of ai (mg) per unit volume	Calculated	mg_i /L	Equivalent calculation as IRS (Table G-2)
Application	Amount of insecticide to be sprayed on surface water	See Table G-15	kg_i /m^2	Najera and Zaim (2002); Natular (Spinosad) brochure
Water_surface area	Total area sprayed each day	500	m^2/day	*Assumption…*
Tank volume	Volume of sprayer tank	10	L/tank	*Assumed equivalent to IRS (Table G-2)*
Exposure rate	Number of tanks prepared per day	3.5 / 5.0 / 7.1	tanks/day	*Assumed equivalent to IRS (Table G-2)*

[1] Low end / average / high end values are based on IRS survey responses (see Annex F)

IRS, ITN retreatment and Larviciding; Disposal of Surplus

Table G-5. Resident's Chronic Drinking Water Ingestion Exposure

$$Dose\,(mg\,/\,kg-day) = \frac{Groundwate\ r\ concentrat\ ion * Water\ \ ingestion\ \ rate * Exposure\ \ Frequency\ \ * Exposure\ \ duration}{Body\ \ weight\ * Averaging\ \ time}$$

Parameter	Explanation	Value[1]	Units	Source
Groundwater concentration	IVM concentration in groundwater	See Table G-15	mg_i /L	EPA SCI-GROW model
Water ingestion rate	Adult	1.4 / 2.3	L/day	Exposure Factors Handbook (U.S. EPA, 1997b); Child Exposure Factors Handbook (U.S. EPA, 2002)
	Child	0.3 / 0.9		
Exposure frequency	Assumes daily exposure	365	days/years	Assumption; 2007 PEA (USAID, 2007)
Exposure duration	For non-cancer endpoints	1	year	Value does not affect risk results; 2007 PEA (USAID, 2007)
	For cancer endpoints, assume resident lives at the same residence for the 50 year lifetime	50		2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007) Child: U.S. EPA, 1997b; Table 7-3
	1-6 year old child	17		
Averaging time	For non-cancer endpoints, assumes chronic exposure	365	day	Equal to exposure duration
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

[1] Average / high end values are based on U.S. population data for drinking water ingestion

IRS, ITN Retreatment and Larviciding; Disposal of Surplus

Table G-6. Resident's Chronic Dermal Exposure from Bathing

$$Dose(mg/kg-day) = \frac{Absorbed\ Dose * Surface\ area\ body * Exposure\ frequency * Exposure\ duration}{Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value[1]	Units	Source
Absorbed dose		Calculated	mg_i /cm^2-event	See below, equation from U.S. EPA (2004) RAGS Dermal Risk Assessment
Surface area body	Whole body; adult	18,000	cm^2	U.S. EPA (2004) RAGS Dermal Risk Assessment
	Whole body; child	6,600		
Exposure frequency	Survey estimates reported 'per month'	276 / 300	baths/year	See Annex F
Exposure duration	For non-cancer and cancer endpoints	1	year	Value does not affect risk results; 2007 PEA (USAID, 2007)
	For cancer endpoints, assume resident lives at the same residence for 50 years	50		2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007) Child: U.S. EPA, 1997b; Table 7-3
	1-6 year old child	17		
Averaging time	For non-cancer endpoints, assumes chronic exposure	365	day	Equal to exposure duration
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

(continued) [1] Average / high end values are based on IRS survey responses (see Annex F) for bathing

Table G-6. (continued)

$$Absorbed\ Dose_{event} = (2 * FA_{aq}) * Permeability\ coefficient * \left(\frac{Groundwater\ concentration}{1E+03} \right) * \sqrt{\frac{6 * \tau_{event} * t_{event}}{\pi}}$$

Parameter	Explanation	Value[1]	Units	Source
FA_{aq}	Chemical-specific; fractional loss of chemical from skin due to desquamation.	Chemical specific data see Table G-15	unitless	2007 PEA (USAID, 2007; Table G-17); assumed to be 1.0 if chemical-specific value unavailable
Permeability coefficient	Chemical-specific	Chemical specific	cm/hr	Calculated, see below (from U.S. EPA, 2004)
Groundwater concentration	Daily average insecticide concentration in the groundwater that is used for bathing	See Table G-15	mg_i /L	EPA SCI-GROW model
1E+03	Conversion factor from L to cm^3	----	cm^3/L	NA
τ_{event}	Lag time of absorption	Chemical specific	hr/event	Calculated, see below (from U.S. EPA, 2004)
t_{event}	Bathing time	0.22 / 0.38	hr/event	See Annex F

[1] Average / high end values are based on IRS survey responses (see Annex F) for bathing

Table G-6. (continued)

$$Permeability\ \ Coefficient = 10\text{^}(-2.80 + 0.66 \log Kow - 0.0056 * MW)$$

$$\tau_{event} = 0.105 * 10^{(0.0056 * MW)}$$

Parameter	Explanation	Values	Units	Source
K_{ow}	Octanol-Water partition coefficient	Chemical specific data	(unitless)	see Table D-1
MW	Molecular Weight	Chemical specific data	g/mol	see Table D-1

Indoor Residual Spraying (IRS); Spraying

Table G-7. Worker's Sub-chronic Inhalation Exposure

$$Dose(mg/kg-day) = \frac{Unit\ exposure * Application * Area\ treated * Housesperday * Exposure\ frequency * Spraycycles}{PPE * Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value[1]	Units	Source
Unit exposure	Based on backpack sprayer application	0.066	mg_i / kg_i	SOPs (U.S. EPA, 1997a)
Application	Amount of insecticide to be sprayed onto walls	Chemical specific data see Table G-15	kg_i /m^2	Najera and Zaim (2002)
Area treated	Total area of the walls of a house on which the insecticide is sprayed	3.58E+01	m^2/house	World Bank (1996); (USAID, 2007)
Houses per day	Number of houses sprayed per day; assumes 3 houses per hour and working 4 hours per day	9 / 11 / 14	houses/day	See Annex F
Exposure frequency	Number of day per spray cycle	33 / 36 / 44	day/cycle	See Annex F
Spray cycles[2]	Number of spray cycles per year	1.0 / 1.25 / 2.0	cycle/yr	See Annex F
PPE	Exposure reduction factor for use of PPE	20	unitless	N95 respirator
Body weight	Adult female mean	60	kg	WHO (2004); 2007 PEA (USAID, 2007)
Averaging time	For non-cancer endpoints, assumes sub-chronic exposure	39 / 42 / 51	day	See Annex F
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

[1] Low end / average / high end values are based on IRS survey responses (see Annex F)
[2] For cancer risk calculations, only a single IRS spray cycle per year is assumed for the long-lasting pesticide DDT.

Indoor Residual Spraying (IRS); Spraying

Table G-8. Worker's Subchronic Dermal Exposure

$$Dose(mg/kg-day) = \frac{Unit\ exposure * FA_{spray} * Application * Area\ treated * Housesperday * Exposure\ frequency * Spraycycles}{PPE * Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value[1]	Units	Source
Unit exposure	Based on airless sprayer application (no data for backpack sprayer)	170	mg_i / kg_i	SOPs (U.S. EPA, 1997a)
FA_{spray}	Fraction of unit exposure absorbed through the skin at application concentration	Chemical specific data see Table G-15	unitless	Manufacturer information, otherwise assumed to be 1.0
Application	Amount of insecticide to be sprayed onto walls	Chemical specific data see Table G-15	kg_i /m^2	Najera and Zaim (2002)
Area treated	Total area of the walls of a house on which the insecticide is sprayed	3.58E+01	m^2/house	World Bank (1996); (USAID, 2007)
Houses per day	Number of houses sprayed per day; assumes 3 houses per hour and working 4 hours per day	9 / 11 / 14	houses/day	See Annex F
Exposure frequency	Number of day per spray cycle	33 / 36 / 44	day/cycle	See Annex F
Spray cycles[2]	Number of spray cycles per year	1.0 / 1.25 / 2.0	cycle/year	See Annex F
PPE	Exposure reduction factor for use of PPE	43	unitless	Machera et al, 2009
Body weight	Adult female mean	60	kg	WHO (2004); 2007 PEA (USAID, 2007)
Averaging time	For noncancer endpoints, assumes subchronic exposure	39 / 42 / 51	day	See Annex F
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

[1] Low end / average / high end values are based on IRS survey responses (see Annex F)
[2] For cancer risk calculations, only a single IRS spray cycle per year is assumed for the long-lasting pesticide DDT.

Indoor Residual Spraying (IRS) Spraying—Post Application

Table G-9. Resident's Chronic Dermal Exposure

$$Dose(mg/kg-day) = \frac{\left(Application * 1E+02 / F_{att}\right) * ABS * Skin\ surface\ area * Exposure\ \ frequency * Exposure\ duration}{Body\ Weight * Averaging\ \ time}$$

Parameter	Explanation	Values	Units	Source
Application	Amount of insecticide to be sprayed onto walls	Chemical specific data see Table G-15	kg_i /m^2	Najera and Zaim (2002)
F_{att}	Initial application attenuation factor	60	unitless	*see text; Section 5.2.3.6*
1E+02	Conversion factor for m^2 to cm^2, and kg to mg	----	m^2-mg / cm^2-kg	NA
ABS	Dermal absorption fraction from particulates	Chemical specific data see Table G-15	unitless	U.S. EPA (2004) RAGS Dermal Risk Assessment; Exhibit 3-4
Skin surface area	½ of 50th percentile hand and forearm; adult	1,039	cm^2	U.S. EPA (2004) RAGS Dermal Risk Assessment; Exhibit C-1
	½ of hand and forearm; child age <1 - <6 yr	375		
Exposure frequency	Assumes daily exposure	365	days/years	Assumption; 2007 PEA (USAID, 2007)
Exposure duration	For non-cancer endpoints	1	year	Value does not affect risk results; 2007 PEA (USAID, 2007)
	For cancer endpoints, assume resident lives at the same residence for 50 years	50		2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007) Child: U.S. EPA, 1997b; Table 7-3
	1-6 year old child	17		
Averaging time	For non-cancer endpoints, assumes chronic exposure	365	day	Equal to exposure duration
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Long-Lasting Insecticidal Net (LLIN), Retreated Insecticide Treated Net (ITN) —Washing

Table G-10. Resident's Dermal Exposure

$$Dose(mg/kg-day) = \frac{Absorbed\ dose * Skin\ surface\ area * Exposure\ \ frequency * Exposure\ duration}{Body\ Weight * Averaging\ \ time}$$

Parameter	Explanation	Value	Units	Source
Absorbed dose		Calculated	mg_i /cm^2-event	See below, equation from U.S. EPA (2004) RAGS Dermal Risk Assessment
Skin surface area	50th percentile hand and forearm; adult	2077	cm^2	U.S. EPA (2004) RAGS Dermal Risk Assessment; Exhibit C-1
Exposure frequency	Acute exposure assessed for non-cancer endpoint	1 day	See value	*Assumption for chronic; CTE and RME washing frequency…*
	Chronic exposure assessed for cancer endpoint	2 day/yr / 4 day/yr		
Exposure duration	Cancer endpoint only; assume resident lives at the same residence for 50 years	50	Year	2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007)
Averaging time	For non-cancer endpoints, assumes an acute exposure	1	day	Equal to length of exposure
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

(continued) [1] Average (CTE) / high end (RME) values are based on deltamethrin in two LLIN products.

Table G-10. (continued)

$$Absorbed\ Dose_{event} = (2 * FA_{aq}) * Permeability\ coefficient * \left(\frac{Washwater\ concentration}{1E+03} \right) * \sqrt{\frac{6 * \tau_{event} * t_{event}}{\pi}}$$

Parameter	Explanation	Value	Units	Source
FA_{aq}	Chemical-specific; fractional loss of chemical from skin due to desquamation.	Chemical specific data see Table G-15	unitless	2007 PEA (USAID, 2007; Table G-17); assumed to be 1.0 if chemical-specific value unavailable
Permeability coefficient	Chemical-specific	Chemical specific	cm/hr	Calculated, see Table G-6
Washwater concentration	Insecticide concentration in water; protectively assumes washing in a basin	Chemical specific	mg_i /L	Calculated, see below
1E+03	Conversion factor from L to cm^3	----	cm^3/L	NA
τ_{event}	Lag time of absorption	Chemical specific	hr/event	Calculated, see Table G-6
t_{event}	Time spent washing net	0.17	hr/event	*Assumed (10 minutes)*

Table G-10. (continued)

$$Washwater\ concentrat\ ion(mg/L) = LLINconcen\ tration * Netweight\ * Netarea\ * Pesticidel\ oss \Big/ Ba\sin volume$$

Parameter	Explanation	Value[1]	Units	Source
LLIN concentration	Concentration of pesticide in net fabric	Product specific data see Table G-15	mg/kg	Manufacturer information
Net weight	Unit weight of net material	Product specific data see Table G-15	kg/m^2	Manufacturer information
Net area	Surface area of net	15	m^2	Najera and Zaim (2002)
Pesticide loss	Fractional loss of pesticide per wash. Range of 2% to 8%; central value of 5%.	0.05 / 0.08	unitless	WHO, 2009; Tables 6 and 12
Basin volume	Volume of water in which pesticide is dissolved	10	L	*Assumed*

[1] Average (CTE) / high end (RME) values are based on deltamethrin in two LLIN products.

Larviciding; Spray Application

Table G-11. Worker's Subchronic Inhalation Exposure

$$Dose(mg/kg-day) = \frac{Unit\ exposure * Application * Area\ treated * Exposure\ frequency * Spraycycles}{PPE * Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value[1]	Units	Source
Unit exposure	Assumes a backpack sprayer	0.066	mg_i / kg_i	SOPs (U.S. EPA, 1997a)
Application	Amount of larvicide to be sprayed onto surface water	Chemical specific data see Table G-15	kg_i /m^2	Najera and Zaim (2002); Natular brochure
Area treated	Total area of water on which the larvicide is sprayed	320 / 390 / 500	m^2/day	*Assumed equivalent to area sprayed during IRS (Table G-7)*
Exposure frequency	Number of day per spray cycle	33 / 36 / 44	day/cycle	*Assumed equivalent to IRS (Table G-7)*
Spray cycles	Number of spray cycles per year	1.0 / 1.25 / 2.0	cycle/yr	*Assumed equivalent to IRS (Table G-7)*
PPE	Exposure reduction factor for use of PPE	20	unitless	N95 respirator
Body weight	Adult female mean	60	kg	WHO (2004); 2007 PEA (USAID, 2007)
Averaging time	For noncancer endpoints, assumes subchronic exposure	39 / 42 / 51	day	See Annex F
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

[1] Low end / average / high end values are based on IRS survey responses (see Annex F)

Larviciding; Spray Application

Table G-12. Worker's Subchronic Dermal Exposure

$$Dose(mg/kg-day) = \frac{Unit\ exposure * FA_{spray} * Application * Area\ treated * Exposure\ frequency * Spraycycles}{PPE * Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value[1]	Units	Source
Unit exposure	Assumes a backpack sprayer	10.8	mg_i / kg_i	SOPs (U.S. EPA, 1997a)
FA_{spray}	Fraction of unit exposure absorbed through the skin at application concentration	Chemical specific data see Table G-15	unitless	Manufacturer information, otherwise assumed to be 1.0
Application	Amount of larvicide to be sprayed onto surface water	Chemical specific data see Table G-15	kg_i /m^2	Najera and Zaim (2002); Natular brochure
Area treated	Total area of water on which the larvicide is sprayed	320 / 390 / 500	m^2/day	*Assumed equivalent to area sprayed during IRS (Table G-7)*
Exposure frequency	Number of day per spray cycle	33 / 36 / 44	day/cycle	*Assumed equivalent to IRS (Table G-7)*
Spray cycles	Number of spray cycles per year	1.0 / 1.25 / 2.0	cycle/yr	*Assumed equivalent to IRS (Table G-7)*
PPE	Exposure reduction factor for use of PPE	43	unitless	Machera et al, 2009
Body weight	Adult female mean	60	kg	WHO (2004); 2007 PEA (USAID, 2007)
Averaging time	For noncancer endpoints, assumes subchronic exposure	39 / 42 / 51	day	See Annex F
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

[1] Low end / average / high end values are based on IRS survey responses (see Annex F)

Risk Estimate, Non-Carcinogenic

Table G-13. Hazard Quotient for Non-carcinogenic Insecticides

Hazard Quotient (HQ) Calculation

$$HQ = \frac{AveragedailyDose}{\mathrm{Re}\ ferenceDose}$$

Parameter	Explanation	Units	Source
Hazard Quotient	The ratio of calculated insecticide dose to a reference dose level below which adverse health effects are unlikely; HQs greater than 1 are of concern	unitless	(U.S. EPA, 1989)
Average daily dose	The body weight normalized average daily dose during the exposure period	mg/kg-day	Calculated (See Tables G-1 to G-12)
Reference dose	The insecticide dose an individual may be exposed to for which adverse effects are unlikely to occur	mg/kg-day	Values presented in Annex D, Table D-3

Risk Estimate: Carcinogenic

Table G-14. Incremental Cancer Risk

Cancer Risk Calculation

$$Incremental\ Cancer\ Risk = LADD * Slope\ factor$$

Parameter	Explanation	Units	Source
Incremental cancer risk	The incremental risk of developing cancer from the lifetime dose calculated in the exposure assessment	risk/lifetime	(U.S. EPA, 1989)
LADD	The body weight normalized lifetime average daily dose	mg/kg-day	Calculated (See Tables G-1 to G-12)
Slope factor	Expresses the relationship between dose and cancer incidence risk	1 / mg/kg-day	Values presented in Annex D, Table D-3

Pesticide-Specific and LLIN-Specific Properties

Table G-15. Pesticide-Specific Properties for Exposure Calculations

Insecticide	IVM Method	Application IRS, ITN or larvicide (1)	IRS, ITN or larvicide concentration (1)	Screening groundwater concentration	Aqueous fraction absorbed (FA_{aq}) (2)	Spraying fraction absorbed (FA_{spray}) (3)	Particle dermal absorption fraction (ABS) (4)	LLIN/ITN concentration	Unit weight of net
		kg_i/m^2	mg_i/L	mg_i/L	unitless	unitless	unitless	mg_i/kg	kg/m^2
Alpha-cypermethrin	IRS, LLIN, ITN	2E-05 - 3E-05	57 - 86	1.3E-05	0.8	1	0.1	5500 (a)/ 20-40 mg/m^2	0.045 (a)
Bendiocarb	IRS	1E-04 - 4E-04	290 - 1150	7.3E-06	1	1	0.1	NA	NA
Bifenthrin	IRS	2.5E-5 - 5E-05	72 - 140	1.3E-05	0.7	1	0.1	NA	NA
Chlorfenapyr	IRS	4E-04 (b)	1150	1.3E-05	0.9	1	0.1	NA	NA
Cyfluthrin	IRS, ITN	2E-5 - 5E-05	57 - 140	3.6E-05	0.8	1	0.1	NA/ 50 mg/m^2	NA
DDT	IRS	1E-03 - 2E-03	2900 - 5700	1.3E-05	0.7	1	0.03	NA	NA
Deltamethrin	IRS, LLIN, ITN	2E-05 - 2.5E-05	57 - 72	1.3E-05	0.6	1	0.1	80 - 100 mg/m^2 (c)/ 15-25mg/m^2	NA
Etofenprox	IRS, ITN	1E-04 - 3E-04	290 - 860	3.2E-05	0.7	1	0.1	NA	NA
Fenitrothion	IRS	2E-03	5700	7.0E-05	1	1	0.1	NA	NA
Lambda-cyhalothrin	IRS, LLIN, ITN	2E-05 - 3E-05	57 - 86	1.3E-05	0.4	1	0.1	50 mg/m^2 (c)/ 10-15 mg/m^2	NA
Malathion	IRS	2E-03	5700	1.1E-03	1	1	0.1	NA	NA

Insecticide	IVM Method	Application IRS, ITN or larvicide (1)	IRS, ITN or larvicide concentration (1)	Screening groundwater concentration	Aqueous fraction absorbed (FA_{aq}) (2)	Spraying fraction absorbed (FA_{spray}) (3)	Particle dermal absorption fraction (ABS) (4)	LLIN/ITN concentration	Unit weight of net
Methoprene	larvicide	2E-06 - 4E-06	21 - 28	1.3E-05	0.9	1	NA	NA	NA
Permethrin	LLIN, ITN	NA	NA	NA	0.7	1	0.1	20,000 (e)/ 200-500 mg/m^2	0.05 (e)
Pirimiphos-methyl	IRS	1E-03 - 2E-03	2900 - 5700	1.2E-05	0.9	0.08 (g)	0.1	NA	NA
Propoxur	IRS	1E-03 - 2E-03	2900 - 5700	7.5E-03	1	1	0.1	NA	NA
Spinosad	Larvicide	9.1E-06 - 2E-05	93 - 140	9.2E-05	0.01	1	NA	NA	NA
Temephos	Larvicide	5.6E-6 - 1.1E-5	57 - 78	1.3E-05	0.6	1	NA	NA	NA
Pyriproxyfen	IRS (f), LLIN, larvicide	5E-7 – 1E-6	5.1 – 7.1	1.3E-05	0.9	1	0.1	(d)	(d)

(1) Range represents low-end and high-end estimates used in the exposure assessment. Single value implies only one (best-estimate) value exists.
(2) Based on Exhibit A-5 of *Dermal Risk Assessment Guidance for Superfund* (U.S.EPA 2004).
(3) Default value of 1.0 used in the absence of manufacturer information.
(4) From Exhibit 3-4 of *Dermal Risk Assessment Guidance for Superfund* (U.S.EPA 2004). Default value of 0.1 for organic chemicals.
(a) http://duranetmosquitonet.com/closer.cfm
(b) Raghavendra et al, 2011
(c) Pesticide loading on DawaPlus brand net (80 mg/m^2); http://www.tananetting.com/products/product-public-dawaplus-spec.php. On PermaNet 3.0 product side walls, deltamethrin content is 84 mg/m^2. Top wall deltamethrin content is 160 mg/m^2, with piperonyl butoxide added to the top panel only at 1,000 mg/m^2 (WHO, 2008). 50 mg/m^2 lambda-cyhalothrin for a Syngenta polyester net (WHO, 2008).
(d) No manufacturer information was found for this LLIN pesticide.
(e) http://www.spartanrelief.com/olyset-mosquito-net.php
(f) Application rate information for use in IRS was not found.
(g) Values of 0.02, 0.03, and 0.08 were measured at 6, 10, and 24 hr periods following unoccluded *in vitro* skin application at 4,500 mg/L (Ward 1996; attached). A reasonable worst case value of 0.08 is used in this risk assessment based on daily spray activities and no effect of bathing or washing by sprayers to limit absorption. In the absence of product-specific information, a default FA_{spray} value of 1.0 is applied.

IRS with DDT

Table G-16. Resident's Chronic Soil Ingestion Exposure

$$Dose\,(mg/kg-day) = \frac{Soil concentration * 1E-06 * Soil ingestion\ rate * Exposure\ Frequency * Exposure\ duration}{Body\ weight * Averaging\ time}$$

Parameter	Explanation	Value	Units	Source
Soil concentration; floor sweepings	DDT concentration in soil from indoors	360	mg_i /kg	Average of mean concentrations in IRS homes (see Table 5-16)
Soil ingestion rate	Adult	100	mg/day	Standard Default Exposure Factors Handbook (U.S. EPA, 1991)
	Child			
1E-06	Conversion factor	----	mg / kg	NA
Exposure frequency	Assumes daily exposure	365	days/years	Assumption; 2007 PEA (USAID, 2007)
Exposure duration	For noncancer endpoints	1	year	Value does not affect risk results; 2007 PEA (USAID, 2007)
	For cancer endpoints, assume resident lives at the same residence for the 50 year lifetime	50		2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007) Child: U.S. EPA, 1997b; Table 7-3
	1-6 year old child	17		
Averaging time	For noncancer endpoints, assumes chronic exposure	365	day	Equal to exposure duration
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

IRS with DDT

Table G-17. Resident's Chronic Inhalation Exposure

$$Dose\,(mg\,/\,kg-day) = \frac{Airconcentration * Inhalation\ \ rate * Exposuretime * Exposure\ \ Frequency\ \ * Exposure\ \ duration}{Body\ \ weight * Averaging\ \ time}$$

Parameter	Explanation	Value	Units	Source
Air concentration	DDT concentration in indoor air	0.0036	$mg_i\ /m^3$	Average of concentrations in IRS homes (see Table 5-16)
Inhalation rate	Adult	0.63	m^3/hr	U.S. EPA, 1997b; Table 5-23 U.S. EPA 2002; Table 7-14
	Child			
Exposure time	Time spent indoors	12	hr / day	Assumption
Exposure frequency	Assumes daily exposure	365	days/years	Assumption; 2007 PEA (USAID, 2007)
Exposure duration	For noncancer endpoints	1	year	Value does not affect risk results; 2007 PEA (USAID, 2007)
	For cancer endpoints, assume resident lives at the same residence for the 50 year lifetime	50		2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007) Child: U.S. EPA, 1997b; Table 7-3
	1-6 year old child	17		
Averaging time	For noncancer endpoints, assumes chronic exposure	365	day	Equal to exposure duration
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

IRS with DDT

Table G-18. Resident's Chronic Dermal Exposure

$$Dose(mg/kg-day) = \frac{Wallconcentration * ABS * 1E-06 * AF * Skin\ surface\ area * Exposure\ \ frequency * Exposure\ duration}{Body\ Weight * Averaging\ \ time}$$

Parameter	Explanation	Values	Units	Source
Wall concentration	Concentration of DDT on wall scrapings	1260	mg_i /kg	Average of mean concentrations in IRS homes (see Table 5-16)
ABS	Dermal absorption fraction	Chemical specific data see Table G-15	unitless	U.S. EPA (2004) RAGS Dermal Risk Assessment; Exhibit 3-4
1E-06	Conversion factor	----	mg / kg	NA
Skin surface area	½ of 50th percentile hand and forearm; adult	1,039	cm^2	U.S. EPA (2004) RAGS Dermal Risk Assessment; Exhibit C-1
	½ of hand and forearm; child age <1 - <6 yr	375		
Skin adherence factor (AF)	Amount of wall material adhering to skin	0.07 (adult)	mg/cm^2-event	U.S. EPA (2004) RAGS Dermal Risk Assessment; recommended values
		0.2 (child)		
Exposure frequency	Assumes daily exposure	365	events/years	Assumption; 2007 PEA (USAID, 2007)
Exposure duration	For noncancer endpoints	1	year	Value does not affect risk results; 2007 PEA (USAID, 2007)
	For cancer endpoints, assume resident lives at the same residence for 50 years	50		2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007) Child: U.S. EPA, 1997b; Table 7-3
	1-6 year old child	17		
Averaging time	For noncancer endpoints, assumes chronic exposure	365	day	Equal to exposure duration
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

IRS with DDT
Table G-19. Resident's Chronic Food Ingestion Exposure

$$Dose\,(mg\,/\,kg\,-\,day) = \frac{Foodconcen\ tration\ *\ 1E-03\ *Foodingest\ ion\ \ rate\ *\ Exposure\ \ Frequency\ \ *\ Exposure\ \ duration}{Body\ \ weight\ *\ Averaging\ \ time}$$

Parameter	Explanation	Value	Units	Source
Food concentration	DDT concentration in vegetables and poultry raised in affected area	0.043 (veg)	mg_i /kg	Mean concentrations in IRS village (see Table 5-17)
		24.5 (chicken) (a)		
Food ingestion rate; home-raised	Vegetable	70 (b)	g/day	Exposure Factors Handbook (U.S. EPA, 1997b; Tables 13-33 and 13-55)
	Chicken	40 (c)		
1E-03	Conversion factor	----	kg / g	NA
Exposure frequency	Assumes daily exposure	365	days/years	Assumption; 2007 PEA (USAID, 2007)
Exposure duration	For noncancer endpoints	1	year	Value does not affect risk results; 2007 PEA (USAID, 2007)
	For cancer endpoints, assume resident lives at the same residence for the 50 year lifetime	50		2007 PEA (USAID, 2007)
Body weight	Adult female mean	60	kg	Adult: WHO (2004); 2007 PEA (USAID, 2007) Child: U.S. EPA, 1997b; Table 7-3
	1-6 year old child	17		
Averaging time	For noncancer endpoints, assumes chronic exposure	365	day	Equal to exposure duration
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption; 2007 PEA (USAID, 2007)

(a) Assumes long-term consumption is 90% muscle and 10% fat.

(b) Based on the 75th percentile of seasonally-adjusted intake of home-grown vegetables in the Western U.S., adjusted by an 18% preparation loss for corn, squash, peppers and tomatoes (U.S.EPA, 1997; Table 13-7) and assuming a 60-kg average body weight (U.S.EPA 1997; Section 13.3).

(c) Based on the 50th percentile of annual-average intake of home-grown poultry in the Western U.S., adjusted by a 31% preparation loss (U.S.EPA, 1997; Table 13-5) and assuming a 60-kg average body weight (U.S.EPA 1997; Section 13.3).

Glossary

Absorbed dose (mg/kg-day)—The amount of pesticide a receptor is predicted to absorb per unit body weight and time.

Application (kg ai/m^2)—The mass of pesticide active ingredient sprayed per unit area.

Averaging time (days)—The period of time over which the toxic effects of the dose are averaged.

Dose (mg/kg-day)—The calculated amount of pesticide to which a receptor is exposed per unit body weight and time.

EC—Emulsifiable concentrate; a liquid pesticide formulation that forms an emulsion when added to water.

Exposure duration (year)—The period of time over which a receptor is exposed (via inhalation, ingestion, or dermal contact) to a pesticide.

Exposure frequency (event/time or time/time)—The number of events in which a specific receptor is exposed within the exposure duration.

Fraction absorbed—The fraction of the pesticide that is absorbed through the skin.

Groundwater concentration (mass ai/L)—The average pesticide concentration in groundwater that is used for drinking water.

IRS—Indoor residual spraying; an IVM process in which the walls of a house are sprayed with insecticide to kill mosquitoes inside the home.

IVM Concentration (mass ai/L)—The mass of active ingredient per unit volume for IRS and larviciding.

Kow—Octanol-water partition coefficient; a chemical-specific property that characterizes a chemical's affinity for water or lipids.

LADD (mg/kg-day)—Lifetime average daily dose; a measure of dose that is used to assess cancer risk.

LLIN—Long-lasting insecticide-treated nets, an IVM process in which bed nets are pre-treated with insecticide to protect residents from mosquitoes.

MW (g/mol)—Molecular weight; a chemical-specific property.

Permeability coefficient (cm/hr)—The rate at which a pesticide moves through the skin.

PPE—Personal protective equipment, such as gloves or masks.

$\square_{event}$ **(hr/event)**—The lag time per event, which is the amount of time for the pesticide to diffuse through the skin.

t_{event} **(hr/event)**—The duration of a dermal exposure event (e.g., a bath or washing a net).

Unit exposure (mg ai/kg ai)—The unit mass of active ingredient to which a receptor will be exposed via an exposure pathway (ingestion, inhalation, dermal) per unit mass of active ingredient from the process/practice (e.g., mixing).

WP—Wettable powder; a fine powder pesticide formulation that must be mixed with water or another liquid before it is applied.

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CENTRAL TOXICOLOGY LABORATORY
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CHESHIRE UK

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STUDY DETAILS

Sponsor:	Zeneca Agrochemicals
Sponsor Reference:	WINO15450
CTL Test Substance Reference Number:	Y00146/081
CTL Study Number:	JV1484

AUTHOR

R J Ward

DATE OF ISSUE

14 November 1996

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STATEMENT OF DATA CONFIDENTIALITY CLAIM

THIS DOCUMENT CONTAINS INFORMATION CONFIDENTIAL AND TRADE SECRET TO ZENECA

It should not be disclosed in any form to an outside party, nor should information contained herein be used by a registration authority to support registration of this product or any other product without the written permission of Zeneca Agrochemicals.

05120035

STATEMENT OF GLP COMPLIANCE AND AUTHENTICATION

I, the undersigned, declare that the objectives laid down in the protocol were achieved and that the data generated are valid. The report fully and accurately reflects the procedures used and the raw data generated in the above study.

The study was conducted in compliance with the UK Principles of Good Laboratory Practice (The United Kingdom GLP Compliance Programme, Department of Health 1989). These Principles are in accordance with the OECD Principles of Good Laboratory Practice (1982) ISBN 9264 12367 9 (OECD Environment Monograph No 45, OCDE/GD(92)32) and are in conformity with, and implement, the requirements of the European Commission (Directives 87/18/EEC and 88/320/EEC).

R J Ward
Study Director

.....RJWard..... 14 November 1996
Date

05120036

This page
may be required
by some
regulatory authorities.

05120037

QUALITY ASSURANCE STATEMENT

In accordance with ZENECA policy and QA procedures for Good Laboratory Practice, this report has been audited and the conduct of this study has been inspected as follows:

Date	Date of QA Report
03 Sep 96	09 Sep 96
13 Nov 96	13 Nov 96
14 Nov 96	14 Nov 96

In addition, procedure inspections associated with this type of study were made as follows:

27 Jun 96	28 Jun 96
02 Jul 96	03 Jul 96
30 Jul 96	30 Jul 96
31 Jul 96	31 Jul 96
27 Sep 96	04 Oct 96

Facilities and process based procedures associated with this type of study were inspected in accordance with QA Standard Operating Procedures.

So far as can be reasonably established, the methods described and the results given in the final report accurately reflect the raw data produced during the study, JV1484.

I H Mills Irene H. Mills 14 November 1996

(CTL Quality Assurance Unit)

05120038

STUDY CONTRIBUTORS

The following contributed to this report in the capacities indicated:

Name	Title
Mr R J Ward	Report Writer
Dr J R Heylings	Study Reviewer
Mrs A Pillai	Study Investigator

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This page is provided for the Regulatory Authority Reviewer's notes.

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1. SUMMARY

1.1 Study design

The absorption of pirimiphos-methyl from a nominal 500g/*l* EC formulation, YF7244C, (actual content 504g pirimiphos-methyl/*l*) has been measured *in vitro* through human epidermis. The formulation was applied as the concentrate formulation and as a 0.9:100v/v (4.54g pirimiphos-methyl/*l*) spray strength dilution of the formulation in water. The concentrate formulation and the spray strength dilution were applied to the epidermal membranes at a rate of 10µl/cm^2; all applications were left unoccluded throughout the entire exposure period. These applications were designed to simulate potential human dermal exposure to the formulation during normal use.

1.2 Results

Absorption of pirimiphos-methyl from both the concentrate and spray strength dilution maintained essentially constant rates over the entire exposure period (54h). The absorption rate measured from the spray dilution (mean 0.155µg/cm^2/h) was approximately 8 times less than the rate obtained from the concentrate (1.172µg/cm^2/h). Mean amounts of pirimiphos-methyl absorbed during typical working day periods from the concentrate varied from 5.72µg/cm^2 (0.11% of dose) at 6h to 10.9µg/cm^2 (0.22% of dose) at 10h. This increased to 28.4µg/cm^2 (0.56% of dose) after 24h exposure. The amounts absorbed from the spray dilution varied from 0.883µg/cm^2 (1.9% of dose) at 6h to 1.53µg/cm^2 (3.4% of dose) at10h. This increased to 3.84µg/cm^2 (8.46% of dose) after 24h exposure.

1.3 Conclusion

The results obtained in this study demonstrate that the absorption of pirimiphos-methyl through human epidermis is slow when compared with the absorption rates of other penetrants measured using this *in vitro* technique (Dugard *et al*, 1984; Dugard and Scott, 1984). These data predict that the dermal absorption of pirimiphos-methyl from normal exposure to this 500g/l EC formulation would be low.

2. INTRODUCTION

2.1 Purpose

Pirimiphos-methyl is intended for use as an insecticide.

The purpose of this study was to determine the *in vitro* absorption of pirimiphos-methyl through human epidermis to aid the quantitative assessment of the hazard from human skin contact with an EC formulation containing a nominal 500g pirimiphos-methyl/*l*.

2.2 Justification for test system selection

In vitro techniques employing glass diffusion cells (Appendix A) have been shown to predict percutaneous absorption of chemicals *in vivo* (Scott *et al*, 1992; Ramsey *et al*, 1994).

Such an *in vitro* technique was used in the study, where the applied doses and conditions of exposure were designed to simulate potential exposure to the formulation during normal use.

2.3 Dates of the experimental work

The experimental phase of the study commenced on 2nd September 1996 and finished on 6th September 1996.

2.4 Data storage

An original report and all raw data pertaining to this study are retained in the Archives, Central Toxicology Laboratory (CTL), Alderley Park, Macclesfield, Cheshire, UK.

3. TEST SUBSTANCES

3.1 500g/l EC formulation of pirimiphos-methyl

pirimiphos-methyl content:	504g/*l*
Source:	Zeneca Agrochemicals, Yalding, Kent, UK
Colour:	Brown
Physical state:	Liquid
Batch reference number:	F5512
CTL test substance reference number:	Y00146/081
Specific gravity:	1.024
Storage conditions:	Ambient temperature in the dark

The sample was tested as supplied and diluted as described in Section 4.4 and Table 1. From information supplied by the Sponsor, the test substance was used within the expiry date. The certificate of analysis is retained in the CTL Archives.

3.2 Standard sample of pirimiphos-methyl

Name:	Pirimiphos-methyl
Source:	Zeneca Agrochemicals, Jealott's Hill Reseach Station, Bracknell, Berks, UK
Colour:	Light amber
Physical state:	Liquid
Batch reference number:	ASJ10084-01S
CTL test substance reference number:	Y00146/078
Purity (% w/w):	99.6
Storage conditions:	Refrigerated

From information supplied by the Sponsor, the test substance was used within the expiry date. The certificate of analysis is retained in the CTL Archives.

4. EXPERIMENTAL PROCEDURES

4.1 Analytical techniques

4.1.1 Gas-liquid chromatography (GLC) conditions

Detector:	Nitrogen-phosphorus
Column:	3% OV17 on Chromosorb WHP (100-120#) 1.2m x 2mm id
Column temperature:	200°C
Detector temperature:	275°C
Injection port temperature:	220°C
Carrier gas:	Helium at 30ml/min
Injection volume:	2µl

The limit of quantitation using the above procedure was set at 0.03µg/ml.

4.2 Preparation of epidermal membranes

4.2.1 Human skin

Extraneous tissue was removed from human whole skin samples. The skin samples were immersed in water at 60°C for 40-45 seconds and the epidermis teased off the dermis. Each epidermal membrane was given an identifying number and stored frozen on aluminium foil until required for use.

4.3 Measurement of membrane integrity

Samples of epidermis were mounted in glass diffusion cells (Appendix A) with an exposed area of 2.54cm^2. The cells were placed in a water bath maintained at 30 ± 1°C.

The integrity of the membranes was determined by measurement of their electrical resistance across the skin membrane. Membranes with a measured resistance <10kΩ were regarded as having a lower integrity than normal and were not used for exposure to the test material.

4.4 Measurement of test substance absorption

The receptor chambers of the cells were filled with a recorded volume of receptor fluid (50% v/v ethanol in water) and placed in a water bath maintained at 30 ± 1°C. A pre-treatment sample (0.5ml) was taken from each receptor chamber for analysis by GLC. An equal volume of fresh receptor fluid was added to each receptor chamber to replace the volume removed.

The formulation was applied to the skin membranes as the concentrate and as a 0.9:100v/v (4.5g pirimiphos-methyl /*l*) aqueous spray strength dilution at the dose rates indicated in Table 1 and left unoccluded for the duration of the exposure period (54h).

At recorded intervals, samples (0.5ml) of the receptor fluid were taken for analysis by GLC. The volume of fluid in the receptor chamber was maintained by the addition of fresh receptor fluid (0.5ml) to the chamber immediately after the removal of each sample.

5. DATA EVALUATION

Results of the assay were expressed as concentrations of pirimiphos-methyl in the receptor solution. The amounts absorbed and rates of absorption, with correction for the volume of sample removed, were determined using the calculation in Appendix B.

6. RESULTS AND DISCUSSION

The results obtained in this study are summarised in Table 1, where data are presented both in terms of absorption rate and in terms of amount and percent of the dose applied during periods representing typical working days (6, 8 and 10h) and at 24h.

The absorption profiles for pirimiphos-methyl from this formulation and the 0.9:100v/v spray strength dilution are displayed in Appendices C and D. The absorption data for each individual cell are given in Appendices E and F.

Absorption of pirimiphos-methyl from both the concentrate and spray strength dilution maintained essentially constant rates over the entire exposure period (54h). The absorption rate measured from the spray dilution (mean 0.155μg/cm^2/h) was approximately 8 times less than the rate obtained from the concentrate (1.172μg/cm^2/h). Mean amounts of pirimiphos-methyl absorbed from the concentrate during typical working day periods from the concentrate varied from 5.72μg/cm^2 (0.11% of dose) at 6h to 10.9μg/cm^2 (0.22% of dose) at 10h. This increased 28.4μg/cm^2 (0.56% of dose) after 24h exposure. The amounts absorbed from the spray dilution varied from 0.883μg/cm^2 (1.9% of dose) at 6h to 1.53μg/cm^2 (3.4% of dose) at10h. This increased 3.84μg/cm^2 (8.46% of dose) after 24h exposure.

7. CONCLUSION

The results obtained in this study demonstrate that the absorption of pirimiphos-methyl through human epidermis is slow when compared with the absorption rates of other penetrants measured using this *in vitro* technique (Dugard *et al*, 1984; Dugard and Scott, 1984). These data predict that the dermal absorption of pirimiphos-methyl from normal exposure to this 500g/l EC formulation would be low.

8. REFERENCES

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Ramsey J D, Woollen B H, Auton T R and Scott R C (1994). The Predictive Accuracy of *In Vitro* Measurements for the Dermal Absorption of a Lipophilic Penetrant (Fluazifop-Butyl) through Rat and Human Skin. Fundam. Appl. Toxicol. **23**, 230-236.

TABLE 1 - SUMMARY OF PIRIMIPHOS-METHYL ABSORPTION

1. DETAILS OF APPLICATION OF TEST MATERIALS	2. MEAN ABSORPTION RATES		3. MEAN AMOUNT AND PERCENT OF DOSE ABSORBED		
	Time period (h)	Absorption rate ($\mu g/cm^2/h \pm SEM$)	Time (h)	Amount ($\mu g/cm^2$)	Percent absorbed
Concentrate Formulation (503.7g ai/l) 10µl/cm² (5037µg ai/cm²) Unoccluded Duration of exposure: 54h n = 5	0.5-54	1.17 ± 0.097	6 8 10 24	5.72 8.32 10.9 28.4	0.11 0.17 0.22 0.56
0.9:100v/v spray dilution (4.536g ai/l) 10µl/cm² (45.36µg ai/cm²) Unoccluded Duration of exposure: 54h n = 6	0.5-54	0.155 ± 0.028	6 8 10 24	0.883 1.20 1.53 3.84	1.9 2.6 3.4 8.5

Active ingredient (ai) = pirimiphos-methyl

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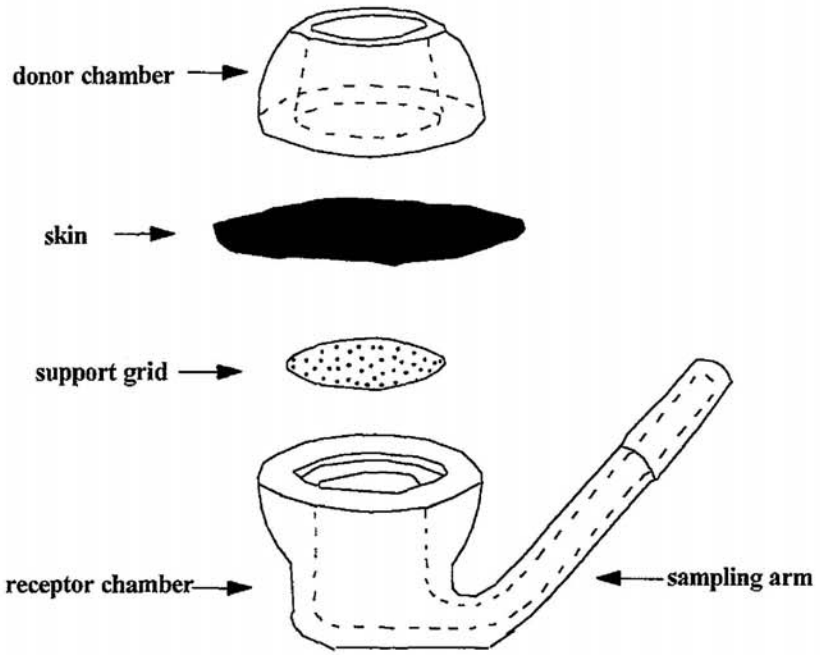
APPENDIX A - DIFFUSION CELL



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APPENDIX B - CALCULATIONS

1. Absorption data

Absorption data were determined using a validated computer program which performs the following calculations:

Equation 1

Receptor volume (ml) = V
Sample replacement volume (ml) = v

Concentrations (µg/ml) at sampling times (h) t_1, t_2, t_3 etc. are c_1, c_2, c_3 etc.

The total amount of penetrant having passed through the epidermal membrane into the receptor fluid, corrected for sample volume removed (c_1v, c_2v, c_3v etc.) at sampling times t_1, t_2, t_3 etc. are:

$t_1 = c_1V$
$t_2 = c_2V + c_1v$
$t_3 = c_3V + c_1v + c_2v$
$t_4 = c_4V + c_1v + c_2v + c_3v$
etc.

The amount of test penetrant at each time point is divided by the area of epidermal membrane ($2.54cm^2$) and the results plotted as amount of penetrant absorbed ($\mu g/cm^2$) versus time (h). The slope of this absorption profile between given time points gives the average rate of absorption of the penetrant per cm^2 of the skin ($\mu g/cm^2/h$) during that period.

The mean 'percent of dose absorbed' for any given time point is:

Equation 2

$$\% \text{ Absorbed} = \frac{\text{Mean amount absorbed } (\mu g/cm^2)}{\text{Mean amount applied } (\mu g/cm^2)} \times 100$$

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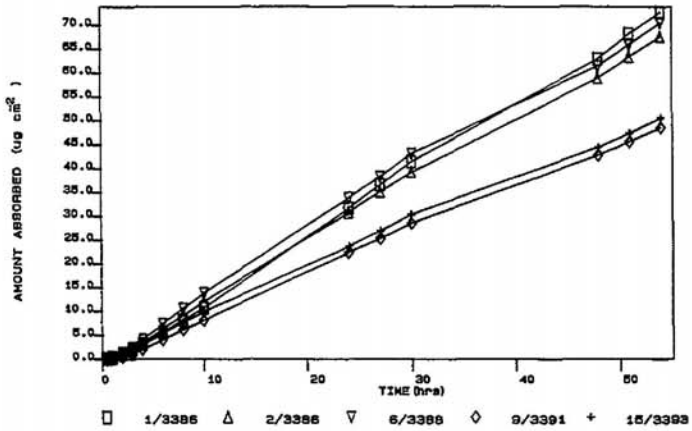
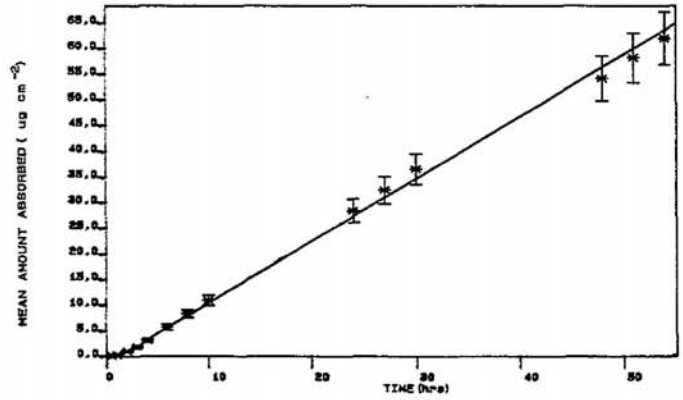
APPENDIX C - ABSORPTION PROFILES FROM THE CONCENTRATE FORMULATION THROUGH HUMAN EPIDERMIS

a) Individual Cell Data (cell no./skin no.)



b) Mean absorption Profile (± SEM n= 5)



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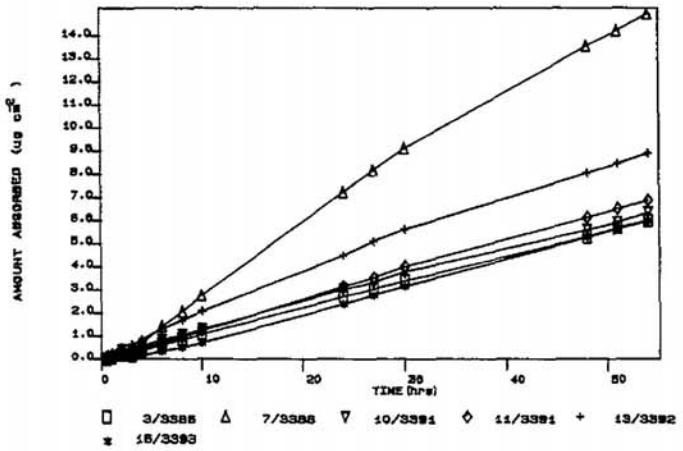
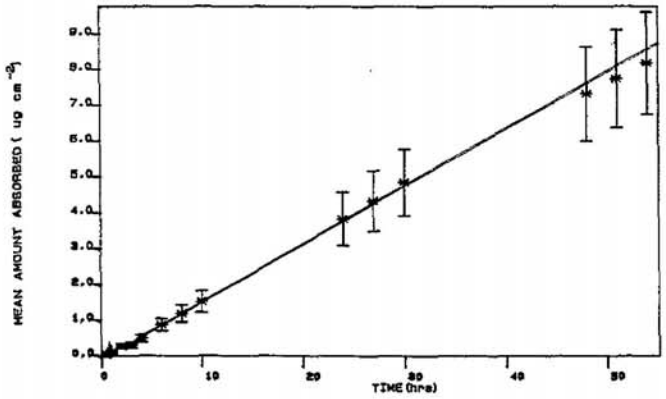
APPENDIX D - ABSORPTION PROFILES FROM THE 0.9:100v/v AQUEOUS SPRAY STRENGTH DILUTION THROUGH HUMAN EPIDERMIS

a) Individual Cell Data (cell no./skin no.)



b) Mean absorption Profile (± SEM; n= 6)



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APPENDIX E - ABSORPTION FROM THE CONCENTRATE FORMULATION

Cell number	Skin ref.	Absorption rate ($\mu g/cm^2/h$)
		0.5-54h
1	3386	1.38
2	3386	1.28
6	3388	1.33
9	3391	0.928
15	3393	0.949
Mean	-	1.17
SD	-	0.216
SEM	-	0.097
n	-	5

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APPENDIX F - ABSORPTION FROM THE 0.9:100v/v AQUEOUS SPRAY STRENGTH DILUTION

Cell number	Skin ref.	Absorption rate (µg/cm²/h)
		0.5-54h
3	3386	0.113
7	3388	0.288
10	3391	0.117
11	3391	0.130
13	3392	0.164
16	3393	0.115
Mean	-	0.155
SD	-	0.068
SEM	-	0.028
n	-	6

ANNEX H: CANCER RISK AND HAZARD QUOTIENT VALUES

Table H-1a. Worker Cancer Risk Results: Preparation of Insecticide for Indoor Residual Spray, ITN Retreatment and Larviciding; without use of PPE

	Inhalation (WP or G)	Dermal (WP or G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
Low-End Exposure Estimates (no PPE)						
DDT	3.2E-07	3.2E-05	8.6E-09	2.1E-05	3E-05	2E-05
Etofenprox	4.8E-10	4.8E-08	1.3E-11	3.2E-08	5E-08	3E-08
Permethrin	NA	NA	NA	NA	NA	NA
Propoxur	3.4E-09	3.5E-07	9.3E-11	2.3E-07	4E-07	2E-07
Mid-Range Exposure Estimates (no PPE)						
DDT	6.3E-07	6.4E-05	1.7E-08	4.2E-05	6E-05	4E-05
Etofenprox	1.6E-09	1.6E-07	4.3E-11	1.1E-07	2E-07	1E-07
Permethrin	NA	NA	NA	NA	NA	NA
Propoxur	8.6E-09	8.7E-07	2.3E-10	5.7E-07	9E-07	6E-07
High-End Exposure Estimates (no PPE)						
DDT	1.3E-06	1.3E-04	3.6E-08	8.8E-05	1E-04	9E-05
Etofenprox	5.9E-09	6.0E-07	1.6E-10	3.9E-07	6E-07	4E-07
Permethrin	NA	NA	NA	NA	NA	NA
Propoxur	2.9E-08	2.9E-06	7.7E-10	1.9E-06	3E-06	2E-06

NA: Pesticide not used for IRS or larviciding.

EC: emulsifiable concentrate. WP: wettable powder. G: granular

Table H-1b. Worker Cancer Risk Results: Preparation of Insecticide for Indoor Residual Spray, ITN Retreatment and Larviciding; with PPE

	Inhalation (WP or G)	Dermal (WP or G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
Low-End Exposure Estimates (with PPE)						
DDT	1.6E-08	6.4E-07	4.3E-10	6.3E-07	7E-07	6E-07
Etofenprox	2.4E-11	9.6E-10	6.4E-13	9.5E-10	1E-09	1E-09
Permethrin	NA	NA	NA	NA	NA	NA

Propoxur	1.7E-10	7.0E-09	4.7E-12	6.9E-09	7E-09	7E-09
Mid-Range Exposure Estimates (with PPE)						
DDT	3.2E-08	1.3E-06	8.6E-10	1.3E-06	1E-06	1E-06
Etofenprox	7.9E-11	3.2E-09	2.1E-12	3.2E-09	3E-09	3E-09
Permethrin	NA	NA	NA	NA	NA	NA
Propoxur	4.3E-10	1.7E-08	1.2E-11	1.7E-08	2E-08	2E-08
High-End Exposure Estimates (with PPE)						
DDT	6.6E-08	2.7E-06	1.8E-09	2.6E-06	3E-06	3E-06
Etofenprox	3.0E-10	1.2E-08	8.0E-12	1.2E-08	1E-08	1E-08
Permethrin	NA	NA	NA	NA	NA	NA
Propoxur	1.4E-09	5.8E-08	3.9E-11	5.7E-08	6E-08	6E-08

NA: Pesticide not used for IRS or larviciding.

EC: emulsifiable concentrate. WP: wettable powder. G: granular

Table H-2a. Worker Subchronic Hazard Quotient Results: Preparation of Insecticide for Indoor Residual Spray, ITN Retreatment and Larviciding; without use of PPE

	Inhalation (WP or G)	Dermal (WP G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
Low-End Exposure Estimates (no PPE)						
IRS Pesticide						
Alpha-cypermethrin	2.2E-06	1.8E-04	5.9E-08	1.2E-04	2E-04	1E-04
Bendiocarb	2.2E-02	2.2E-02	5.9E-04	1.5E-02	4E-02	2E-02
Bifenthrin	1.6E-03	5.5E-03	4.2E-05	3.6E-03	7E-03	4E-03
Chlorfenapyr	NA	NA	NA	NA	NA	NA
Cyfluthrin	4.4E-02	2.9E-04	1.2E-03	1.9E-04	4E-02	1E-03
DDT	8.7E-01	8.8E+01	2.4E-02	5.8E+01	9E+01	6E+01
Deltamethrin	8.7E-04	8.8E-05	2.4E-05	5.8E-05	1E-03	8E-05
Etofenprox	4.4E-04	1.1E-02	1.2E-05	7.3E-03	1E-02	7E-03
Fenitrothion	NA	NA	NA	NA	NA	NA
Lambda-cyhalothrin	1.1E-02	8.8E-03	3.0E-04	5.8E-03	2E-02	6E-03
Malathion	NA	NA	NA	NA	NA	NA
Permethrin	NA	NA	NA	NA	NA	NA
Pirimiphos-methyl	NA	NA	1.7E-02	4.2E+01	NA	4E+01
Propoxur	1.1E-01	4.4E-03	3.0E-03	2.9E-03	1E-01	6E-03
Larvicide						
Methoprene	1.3E-09	6.0E-07	9.5E-10	5.8E-05	6E-07	6E-05

	Inhalation (WP or G)	Dermal (WP G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
Spinosad	5.7E-06	1.0E-04	4.0E-06	9.8E-03	1E-04	1E-02
Temephos	3.1E-05	5.6E-04	2.2E-05	5.4E-02	6E-04	5E-02
Pyriproxyfen	2.4E-08	4.3E-07	1.7E-08	4.2E-05	5E-07	4E-05
Mid-Range Exposure Estimates (no PPE)						
IRS Pesticide						
Alpha-cypermethrin	3.4E-06	2.7E-04	9.1E-08	1.8E-04	3E-04	2E-04
Bendiocarb	6.8E-02	6.8E-02	1.8E-03	4.5E-02	1E-01	5E-02
Bifenthrin	2.9E-03	1.0E-02	7.8E-05	6.8E-03	1E-02	7E-03
Chlorfenapyr	7.2E-02	7.3E+00	2.0E-03	4.8E+00	7E+00	5E+00
Cyfluthrin	9.5E-02	6.4E-04	2.6E-03	4.2E-04	1E-01	3E-03
DDT	1.6E+00	1.6E+02	4.4E-02	1.1E+02	2E+02	1E+02
Deltamethrin	1.2E-03	1.2E-04	3.3E-05	8.1E-05	1E-03	1E-04
Etofenprox	1.1E-03	2.7E-02	2.9E-05	1.8E-02	3E-02	2E-02
Fenitrothion	2.7E+00	1.1E+01	7.3E-02	7.2E+00	1E+01	7E+00
Lambda-cyhalothrin	1.7E-02	1.4E-02	4.6E-04	9.0E-03	3E-02	9E-03
Malathion	1.1E+00	8.6E-02	2.9E-02	5.7E-02	1E+00	9E-02
Permethrin	NA	NA	NA	NA	NA	NA
Pirimiphos-methyl	NA	NA	3.1E-02	7.7E+01	NA	8E+01
Propoxur	2.0E-01	8.2E-03	5.5E-03	5.4E-03	2E-01	1E-02
Larvicide						
Methoprene	2.5E-09	1.1E-06	1.8E-09	1.1E-04	1E-06	1E-04
Spinosad	1.1E-05	2.0E-04	7.9E-06	1.9E-02	2E-04	2E-02
Temephos	5.8E-05	1.0E-03	4.0E-05	1.0E-01	1E-03	1E-01
Pyriproxyfen	4.5E-08	8.0E-07	3.1E-08	7.7E-05	8E-07	8E-05
High-End Exposure Estimates (no PPE)						
IRS Pesticide						
Alpha-cypermethrin	5.2E-06	4.2E-04	1.4E-07	2.8E-04	4E-04	3E-04
Bendiocarb	1.4E-01	1.4E-01	3.7E-03	9.2E-02	3E-01	1E-01
Bifenthrin	4.9E-03	1.7E-02	1.3E-04	1.2E-02	2E-02	1E-02
Chlorfenapyr	NA	NA	NA	NA	NA	NA
Cyfluthrin	1.7E-01	1.2E-03	4.7E-03	7.7E-04	2E-01	5E-03
DDT	2.8E+00	2.8E+02	7.5E-02	1.8E+02	3E+02	2E+02
Deltamethrin	1.7E-03	1.7E-04	4.7E-05	1.2E-04	2E-03	2E-04
Etofenprox	2.1E-03	5.2E-02	5.6E-05	3.5E-02	5E-02	3E-02

	Inhalation (WP or G)	Dermal (WP G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
Fenitrothion	NA	NA	NA	NA	NA	NA
Lambda-cyhalothrin	2.6E-02	2.1E-02	7.0E-04	1.4E-02	5E-02	1E-02
Malathion	NA	NA	NA	NA	NA	NA
Permethrin	NA	NA	NA	NA	NA	NA
Pirimiphos-methyl	NA	NA	5.4E-02	1.3E+02	NA	1E+02
Propoxur	3.5E-01	1.4E-02	9.4E-03	9.2E-03	4E-01	2E-02
Larvicide						
Methoprene	4.3E-09	1.9E-06	3.0E-09	1.8E-04	2E-06	2E-04
Spinosad	2.0E-05	3.5E-04	1.4E-05	3.4E-02	4E-04	3E-02
Temephos	9.8E-05	1.7E-03	6.9E-05	1.7E-01	2E-03	2E-01
Pyriproxyfen	7.6E-08	1.4E-06	5.4E-08	1.3E-04	1E-06	1E-04

NA: Pesticide not used for IRS or larviciding, or (if only 1 or 2 estimates are zero) no exposure estimate is available for that intensity class (low-mid-high)

EC: emulsifiable concentrate. WP: wettable powder. G: granular

Table H-2b. Worker Subchronic Hazard Quotient Results: Preparation of Insecticide for Indoor Residual Spray, ITN Retreatment and Larviciding; with PPE

	Inhalation (WP or G)	Dermal (WP or G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
	Low-End Exposure Estimates (with PPE)					
IRS Pesticide						
Alpha-cypermethrin	1.1E-07	3.5E-06	3.0E-09	3.5E-06	4E-06	3E-06
Bendiocarb	1.1E-03	4.4E-04	3.0E-05	4.4E-04	2E-03	5E-04
Bifenthrin	7.8E-05	1.1E-04	2.1E-06	1.1E-04	2E-04	1E-04
Chlorfenapyr	NA	NA	NA	NA	NA	NA
Cyfluthrin	2.2E-03	5.9E-06	5.9E-05	5.8E-06	2E-03	6E-05
DDT	4.4E-02	1.8E+00	1.2E-03	1.7E+00	2E+00	2E+00
Deltamethrin	4.4E-05	1.8E-06	1.2E-06	1.7E-06	5E-05	3E-06
Etofenprox	2.2E-05	2.2E-04	5.9E-07	2.2E-04	2E-04	2E-04
Fenitrothion	NA	NA	NA	NA	NA	NA
Lambda-cyhalothrin	5.5E-04	1.8E-04	1.5E-05	1.7E-04	7E-04	2E-04
Malathion	NA	NA	NA	NA	NA	NA
Permethrin	NA	NA	NA	NA	NA	NA
Pirimiphos-methyl	NA	NA	8.4E-04	1.2E+00	NA	1E+00
Propoxur	5.5E-03	8.8E-05	1.5E-04	8.7E-05	6E-03	2E-04
Larvicide						

	Inhalation (WP or G)	Dermal (WP or G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
Methoprene	6.7E-11	1.2E-08	4.7E-11	1.7E-06	1E-08	2E-06
Spinosad	2.8E-07	2.0E-06	2.0E-07	2.9E-04	2E-06	3E-04
Temephos	1.6E-06	1.1E-05	1.1E-06	1.6E-03	1E-05	2E-03
Pyriproxyfen	1.2E-09	8.6E-09	8.4E-10	1.2E-06	1E-08	1E-06
Mid-Range Exposure Estimates (with PPE)						
IRS Pesticide						
Alpha-cypermethrin	1.7E-07	5.5E-06	4.6E-09	5.4E-06	6E-06	5E-06
Bendiocarb	3.4E-03	1.4E-03	9.1E-05	1.4E-03	5E-03	1E-03
Bifenthrin	1.4E-04	2.0E-04	3.9E-06	2.0E-04	3E-04	2E-04
Chlorfenapyr	3.6E-03	1.5E-01	9.8E-05	1.4E-01	1E-01	1E-01
Cyfluthrin	4.7E-03	1.3E-05	1.3E-04	1.3E-05	5E-03	1E-04
DDT	8.1E-02	3.3E+00	2.2E-03	3.2E+00	3E+00	3E+00
Deltamethrin	6.1E-05	2.5E-06	1.6E-06	2.4E-06	6E-05	4E-06
Etofenprox	5.4E-05	5.5E-04	1.5E-06	5.4E-04	6E-04	5E-04
Fenitrothion	1.4E-01	2.2E-01	3.7E-03	2.2E-01	4E-01	2E-01
Lambda-cyhalothrin	8.4E-04	2.7E-04	2.3E-05	2.7E-04	1E-03	3E-04
Malathion	5.4E-02	1.7E-03	1.5E-03	1.7E-03	6E-02	3E-03
Permethrin	NA	NA	NA	NA	NA	NA
Pirimiphos-methyl	NA	NA	1.6E-03	2.3E+00	NA	2E+00
Propoxur	1.0E-02	1.6E-04	2.7E-04	1.6E-04	1E-02	4E-04
Larvicide						
Methoprene	1.2E-10	2.2E-08	8.8E-11	3.2E-06	2E-08	3E-06
Spinosad	5.6E-07	4.0E-06	3.9E-07	5.8E-04	5E-06	6E-04
Temephos	2.9E-06	2.1E-05	2.0E-06	3.0E-03	2E-05	3E-03
Pyriproxyfen	2.2E-09	1.6E-08	1.6E-09	2.3E-06	2E-08	2E-06
High-End Exposure Estimates (with PPE)						
IRS Pesticide						
Alpha-cypermethrin	2.6E-07	8.4E-06	7.0E-09	8.3E-06	9E-06	8E-06
Bendiocarb	6.9E-03	2.8E-03	1.9E-04	2.8E-03	1E-02	3E-03
Bifenthrin	2.5E-04	3.5E-04	6.7E-06	3.5E-04	6E-04	4E-04
Chlorfenapyr	NA	NA	NA	NA	NA	NA
Cyfluthrin	8.6E-03	2.3E-05	2.3E-04	2.3E-05	9E-03	3E-04
DDT	1.4E-01	5.6E+00	3.7E-03	5.5E+00	6E+00	6E+00
Deltamethrin	8.6E-05	3.5E-06	2.3E-06	3.5E-06	9E-05	6E-06

	Inhalation (WP or G)	Dermal (WP or G)	Inhalation (EC)	Dermal (EC)	SUM (WP or G)	SUM (EC)
Etofenprox	1.0E-04	1.0E-03	2.8E-06	1.0E-03	1E-03	1E-03
Fenitrothion	NA	NA	NA	NA	NA	NA
Lambda-cyhalothrin	1.3E-03	4.2E-04	3.5E-05	4.2E-04	2E-03	5E-04
Malathion	NA	NA	NA	NA	NA	NA
Permethrin	NA	NA	NA	NA	NA	NA
Pirimiphos-methyl	NA	NA	2.7E-03	4.0E+00	NA	4E+00
Propoxur	1.7E-02	2.8E-04	4.7E-04	2.8E-04	2E-02	7E-04
Larvicide						
Methoprene	2.1E-10	3.8E-08	1.5E-10	5.5E-06	4E-08	6E-06
Spinosad	9.9E-07	7.0E-06	6.9E-07	1.0E-03	8E-06	1E-03
Temephos	4.9E-06	3.5E-05	3.4E-06	5.1E-03	4E-05	5E-03
Pyriproxyfen	3.8E-09	2.7E-08	2.7E-09	4.0E-06	3E-08	4E-06

NA: Pesticide not used for IRS or larviciding, or (if only 1 or 2 estimates are zero) no exposure estimate is available for that intensity class (low-mid-high)

EC: emulsifiable concentrate. WP: wettable powder. G: granular

Table H-3a. Worker Cancer Risk Results: Spray Application for Indoor Residual Spray and Larviciding; without use of PPE

	Inhalation	Dermal	SUM
	Low-End Exposure Estimates (no PPE)		
DDT	2.2E-07	5.6E-04	6E-04
Etofenprox	3.3E-10	8.4E-07	8E-07
Permethrin	NA	NA	NA
Propoxur	2.4E-09	6.1E-06	6E-06
	Mid-Range Exposure Estimates (no PPE)		
DDT	4.4E-07	1.1E-03	1E-03
Etofenprox	1.1E-09	2.8E-06	3E-06
Permethrin	NA	NA	NA
Propoxur	5.9E-09	1.5E-05	2E-05
	High-End Exposure Estimates (no PPE)		
DDT	9.0E-07	2.3E-03	2E-03
Etofenprox	4.1E-09	1.0E-05	1E-05
Permethrin	NA	NA	NA
Propoxur	2.0E-08	5.1E-05	5E-05

NA: Pesticide not used for IRS or larviciding.

Table H-3b. Worker Cancer Risk Results: Spray Application for Indoor Residual Spray and Larviciding; with PPE

	Inhalation	Dermal	SUM
	Low-End Exposure Estimates (with PPE)		
DDT	1.1E-08	1.3E-05	1E-05
Etofenprox	1.6E-11	1.9E-08	2E-08
Permethrin	NA	NA	NA
Propoxur	1.2E-10	1.4E-07	1E-07
	Mid-Range Exposure Estimates (with PPE)		
DDT	2.2E-08	2.6E-05	3E-05
Etofenprox	5.4E-11	6.5E-08	6E-08
Permethrin	NA	NA	NA
Propoxur	3.0E-10	3.5E-07	4E-07
	High-End Exposure Estimates (with PPE)		
DDT	4.5E-08	5.4E-05	5E-05
Etofenprox	2.0E-10	2.4E-07	2E-07
Permethrin	NA	NA	NA
Propoxur	9.8E-10	1.2E-06	1E-06

NA: Pesticide not used for IRS or larviciding.

Table H-4a. Worker Subchronic Hazard Quotient Results: Spray Application for Indoor Residual Spray and Larviciding; without use of PPE

	Inhalation	Dermal	SUM
	Low-End Exposure Estimates (no PPE)		
IRS Pesticide			
Alpha-cypermethrin	1.5E-06	3.1E-03	3E-03
Bendiocarb	1.5E-02	3.9E-01	4E-01
Bifenthrin	1.1E-03	9.7E-02	1E-01
Chlorfenapyr	NA	NA	NA
Cyfluthrin	3.0E-02	5.1E-03	4E-02
DDT	6.0E-01	1.5E+03	2E+03
Deltamethrin	6.0E-04	1.5E-03	2E-03
Etofenprox	3.0E-04	1.9E-01	2E-01
Fenitrothion	NA	NA	NA
Lambda-cyhalothrin	7.5E-03	1.5E-01	2E-01
Malathion	NA	NA	NA

	Inhalation	Dermal	SUM
Permethrin	NA	NA	NA
Pirimiphos-methyl	4.3E-01	8.8E+01	9E+01
Propoxur	7.5E-02	7.7E-02	2E-01
Larvicide			
Methoprene	2.4E-08	1.5E-03	2E-03
Spinosad	1.0E-04	2.6E-01	3E-01
Temephos	5.6E-04	1.4E+00	1E+00
Pyriproxyfen	4.3E-07	1.1E-03	1E-03
	Mid-Range Exposure Estimates (no PPE)		
IRS Pesticide			
Alpha-cypermethrin	2.3E-06	4.8E-03	5E-03
Bendiocarb	4.6E-02	1.2E+00	1E+00
Bifenthrin	2.0E-03	1.8E-01	2E-01
Chlorfenapyr	5.0E-02	1.3E+02	1E+02
Cyfluthrin	6.5E-02	1.1E-02	8E-02
DDT	1.1E+00	2.9E+03	3E+03
Deltamethrin	8.4E-04	2.2E-03	3E-03
Etofenprox	7.4E-04	4.8E-01	5E-01
Fenitrothion	1.9E+00	1.9E+02	2E+02
Lambda-cyhalothrin	1.2E-02	2.4E-01	3E-01
Malathion	7.4E-01	1.5E+00	2E+00
Permethrin	NA	NA	NA
Pirimiphos-methyl	8.0E-01	1.6E+02	2E+02
Propoxur	1.4E-01	1.4E-01	3E-01
Larvicide			
Methoprene	4.5E-08	2.9E-03	3E-03
Spinosad	2.0E-04	5.2E-01	5E-01
Temephos	1.0E-03	2.6E+00	3E+00
Pyriproxyfen	8.0E-07	2.0E-03	2E-03
	High-End Exposure Estimates (no PPE)		
IRS Pesticide			
Alpha-cypermethrin	3.6E-06	7.4E-03	7E-03
Bendiocarb	9.5E-02	2.5E+00	3E+00
Bifenthrin	3.4E-03	3.1E-01	3E-01

	Inhalation	Dermal	SUM
Chlorfenapyr	NA	NA	NA
Cyfluthrin	1.2E-01	2.0E-02	1E-01
DDT	1.9E+00	4.9E+03	5E+03
Deltamethrin	1.2E-03	3.1E-03	4E-03
Etofenprox	1.4E-03	9.2E-01	9E-01
Fenitrothion	NA	NA	NA
Lambda-cyhalothrin	1.8E-02	3.7E-01	4E-01
Malathion	NA	NA	NA
Permethrin	NA	NA	NA
Pirimiphos-methyl	1.4E+00	2.8E+02	3E+02
Propoxur	2.4E-01	2.5E-01	5E-01
Larvicide			
Methoprene	7.6E-08	4.9E-03	5E-03
Spinosad	3.5E-04	9.1E-01	9E-01
Temephos	1.7E-03	4.5E+00	4E+00
Pyriproxyfen	1.4E-06	3.5E-03	4E-03

NA: Pesticide not used for IRS or larviciding, or (if only 1 or 2 estimates are zero) no exposure estimate is available for that intensity class (low-mid-high).

Table H-4b. Worker Subchronic Hazard Quotient Results: Spray Application for Indoor Residual Spray and Larviciding; with PPE

	Inhalation	Dermal	SUM
	Low-End Exposure Estimates (with PPE)		
IRS Pesticide			
Alpha-cypermethrin	7.5E-08	7.1E-05	7E-05
Bendiocarb	7.5E-04	8.9E-03	1E-02
Bifenthrin	5.4E-05	2.2E-03	2E-03
Chlorfenapyr	NA	NA	NA
Cyfluthrin	1.5E-03	1.2E-04	2E-03
DDT	3.0E-02	3.6E+01	4E+01
Deltamethrin	3.0E-05	3.6E-05	7E-05
Etofenprox	1.5E-05	4.4E-03	4E-03
Fenitrothion	NA	NA	NA
Lambda-cyhalothrin	3.7E-04	3.6E-03	4E-03
Malathion	NA	NA	NA

	Inhalation	Dermal	SUM
Permethrin	NA	NA	NA
Pirimiphos-methyl	2.1E-02	2.0E+00	2E+00
Propoxur	3.7E-03	1.8E-03	6E-03
Larvicide			
Methoprene	1.2E-09	3.6E-05	4E-05
Spinosad	5.1E-06	6.0E-03	6E-03
Temephos	2.8E-05	3.3E-02	3E-02
Pyriproxyfen	2.1E-08	2.5E-05	3E-05
	Mid-Range Exposure Estimates (with PPE)		
IRS Pesticide			
Alpha-cypermethrin	1.2E-07	1.1E-04	1E-04
Bendiocarb	2.3E-03	2.7E-02	3E-02
Bifenthrin	9.9E-05	4.1E-03	4E-03
Chlorfenapyr	2.5E-03	2.9E+00	3E+00
Cyfluthrin	3.2E-03	2.6E-04	4E-03
DDT	5.6E-02	6.6E+01	7E+01
Deltamethrin	4.2E-05	4.9E-05	9E-05
Etofenprox	3.7E-05	1.1E-02	1E-02
Fenitrothion	9.3E-02	4.4E+00	4E+00
Lambda-cyhalothrin	5.8E-04	5.5E-03	6E-03
Malathion	3.7E-02	3.5E-02	7E-02
Permethrin	NA	NA	NA
Pirimiphos-methyl	4.0E-02	3.8E+00	4E+00
Propoxur	7.0E-03	3.3E-03	1E-02
Larvicide			
Methoprene	2.2E-09	6.6E-05	7E-05
Spinosad	1.0E-05	1.2E-02	1E-02
Temephos	5.1E-05	6.1E-02	6E-02
Pyriproxyfen	4.0E-08	4.7E-05	5E-05
	High-End Exposure Estimates (with PPE)		
IRS Pesticide			
Alpha-cypermethrin	1.8E-07	1.7E-04	2E-04
Bendiocarb	4.8E-03	5.6E-02	6E-02
Bifenthrin	1.7E-04	7.0E-03	7E-03

	Inhalation	Dermal	SUM
Chlorfenapyr	NA	NA	NA
Cyfluthrin	5.9E-03	4.7E-04	6E-03
DDT	9.5E-02	1.1E+02	1E+02
Deltamethrin	5.9E-05	7.0E-05	1E-04
Etofenprox	7.1E-05	2.1E-02	2E-02
Fenitrothion	NA	NA	NA
Lambda-cyhalothrin	8.9E-04	8.5E-03	9E-03
Malathion	NA	NA	NA
Permethrin	NA	NA	NA
Pirimiphos-methyl	6.8E-02	6.4E+00	6E+00
Propoxur	1.2E-02	5.6E-03	2E-02
Larvicide			
Methoprene	3.8E-09	1.1E-04	1E-04
Spinosad	1.8E-05	2.1E-02	2E-02
Temephos	8.7E-05	1.0E-01	1E-01
Pyriproxyfen	6.8E-08	8.1E-05	8E-05

NA: Pesticide not used for IRS or larviciding, or (if only 1 or 2 estimates are zero) no exposure estimate is available for that intensity class (low-mid-high).

Table H-5. Resident Cancer Risk Results: Domestic Use of Groundwater Contaminated by Pesticide Disposal

	Ingestion	Dermal	SUM
		CTE Estimates	
DDT	1.0E-07	1.8E-06	2E-06
Etofenprox	3.7E-09	7.1E-08	7E-08
Permethrin	NA	NA	NA
Propoxur	6.3E-07	1.2E-08	6E-07
		RME Estimates	
DDT	1.8E-07	2.6E-06	3E-06
Etofenprox	6.5E-09	1.0E-07	1E-07
Permethrin	NA	NA	NA
Propoxur	1.1E-06	1.7E-08	1E-06

NA: Pesticide not used for IRS or larviciding.

Table H-6a. Resident Chronic Hazard Quotient Results: Domestic Use of Groundwater Contaminated by Pesticide Disposal; Child

	Ingestion	Dermal	SUM
		CTE Estimates (child)	
IRS/ITN Pesticide			
Alpha-cypermethrin	3.9E-06	7.2E-08	4E-06
Bendiocarb	1.0E-04	3.5E-06	1E-04
Bifenthrin	1.8E-05	5.4E-06	2E-05
Chlorfenapyr	7.8E-05	8.6E-05	2E-04
Cyfluthrin	2.6E-05	9.6E-07	3E-05
DDT	4.7E-04	1.3E-02	1E-02
Deltamethrin	2.3E-05	2.3E-08	2E-05
Etofenprox	1.5E-05	4.7E-04	5E-04
Fenitrothion	9.6E-04	2.8E-05	1E-03
Lambda-cyhalothrin	4.7E-05	2.4E-05	7E-05
Malathion	2.8E-04	3.3E-05	3E-04
Permethrin	NA	NA	NA
Pirimiphos-methyl	3.2E-03	2.2E-04	3E-03
Propoxur	2.6E-02	4.1E-07	3E-02
Larvicide			
Methoprene	5.8E-07	1.3E-06	2E-06
Spinosad	6.0E-05	2.6E-08	6E-05
Temephos	1.2E-05	2.2E-04	2E-04
Pyriproxyfen	6.7E-07	2.9E-06	4E-06
		RME Estimates (child)	
IRS/ITN Pesticide			
Alpha-cypermethrin	1.2E-05	1.0E-07	1E-05
Bendiocarb	3.0E-04	4.9E-06	3E-04
Bifenthrin	5.4E-05	7.7E-06	6E-05
Chlorfenapyr	2.3E-04	1.2E-04	4E-04
Cyfluthrin	7.7E-05	1.4E-06	8E-05
DDT	1.4E-03	1.9E-02	2E-02
Deltamethrin	7.0E-05	3.3E-08	7E-05
Etofenprox	4.6E-05	6.7E-04	7E-04
Fenitrothion	2.9E-03	4.0E-05	3E-03

	Ingestion	Dermal	SUM
Lambda-cyhalothrin	1.4E-04	3.4E-05	2E-04
Malathion	8.3E-04	4.8E-05	9E-04
Permethrin	NA	NA	NA
Pirimiphos-methyl	9.6E-03	3.2E-04	1E-02
Propoxur	7.9E-02	5.8E-07	8E-02
Larvicide			
Methoprene	1.7E-06	1.9E-06	4E-06
Spinosad	1.8E-04	3.8E-08	2E-04
Temephos	3.5E-05	3.1E-04	3E-04
Pyriproxyfen	2.0E-06	4.2E-06	6E-06

Table H-6b. Resident Chronic Hazard Quotient Results: Domestic Use of Groundwater Contaminated by Pesticide Disposal; Adult

	Ingestion	Dermal	SUM
	CTE Estimates (adult)		
IRS/ITN Pesticide			
Alpha-cypermethrin	5.1E-06	5.5E-08	5E-06
Bendiocarb	1.3E-04	2.7E-06	1E-04
Bifenthrin	2.4E-05	4.2E-06	3E-05
Chlorfenapyr	1.0E-04	6.7E-05	2E-04
Cyfluthrin	3.4E-05	7.4E-07	3E-05
DDT	6.2E-04	1.0E-02	1E-02
Deltamethrin	3.1E-05	1.8E-08	3E-05
Etofenprox	2.0E-05	3.6E-04	4E-04
Fenitrothion	1.3E-03	2.2E-05	1E-03
Lambda-cyhalothrin	6.2E-05	1.8E-05	8E-05
Malathion	3.7E-04	2.6E-06	4E-04
Permethrin	NA	NA	NA
Pirimiphos-methyl	4.2E-03	1.7E-04	4E-03
Propoxur	3.5E-02	3.1E-07	3E-02
Larvicide			
Methoprene	7.7E-07	1.0E-06	2E-06
Spinosad	7.9E-05	2.0E-08	8E-05
Temephos	1.5E-05	1.7E-04	2E-04

	Ingestion	Dermal	SUM
Pyriproxyfen	8.8E-07	2.3E-06	3E-06
		RME Estimates (adult)	
IRS/ITN Pesticide			
Alpha-cypermethrin	8.4E-06	7.9E-08	9E-06
Bendiocarb	2.2E-04	3.8E-06	2E-04
Bifenthrin	3.9E-05	5.9E-06	4E-05
Chlorfenapyr	1.7E-04	9.5E-05	3E-04
Cyfluthrin	5.6E-05	1.1E-06	6E-05
DDT	1.0E-03	1.5E-02	2E-02
Deltamethrin	5.1E-05	2.5E-08	5E-05
Etofenprox	3.3E-05	5.2E-04	6E-04
Fenitrothion	2.1E-03	3.1E-05	2E-03
Lambda-cyhalothrin	1.0E-04	2.6E-05	1E-04
Malathion	6.0E-04	3.7E-06	6E-04
Permethrin	NA	NA	NA
Pirimiphos-methyl	7.0E-03	2.5E-04	7E-03
Propoxur	5.7E-02	4.5E-07	6E-02
Larvicide			
Methoprene	1.3E-06	1.5E-06	3E-06
Spinosad	1.3E-04	2.9E-08	1E-04
Temephos	2.5E-05	2.4E-04	3E-04
Pyriproxyfen	1.4E-06	3.2E-06	5E-06

NA: Pesticide not used for IRS or larviciding.

Table H-7. Resident Cancer Risk Results: Contact with Indoor Residual Spray Pesticide on Walls

	Dermal
DDT	*separate analysis, see text Section 5.2.5.3*
Etofenprox	3E-06
Permethrin	NA
Propoxur	2E-05

Only a single (screening) estimate using mid-range IRS application rate is provided pending refinement of IRS wall loading attenuation factor.

NA: Pesticide not used for IRS.

Table H-8a. Resident Chronic Hazard Quotient Results: Contact with Indoor Residual Spray Pesticide on Walls; Child

	Dermal
Alpha-cypermethrin	2E-05
Bendiocarb	7E-01
Bifenthrin	7E-04
Chlorfenapyr	5E-01
Cyfluthrin	4E-05
DDT	*separate analysis, see text Section 5.2.5.3*
Deltamethrin	8E-06
Etofenprox	2E-02
Fenitrothion	7E-01
Lambda-cyhalothrin	9E-04
Malathion	1E-01
Permethrin	NA
Pirimiphos-methyl	8E+00
Propoxur	6E-04

Only a single (screening) estimate using mid-range IRS application rate is provided pending refinement of IRS wall loading attenuation factor.

NA: Pesticide not used for IRS.

Table H-8b. Resident Chronic Hazard Quotient Results: Contact with Indoor Residual Spray Pesticide on Walls; Adult

	Dermal
Alpha-cypermethrin	1E-05
Bendiocarb	6E-01
Bifenthrin	5E-04
Chlorfenapyr	4E-01
Cyfluthrin	3E-05
DDT	*separate analysis, see text Section 5.2.5.3*
Deltamethrin	6E-06
Etofenprox	2E-02
Fenitrothion	6E-01
Lambda-cyhalothrin	7E-04
Malathion	1E-02
Permethrin	NA
Pirimiphos-methyl	6E+00
Propoxur	4E-04

Only a single (screening) estimate using mid-range IRS application rate is provided pending refinement of IRS wall loading attenuation factor.

NA: Pesticide not used for IRS.

Table H-9. Resident Cancer Risk Results: Washing of Long-Lasting Insecticidal Nets and Retreated ITNs

	Dermal
	CTE Estimates
DDT	NA
Etofenprox	NA
Permethrin	8E-05
Propoxur	NA
	RME Estimates
DDT	NA
Etofenprox	NA
Permethrin	2E-04
Propoxur	NA

Pesticides used in LLINs are indicated by bold font.

NA: Pesticide not used for LLINs.

Table H-10. Resident Acute Hazard Quotient Results: Washing of Long-Lasting Insecticidal Nets and Retreated ITNs

	Dermal
	CTE Estimates
LLIN/ITN Pesticide	
Alpha-cypermethrin	1E-02
Bendiocarb	NA
Bifenthrin	NA
Chlorfenapyr	NA
Cyfluthrin	NA
DDT	NA
Deltamethrin (1)	1E-03
Etofenprox	NA
Fenitrothion	NA
Lambda-cyhalothrin	7E-01
Malathion	NA
Permethrin	3E-01
Pirimiphos-methyl	NA
Propoxur	NA
Larvicide	
Methoprene	NA
Spinosad	NA
Temephos	NA
Pyriproxyfen (2)	NA
	RME Estimates
LLIN Pesticide	
Alpha-cypermethrin	2E-02
Bendiocarb	NA
Bifenthrin	NA
Chlorfenapyr	NA
Cyfluthrin	NA
DDT	NA
Deltamethrin (1)	2E-03
Etofenprox	NA
Fenitrothion	NA
Lambda-cyhalothrin	1E+00
Malathion	NA

	Dermal
Permethrin	5E-01
Pirimiphos-methyl	NA
Propoxur	NA
Larvicide	
Methoprene	NA
Spinosad	NA
Temephos	NA
Pyriproxyfen (2)	NA

(1) RME HQ for piperonyl butoxide synergist in the roof panel of PermaNet 3.0 is 0.012, resulting in a potential RME hazard index of 0.013.

(2) No LLIN product was found that uses pyriproxyfen.

Pesticides used in LLINs are indicated by bold font.

NA: Pesticide not used for LLINs.

ANNEX I: TREATMENT GUIDELINES FOR WHO-RECOMMENDED INSECTICIDES FOR INDOOR RESIDUAL SPRAYING

SECTION 1: SPECIFIC TREATMENT GUIDELINES FOR WHO-RECOMMENDED INSECTICIDES FOR INDOOR RESIDUAL SPRAYING (IRS) FOR MALARIA

Organochlorines

DDT is the only insecticide of this chemical group which is still recommended for indoor residual spraying (IRS). Previously used organochlorines belonged to the cyclodiene sub-class, which included dieldrin and HCH. Dieldrin was abandoned because of its high acute toxicity to humans. Eventually, the whole subgroup became unusable because a mechanism common to all cyclodienes caused the rapid development of resistance.

DDT

DDT is an organochlorine insecticide with low volatility and very low solubility in water, but soluble in fats and organic solvents. DDT is highly persistent, and has a long residual effect on most sprayed surfaces. The long persistence in the environment and its high bioaccumulation in fatty tissues have contributed to the dispersal of DDT residues everywhere (including arctic ice) from its agricultural use in the 1950s and 1960s. This bioaccumulation has resulted in highly toxic effects at the top of food chains, particularly in sharks, eagles, and falcons.

The main danger of environmental contamination from using DDT as an indoor residual spray comes from diverting the insecticide from malaria control to agricultural use. A similar danger would occur if containers were inadequately disposed of or pumps indiscriminately washed in surface waters. These risks could be prevented by proper education and strict supervision.

Toxicology

Absorption route: Absorbed from the gastrointestinal tract and by inhalation. DDT in oily solution may also be absorbed through intact skin. This is not applicable to the WP formulations used for malaria control.

Mode of action: DDT is a central nervous system stimulant that produces hyperactivity and tremor; convulsions may occur but are less common than with other organochlorine insecticides.

Symptoms of poisoning

Acute poisoning by DDT is very rare, particularly when used for indoor residual spraying. Nevertheless, it could potentially occur if there is gross mishandling. Early symptoms may include paresthesia (tingling) of the tongue, lips and parts of the face, which in severe cases extends to the extremities. The patient may have a sense of apprehension and disturbance of equilibrium, dizziness, confusion, and a characteristic tremor.

Emergency Treatment

Remove contaminated clothing and wash the affected skin with clean water and soap, and flush the affected area with large quantities of clean water. Keep the patient calm and in quiet, shaded conditions and seek medical assistance. Do not give the patient oils and fats.

Treatment by Medical Professional

1. **Observation**. Persons exposed to high levels of organochlorine pesticides by any route should be observed for sensory disturbances, incoordination, speech slurring, mental aberrations, and involuntary motor activity that would warn of imminent convulsions.

2. **Convulsions**. If convulsions occur, place the victim in the left lateral decubitus position with the head down. Move away furniture or other solid objects that could be a source of injury. If jaw movements are violent, place padded tongue blades between the teeth to protect the tongue. Whenever possible, remove dentures and other removable dental work. Aspirate oral and pharyngeal secretion, and when possible, insert an oropharyngeal airway to maintain an open passage unobstructed by the tongue. Minimize noise and any manipulation of the patient that may trigger seizure activity.

Dosage of Diazepam:

- *Adults*: 5-10 mg IV and repeat every 5-10 minutes to maximum of 30 mg.
- *Children*: 0.2 to 0.5 mg/kg every 5 minutes to maximum of 10 mg in children over 5 years, and maximum of 5 mg in children under 5 years.

Although lorazepam is widely accepted as a treatment of choice for status epilepticus, there are no reports of its use for organochlorine intoxication. Some cases have required aggressive management that included the addition of phenobarbital or barbiturate–induced coma

Seizures in patients caused by organochlorine toxicity are likely to be prolonged and difficult to control. Status epilepticus is common. For this reason, patients with seizures that do not respond immediately to anticonvulsants should be transferred as soon as possible to a trauma center and will generally require intensive care admission until seizures are controlled and neurologic status is improved. Initial therapy with benzodiazepines should be instituted.

3. **Oxygen.** Administer oxygen by mask. Maintain pulmonary gas exchange by mechanically assisted ventilation whenever respiration is depressed.

4. **Skin decontamination.** Thoroughly decontaminate the skin.

5. **Gastrointestinal decontamination.** If organochlorine has been ingested in a quantity sufficient to cause poisoning and the patient presents within an hour, consider gastric decontamination procedures. If the patient presents more than an hour after ingestion, activated charcoal may still be beneficial. If the victim is convulsing, it is almost always

necessary first to control seizures before attempting gastric decontamination. Activated charcoal administration has been advocated in such poisonings, but there is little human or experimental evidence to support it.

6. **Respiratory failure.** Particularly in poisonings by large doses of organochlorine, **monitor pulmonary ventilation** carefully to forestall respiratory failure. Assist pulmonary ventilation mechanically with oxygen whenever respiration is depressed. Since these compounds are often formulated in a hydrocarbon vehicle, hydrocarbon aspiration may occur with ingestion of these agents. The hydrocarbon aspiration should be managed in accordance with accepted medical practice as a case of acute respiratory distress syndrome, which will usually require intensive care management.

7. **Cardiac monitoring.** In severely poisoned patients, monitor cardiac status by continuous ECG recording to detect arrhythmia.

8. **Contraindications.** Do not give epinephrine, other adrenergic amines, or atropine unless absolutely necessary because of the enhanced myocardial irritability induced by chlorinated hydrocarbons, which predisposes to ventricular fibrillation. Do not give animal or vegetable oils or fats by mouth. They enhance gastrointestinal absorption of the lipophilic organochlorines.

9. **Phenobarbital.** To control seizures and myoclonic movements that sometimes persist for several days following acute poisoning by the more slowly excreted organochlorines, phenobarbital given orally is likely to be effective. Dosage should be based on manifestations in the individual case and on information contained in the package insert.

10. **Cholestryamine resin** accelerates the biliary-fecal excretion of the more slowly eliminated organochlorine compounds. It is usually administered in 4 g doses, 4 times a day, before meals and at bedtime. The usual dose for children is 240 mg/kg/24 hours, divided Q 8 hours. The dose may be mixed with a pulpy fruit or liquid. It should never be given in its dry form and must always be administered with water, other liquids, or a pulpy fruit. Prolonged treatment (several weeks or months) may be necessary.

11. **Convalescence.** During convalescence, enhance carbohydrate, protein, and vitamin intake by diet or parenteral therapy.

Organophosphates

Organophosphates, although rapidly metabolized and eliminated, produce prolonged inhibition of acetylcholinesterase, therefore disturbing the transmission of nerve impulses at the synapses. Organophosphates may thus produce a cumulative effect after repeated exposure, with recovery requiring the production of fresh acetylcholinesterase.

Toxicology

This family includes some extremely toxic insecticides, such as parathion. The insecticides recommended for indoor residual spraying have very low (malathion and pirimiphos-methyl) or moderate toxicity (fenitrothion). Specific data on LD_{50} is presented below for each insecticide. Periodical or daily determination of cholinesterase activity in spraymen and other insecticide handlers is recommended when spraying organophosphates. Specific toxicology of the three approved organophosphates follows.

Malathion

Malathion is an organophosphate insecticide. The pure insecticidal compound (technical grade) of malathion is a liquid with relatively low vapor pressure, moderate water solubility, and relatively low toxicity.

Toxicology

Absorption route: Malathion may be absorbed by inhalation, from the gastrointestinal tract, or through the intact skin. Malathion has low mammal toxicity and a very good safety record, having been safely used with light protective clothing, including overalls and hats. Nevertheless, when stored at high temperature, an inadequately formulated product once produced a very toxic isomer—iso-malathion. Testing for iso-malathion and for its possible production under storage conditions is now part of the WHO specifications.

Mode of action: Malathion is an indirect cholinesterase inhibitor, after metabolism to malaoxon (its oxygen analogue).

Fenitrothion

Fenitrothion is an organophosphate insecticide. It has been used extensively as an indoor residual spray for malaria control since the 1970s. It is the most toxic to man of the insecticides approved for residual house spraying, and has a relatively low margin of safety.

Toxicology

Absorption route: Absorbed through the gastrointestinal tract as well as through intact skin and by inhalation.

Mode of action: A cholinesterase inhibitor.

Pirimiphos-methyl

Toxicology

Absorption route: Pirimiphos-methyl may be absorbed from the gastrointestinal tract, through the intact skin and less commonly, by inhaling fog, smoke, or spray mist.

Mode of action: A cholinesterase inhibitor. The degradation products desethyl pirimiphos-methyl and pirimiphos-methyloxon are also active but of transient stability, and have not figured significantly in mammalian studies.

Symptoms of poisoning

Early symptoms of poisoning may include excessive sweating, headache, weakness, giddiness, nausea, vomiting, stomach pains, blurred vision, constricted pupils, slurred speech, and muscle twitching. Later there may be convulsions, coma, loss of reflexes, and loss of sphincter control.

Emergency Treatment

Organophosphate poisoning is a medical emergency and requires immediate treatment. All supervisors and individual spraymen (in the case of dispersed operations) should be trained in first-aid and emergency treatment of organophosphate intoxication.

The affected person should stop work immediately, remove any contaminated clothing, wash the affected skin with soap and clean water and flush the skin with large quantities of clean water. Care must be taken not to contaminate others, including medical or paramedical workers.

Automatic injectors loaded with atropine sulfate and obidoxime chloride can be made available in the field whenever relatively toxic organophosphate insecticides are used in areas without easy access to medical care. Once given the emergency treatment, the patient should be rapidly referred to a hospital for full treatment.

Treatment by Medical Professional

Caution: Persons attending the victim should avoid direct contact with heavily contaminated clothing and vomitus. Wear rubber gloves while washing pesticide from skin and hair. Vinyl gloves provide no protection.

1. **Airway protection**. Ensure that a clear airway exists. Intubate the patient and aspirate the secretions with a large-bore suction device if necessary. Administer oxygen by mechanically assisted pulmonary ventilation if respiration is depressed. Improve tissue oxygenation as much as possible before administering atropine, so as to minimize the risk of ventricular fibrillation. In severe poisonings, it may be necessary to support pulmonary ventilation mechanically for several days.

2. **Atropine sulfate**. Administer atropine sulfate intravenously or intramuscularly if intravenous injection is not possible. Remember that atropine can be administered through an endotracheal tube if initial IV access is difficult to obtain. Depending on the severity of poisoning, doses of atropine ranging from very low to as high as 300 mg per day may be required, or even a continuous infusion.

The objective of atropine antidotal therapy is to antagonize the effects of excessive concentrations of acetylcholine at end-organs having muscarinic receptors. Atropine does not reactivate the cholinesterase enzyme or accelerate disposition of organophosphate. Recrudescence of poisoning may occur if tissue concentrations of organophosphate remain high when the effect of atropine wears off. Atropine is effective against muscarinic manifestations, but it is ineffective against nicotinic actions, specifically muscle weakness and twitching, and respiratory depression.

Despite these limitations, atropine is often a life-saving agent in organophosphate poisonings. Favorable response to a test dose of atropine (1 mg in adults, 0.01 mg/kg in children under 12 years) can help differentiate poisoning by anticholinesterase agents from other conditions. However, lack of response, with no evidence of atropinization (atropine refractoriness) is typical of more severe poisonings. The adjunctive use of nebulized atropine has been reported to improve respiratory distress, decrease bronchial secretions, and increase oxygenation.

3. **Glycopyrolate** has been studied as an alternative to atropine and found to have similar outcomes using continuous infusion. Ampules of 7.5 mg of glycopyrolate were added to 200 mL of saline and this infusion was titrated to the desired effects of dry mucous membranes and heart rate above 60 beats/min. During this study, atropine was used as a bolus for a heart rate less than 60 beats/min. The other apparent advantage to this regimen was a decreased number of respiratory infections. This may represent an alternative when there is a concern for respiratory infection due to excessive and difficult-to-control secretions, and in the presence of an altered level of consciousness where the distinction between atropine toxicity or relapse of organophosphate poisoning is unclear.

4. **Pralidoxime**. Before administering pralidoxime, draw a blood sample (heparinized) for cholinesterase analysis (since pralidoxime tends to reverse the cholinesterase depression).

Administer pralidoxime (Protopam, 2-PAM, a cholinesterase reactivator) in cases of severe poisoning by organophosphate pesticides in which respiratory depression, muscle weakness, and/or twitching are severe. When administered early (usually less than 48 hours after poisoning), pralidoxime relieves the nicotinic as well as the muscarinic effects of poisoning. Pralidoxime works by reactivating the cholinesterase and also by slowing the "aging" process of phosphorylated cholinesterase to a non-reactivatable form.

Note: Pralidoxime is of limited value and may actually be hazardous in poisonings caused by the cholinesterase-inhibiting carbamate compounds.

Dosage of Atropine:

In ***moderately severe poisoning*** (hypersecretion and other end-organ manifestations without central nervous system depression), the following dosage schedules have been used:

• *Adults and children over 12 years:* 2.0 4.0 mg, repeated every 15 minutes until pulmonary secretions are controlled, which may be accompanied by other signs of atropinization, including flushing, dry mouth, dilated pupils, and tachycardia (pulse of 140 per minute). **Warning:** In cases of ingestion of liquid concentrates of organophosphate pesticides, hydrocarbon aspiration may complicate these poisonings. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as a case of acute respiratory distress syndrome.

•*Children under 12 years:* 0.05-0.1 mg/kg body weight, repeated every 15 minutes until atropinization is achieved. There is a minimum dose of 0.1 mg in children. Maintain atropinization by repeated doses based on recurrence of symptoms for 2-12 hours or longer, depending on severity of poisoning. Maintain atropinization with repeated dosing as indicated by clinical status. Crackles in the lung bases nearly always indicate inadequate atropinization. Pulmonary improvement may not parallel other signs of atropinization. Continuation of, or return of, cholinergic signs indicates the need for more atropine. When symptoms are stable for as much as six hours, the dosing may be decreased.

Severely poisoned individuals may exhibit remarkable tolerance to atropine; two or more times the dosages suggested above may be needed. The dose of atropine may be increased and the dosing interval decreased as needed to control symptoms. Continuous intravenous infusion of atropine may be necessary when atropine requirements are massive. **The desired end-point is the reversal of muscarinic symptoms and signs with improvement in pulmonary status and oxygenation,** without an arbitrary dose limit. Preservative-free atropine products should be used whenever possible.

Note: Persons not poisoned or only slightly poisoned by organophosphates may develop signs of atropine toxicity from such large doses. Fever, muscle fibrillations, and delirium are the main signs of atropine toxicity. If these appear while the patient is fully atropinized, atropine administration should be discontinued, at least temporarily, while the severity of poisoning is reevaluated.

Dosage of Pralidoxime:

- *Adults and children over 12 years:* 1.0-2.0 g by intravenous infusion at a rate of no more than 0.2 g per minute. Slow administration of pralidoxime is strongly recommended and may be achieved by administering the total dose in 100 mL of normal saline over 30 minutes, or longer.
- *Children under 12 years:* 20-50 mg/kg body weight (depending on severity of poisoning) intravenously, mixed in 100 mL of normal saline and infused over 30 minutes.

Dosage of pralidoxime may be repeated in 1-2 hours, then at 10-12 hour intervals if needed. In very severe poisonings, dosage rates may be doubled. Repeated doses of pralidoxime are usually required. In cases that involve continuing absorption of organophosphate (as after ingestion of large amount), or continuing transfer of highly lipophilic organophosphate from fat into blood, it may be necessary to continue administration of pralidoxime for several days beyond the 48 hour post-exposure interval usually cited as the limit of its effectiveness. Pralidoxime may also be given as a continuous infusion of approximately 500 mg/hour, based on animal case studies and adult patient reports.

Monitor blood pressure during administration because of the occasional occurrence of hypertensive crisis. Slow or stop administration if blood pressure rises to hazardous levels. Be prepared to assist pulmonary ventilation mechanically if respiration is depressed during or after pralidoxime administration. If intravenous injection is not possible, pralidoxime may be given by deep intramuscular injection.

5. **Skin decontamination**. In patients who have been poisoned by organophosphate contamination of skin, clothing, hair, and/or eyes, decontamination must proceed concurrently with whatever resuscitative and antidotal measures are necessary to preserve life. Flush the chemical from the eyes with copious amounts of clean water. If no symptoms are evident in a patient who remains alert and physically stable, a prompt shower and shampoo may be appropriate, provided the patient is carefully observed to insure against any sudden appearance of poisoning. If there are any indications of weakness, ataxia, or other neurologic impairment, remove the victim's clothing, have the victim lie down, and give the victim a complete bath and shampoo using copious amounts of soap and water. Surgical green soap is excellent for this purpose, but ordinary soap is about as good. Wash the chemical from skin folds and from under fingernails. Contaminated clothing should be promptly removed, bagged, and laundered before returning. Contaminated leather shoes should be discarded. Note that the pesticide can contaminate the inside surfaces of gloves, boots, and headgear. Attendants should wear rubber gloves, because vinyl provides no protection against skin absorption.

6. **Gastrointestinal decontamination**. If organophosphate has been ingested in quantity probably sufficient to cause poisoning, consider giving gastrointestinal (GI) decontamination. If the patient has already vomited, which is most likely in serious exposures, further efforts at GI decontamination may not be indicated. In significant ingestions, diarrhea and/or vomiting are so constant that charcoal adsorption and catharsis are not indicated.

7. **Observation**. Observe the patient closely for at least 72 hours to ensure that symptoms (sweating, visual disturbances, vomiting, diarrhea, chest and abdominal distress, and

sometimes pulmonary edema) do not recur as atropinization is withdrawn. In very severe poisonings by ingested organophosphates, particularly the more lipophilic and slowly hydrolyzed compounds, metabolic disposition of toxicant may require as many as 5-14 days. In some cases, this slow elimination may combine with profound cholinesterase inhibition to require atropinization for several days or even weeks. As dosage is reduced, the lung bases should be checked frequently for crackles. If crackles are heard, or if there is a return of miosis, bradycardia, sweating, or other cholinergic signs, atropinization must be re-established promptly.

8. **Furosemide** may be considered if pulmonary edema persists in the lungs even after full atropinization. It should not be used until the maximum benefit of atropine has been realized. Consult package insert for dosage and administration.

9. **Pulmonary ventilation**. Monitor pulmonary ventilation carefully to forestall respiratory failure even after the patient recovers from muscarinic symptomatology, particularly in poisonings by large ingested doses of organophosphate. In some cases, respiratory failure has developed several days following organophosphate ingestion, and has persisted for days to weeks.

10. **Hydrocarbon aspiration** may complicate poisonings that involve ingestion of liquid concentrates of organophosphate pesticides. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as a case of acute respiratory distress syndrome.

11. **Cardiopulmonary monitoring**. In severely poisoned patients, monitor cardiac status by continuous ECG recording. Some organophosphates have significant cardiac toxicity.

12. **Seizure control**. Though rare, convulsions occur despite therapy with atropine and pralidoxime in severe organophosphate poisonings. Make sure that causes unrelated to pesticide toxicity are not responsible, including head trauma, cerebral anoxia, or mixed poisoning. The benzodiazepines (diazepam or lorazepam) are the agents of choice as initial therapy to control convulsions.

13. **Contraindications**. The following drugs are contraindicated in nearly all organophosphate poisoning cases: morphine, succinylcholine, theophylline, phenothiazines, and reserpine. Adrenergic amines should be given only if there is a specific indication, such as marked hypotension.

14. **Re-exposures**. Persons who have been clinically poisoned by organophosphate pesticides should not be re-exposed to cholinesterase-inhibiting chemicals until symptoms and signs have resolved completely and blood cholinesterase activities have returned to at least 80 percent of pre-poisoning levels. If blood cholinesterase was not measured prior to poisoning, blood enzyme activities should reach at least minimum normal levels before the patient is returned to a pesticide-contaminated environment.

15. **Prophylaxis.** Do not administer atropine or pralidoxime prophylactically to workers exposed to organophosphate pesticides. Prophylactic dosage with either atropine or pralidoxime may mask early signs and symptoms of organophosphate poisoning and thus allow the worker to continue exposure and possibly progress to more severe poisoning. Atropine itself may increase the health hazards of an agricultural work setting by causing impaired heat loss due to reduced sweating and impaired ability to operate mechanical equipment due to blurred vision (mydriasis).

Carbamates

Carbamates are fast-acting anticholinesterase (AchE) compounds, with relatively high acute oral toxicity.

Toxicology

The inhibition of AchE induced by carbamates is relatively labile. As a result, although symptoms may occur during operational exposure, the patient recovers normally follows once exposure stops. Specific toxicology information on the approved carbamates is as follows:

Bendiocarb

Bendiocarb is a carbamate insecticide with low vapor pressure, low odor and no corrosive and staining properties. This makes it acceptable to most householders. It is rapidly hydrolyzesd in alkaline media (such as whitewash) and rapidly degraded in soil. Like other N-methylcarbamates, bendiocarb is a fast-acting anticholinesterase compound, with high acute oral toxicity.

Toxicology

Bendiocarb may be absorbed from the gastrointestinal tract or, to a limited extent, through intact skin. It is mainly metabolized through hydrolysis and excreted rapidly; there is no accumulation in organs and tissues. Its low vapor pressure makes inhalation unlikely except from airborne spray mist.

Mode of action: Bendiocarb inhibits cholinesterase activity, which is rapidly reversible. The half-life of the inhibited enzyme is approximately 30 minutes.

Propoxur

Toxicology

Absorption route: Propoxur can be absorbed by inhalation, from the gastrointestinal tract and, to a lesser extent, through intact skin. The compound is rapidly metabolized and does not accumulate in tissues.

Mode of action: Inhibition of cholinesterase, which is relatively rapidly reversible.

Symptoms of poisoning

Symptoms of mild carbamate poisoning are similar to those of organophosphate poisoning. They include excessive sweating, headache, nausea, blurred vision, chest pain, vomiting, excessive salivation, and slurred speech. Severe intoxication causes narrowed pupils, muscle twitching, spasms, intestinal convulsions, diarrhea, and labored respiration. These symptoms rapidly subside when spraying is stopped and heavily contaminated clothes are removed, particularly if some atropine is given to the patient.

Emergency Treatment

The affected person should stop work immediately, remove any contaminated clothing and wash the affected skin with soap and clean water. The whole contaminated area (including the eyes, if necessary) should be flushed with large quantities of clean water. The patient should be kept at rest and immediate medical aid obtained (show medical personnel the product label).

The patient can be treated by atropine, but it is often no longer necessary by the time the patient reaches the place where atropine is available. Oximes are contraindicated for the treatment of

carbamate poisoning. Morphine should not be used, but diazepam may be useful for convulsions.

Treatment by Medical Professional

Caution: Persons attending the victim should avoid direct contact with heavily contaminated clothing and vomitus. Wear rubber gloves while washing pesticide from skin and hair. Vinyl gloves provide no protection.

1. **Airway protection**. Ensure that a clear airway exists. Intubate the patient and aspirate the secretions with a large-bore suction device if necessary. Administer oxygen by mechanically assisted pulmonary ventilation if respiration is depressed. Improve tissue oxygenation as much as possible before administering atropine to minimize the risk of ventricular fibrillation. In severe poisonings, it may be necessary to support pulmonary ventilation mechanically for several days.

2. **Atropine**. Administer atropine sulfate intravenously or intramuscularly if intravenous injection is not possible. Remember that atropine can be administered through an endotracheal tube if initial IV access is difficult to obtain. Carbamates usually reverse with much smaller dosages of atropine than those required to reverse organophosphates. (See dosage on next page.)

   The objective of atropine antidotal therapy is to antagonize the effects of excessive concentrations of acetylcholine at end-organs having muscarinic receptors. Atropine does not reactivate the cholinesterase enzyme or accelerate excretion or breakdown of carbamate. Recrudescence of poisoning may occur if tissue concentrations of toxicant remain high when the effect of atropine wears off. Atropine is effective against muscarinic manifestations, but is ineffective against nicotinic actions, specifically, muscle weakness and twitching, and respiratory depression.

   Despite these limitations, atropine is often a life-saving agent in N-methyl carbamate poisonings. Favorable response to a test dose of atropine (1 mg in adults, 0.01 mg/kg in children under 12 years) given intravenously can help differentiate poisoning by anticholinesterase agents from other conditions such as cardiogenic pulmonary edema and hydrocarbon ingestion. However, lack of response to the test dose, indicating no atropinization (atropine refractoriness), is characteristic of moderately severe to severe poisoning and indicates a need for further atropine. If the test dose does not result in mydriasis and drying of secretions, the patient can be considered atropine refractory.

3. **Skin decontamination**. In patients with contaminated skin, clothing, hair, and/or eyes, decontamination must proceed concurrently with whatever resuscitative and antidotal measures are needed to preserve life. Flush the chemical from eyes with copious amounts of clean water. For asymptomatic individuals who are alert and physically able, a prompt shower and shampoo may be appropriate for thorough skin decontamination, provided the patient is carefully observed to insure against sudden appearance of poisoning. If there are any indications of weakness, ataxia, or other neurologic impairment, remove the victim's clothing, have the victim lie down, and give the victim a complete bath and shampoo using copious amounts of soap and water. Wash the chemical from skin folds and from under fingernails. Attendants should wear rubber gloves, as vinyl provides no protection against skin absorption.

Contaminated clothing should be promptly removed, bagged, and laundered before returning. Contaminated leather shoes should be discarded. Note that the pesticide can contaminate the inside surfaces of gloves, boots, and headgear.

Dosage of Atropine:

In ***moderately severe poisoning*** (hypersecretion and other end-organ manifestations without central nervous system depression), the following dosage schedules have proven effective:

- *Adults and children over 12 years:* 2.0-4.0 mg, repeated every 15 minutes until pulmonary secretions are controlled, which may be accompanied by other signs of atropinization, including flushing, dry mouth, dilated pupils, and tachycardia (pulse of 140 per minute). **Warning:** In cases of ingestion of liquid concentrates of carbamate pesticides, hydrocarbon aspiration may complicate these poisonings. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as a case of acute respiratory distress syndrome.
- *Children under 12 years:* 0.05-0.1 mg/kg body weight, repeated every 15 minutes until pulmonary secretions are controlled, which may be accompanied by other signs of atropinization as above (heart rates vary depending on age of child with young toddlers having a rate approaching 200). There is a minimum dose of 0.1 mg in children.

Maintain atropinization by repeated doses based on recurrence of symptoms for 2-12 hours or longer depending on severity of poisoning. Crackles in the lung bases nearly always indicate inadequate atropinization and pulmonary improvement may not parallel other signs. Continuation or return of cholinergic signs indicates the need for more atropine.

Severely poisoned individuals may exhibit remarkable tolerance to atropine; two or more times the dosages suggested above may be needed. Reversal of muscarinic manifestations, rather than a specific dosage, is the object of atropine therapy. However, prolonged intensive intravenous administration of atropine sometimes required in organophosphate poisonings is rarely needed in treating carbamate poisoning.

Note: Persons not poisoned or only slightly poisoned by N-methyl carbamates may develop signs of atropine toxicity from such large doses. Fever, muscle fibrillations, and delirium are the main signs of atropine toxicity. If these signs appear while the patient is fully atropinized, atropine administration should be discontinued, at least temporarily, while the severity of poisoning is reevaluated.

4. **Gastrointestinal decontamination**. If N-methyl carbamate has been ingested in a quantity probably sufficient to cause poisoning, consider giving gastrointestinal decontamination as outlined in Chapter 2. If the patient has presented with a recent ingestion and is still asymptomatic, adsorption of poison with activated charcoal may be beneficial. In significant ingestions, diarrhea and/or vomiting are so constant that charcoal adsorption and catharsis are not indicated. Attention should be given to oxygen, airway management, and atropine.

5. **Urine sample**. Save a urine sample for metabolite analysis if there is need to identify the agent responsible for the poisoning.

6. **Pralidoxime** is probably of little value in N-methyl carbamate poisonings because atropine alone is effective. Although not indicated in isolated carbamate poisoning, pralidoxime appears to be useful in cases of mixed carbamate/organophosphate poisonings and cases of an unknown pesticide that present with muscarinic symptoms.

7. **Observation**. Observe patient closely for at least 24 hours to ensure that symptoms (sweating, visual disturbances, vomiting, diarrhea, chest and abdominal distress, and sometimes pulmonary edema) do not recur as atropinization is withdrawn. The observation period should be longer in the case of mixed pesticide ingestion, because of the prolonged and delayed symptoms associated with organophosphate poisoning. As the dosage of atropine is reduced over time, check the lung bases frequently for crackles. Atropinization must be re-established promptly, if crackles are heard, or if there is a return of miosis, sweating, or other signs of poisoning.

8. **Furosemide** may be considered for relief of pulmonary edema if crackles persist in the lungs even after full atropinization. Furosemide should not be considered until the maximum effect of atropine has been achieved. Consult package insert for dosage and administration.

9. **Pulmonary ventilation**. Particularly in poisonings by large doses of N-methyl carbamates, monitor pulmonary ventilation carefully to forestall respiratory failure, even after the patient recovers from muscarinic symptomatology.

10. **Cardiopulmonary monitoring**. In severely poisoned patients, monitor cardiac status by continuous ECG recording.

11. **Contraindications**. The following drugs are probably contraindicated in nearly all N-methyl carbamate poisoning cases: morphine, succinlycholine, theophylline, phenothiazines, and reserpine. Adrenergic amines should be given only if there is a specific indication, such as marked hypotension.

12. **Hydrocarbon** aspiration may complicate poisonings that involve ingestion of liquid concentrates of some carbamates formulated in a petroleum product base. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as cases of acute respiratory distress syndrome.

13. **Prophylaxis**. Do not administer atropine prophylactically to workers exposed to N-methyl carbamate pesticides. Prophylactic dosage may mask early symptoms and signs of carbamate poisoning and thus allow the worker to continue exposure and possibly progress to more severe poisoning. Atropine itself may increase the health hazards of the agricultural work setting, including impaired heat loss due to reduced sweating and impaired ability to operate mechanical equipment due to blurred vision (mydriasis).

Pyrethroids

These modern synthetic insecticides are similar chemically to natural pyrethrins, but modified to increase stability in the natural environment. They are now widely used in agriculture, in homes and gardens, and to treat ectoparasitic disease.

Pyrethroids are formulated as emulsifiable concentrates, wettable powders, granules, and concentrates for ultra low volume application. They may be combined with additional pesticides (sometimes highly toxic) in the technical product or tank-mixed with other pesticides at the time of application.

Toxicology

Certain pyrethroids exhibit striking neurotoxicity in laboratory animals when administered by intravenous injection, and some are toxic when ingested orally. However, systemic toxicity by inhalation and dermal absorption is low. Although limited absorption may account for the low toxicity of some pyrethroids, rapid biodegradation by mammalian liver enzymes (ester hydrolysis and oxidation) is probably the major factor responsible for this phenomenon. Most pyrethroid metabolites are promptly excreted (at least in part) by the kidney. Fatalities have occurred rarely after pyrethroid exposure, usually following ingestion (He et al., 1989).

The most severe toxicity is to the central nervous system, although more uncommon. Seizures have been reported in severe cases of pyrethroid intoxication. Seizures are more common with exposure to the more toxic cyano-pyrethroids, which include fenvalerate, flucythrinate, cypermethrin, deltapermethrin, and fluvalinate. There are no reports in the literature of seizures in humans from exposure to permethrin.

Apart from central nervous system toxicity, some pyrethroids do cause distressing paresthesia when liquid or volatilized materials contact human skin. Again, these symptoms are more common with exposure to the pyrethroids whose structures include cyano-groups. Sensations are described as stinging, burning, itching, and tingling, progressing to numbness. The skin of the face seems to be most commonly affected, but the hands, forearms, and neck are sometimes involved. Sweating, exposure to sun or heat, and applying water increase the disagreeable sensations. Sometimes the effect is noted within minutes of exposure, but a 1-2 hour delay in the appearance of symptoms is more common. Sensations rarely persist more than 24 hours. Little or no inflammatory reaction is apparent where the paresthesia is reported; the effect is presumed to result from pyrethroid contact with sensory nerve endings in the skin. The paraesthesia is not allergic in nature, although sensitization and allergic responses have been reported as an independent phenomenon with pyrethroid exposure. Race, skin type, or disposition to allergic disease does not affect the likelihood or severity of the reaction.

Persons treated with permethrin for lice or flea infestations sometimes experience itching and burning at the site of application, but this is chiefly an exacerbation of sensations caused by the parasites themselves, and is not typical of the paraesthesia described above.

Other signs and symptoms of toxicity include abnormal facial sensations, dizziness, salivation, headache, fatigue, vomiting, diarrhea, and irritability to sound and touch. In more severe cases, pulmonary edema and muscle fasciculations can develop. Due to the inclusion of unique solvent ingredients, certain formulations of fluvalinate are corrosive to the eyes. Pyrethroids are not cholinesterase inhibitors. However, there have been some cases in which pyrethroid poisoning has been misdiagnosed as organophosphate poisoning, due to some of the similar presenting signs, and some patients have died from atropine toxicity.

Specific toxicology for the 5 recommended pyrethroids is described below.

Alpha-cypermethrin

Alpha-cypermethrin is a synthetic pyrethroid.

Toxicology

Absorption may occur to some extent after inhalation or dermal exposure but, as with other pyrethroids, alpha-cypermethrin is rapidly metabolized and excreted from the body.

Mode of action: Neurotoxicity through disruption of nerve fiber impulse transmission.

Cyfluthrin

Cyfluthrin is a synthetic pyrethroid with very low vapor pressure. It is readily hydrolyzesd under alkaline conditions, but quite stable at pH 7 or below. Cyfluthrin is very strongly adsorbed to organic matter and can be classified as immobile in soil.

Toxicology

The acute toxicity of cyfluthrin varies depending on the vehicle. Toxicity is high by ingestion but cyfluthrin has poor skin penetration. Although as other α-cyano-pyrethroids, it may irritate the eye and skin, 10 percent WP cyfluthrin is not irritating to the skin and only slightly irritating to mucous membranes.

Absorption route: After oral administration, about 90 percent was absorbed in the intestine. Absorption after inhalation is also possible. Dermal absorption is very low.

Mode of action: Cyfluthrin acts upon the peripheral nervous system as well as on regions of the central nervous system (e.g., certain binding sites—GABA-receptors—in the brain).

Deltamethrin

Deltamethrin is a synthetic pyrethroid of the alpha-cyano group. It is related to cypermethrin and lambda-cyhalothrin, and is a single isomer pyrethroid. Deltamethrin has been used in malaria control since the late 1970s, and has been impregnated in bednets or curtains and used for indoor residual spraying in spite of its marked excito-repellency, which in some situations may be an advantage as it reduces human-vector contact.

Deltamethrin is used at dosages of 10-25 mg/m^2 giving a residual effect of 3-6 months. Protective clothing for spraymen should consist of overalls (washed daily), canvas or rubber boots, and hats.

Toxicology

Deltamethrin is primarily absorbed from the gastrointestinal tract, but also by inhalation of spray mist.

Mode of action: A neurotoxin, acting primarily on the basal ganglia of the central nervous system, causing repetitive nerve action.

Etofenprox

Etofenprox is a synthetic non-ester pyrethroid with high vapor pressure and low water solubility. Etofenprox is the insecticide with lowest acute toxicity to mammals of those recommended for indoor residual spraying. It is used as a WP 20 percent formulation, at a dosage of 100-300 mg/m^2 giving a residual effect of 3-6 months.

Toxicology

Absorption route: Etofenprox may be absorbed from the gastrointestinal tract or through the intact skin.

Mode of action: Etofenprox disturbs nerve impulses in insect nerve axons.

Lambda-cyhalothrin

Lambda-cyhalothrin is a synthetic pyrethroid, of the alpha-cyano group, with a core (-CCOOCHCN-), as in alpha-cypermethrin and deltamethrin. Lambda-cyhalothrin has low vapor pressure, is essentially insoluble in water, and has low volatility. It is available in WP formulation and is used at a dosage of 20-30 mg/m^2 giving a residual effect of 3-6 months.

Toxicology

Absorption route: Lambda-cyhalothrin may be absorbed through the gastrointestinal tract, by inhalation, or through the skin. Skin absorption of lambda-cyhalothrin is very low and no systemic effects from skin absorption have been described. Dermal and inhalational exposures usually have mild or no adverse effects. Following substantial ingestion, patients may develop coma, convulsions, and severe muscle fasciculations, and may take several days and occasionally weeks to recover. No known fatalities have been reported after lambda-cyhalothrin exposure.

Mode of action: Lambda-cyhalothrin's mode of action is the same as that of other alpha-cyano pyrethroids, primarily affecting the sodium channels in the nerve membrane and causing a long-lasting prolongation of the transient increase in sodium permeability of the membrane during excitation.

Symptoms of poisoning

In normal use, only local skin reactions have been reported. Any pyrethroid reaching the systemic circulation will be metabolized rapidly to much less toxic metabolites. The risk of toxicity of any kind to humans exposed by the usual routes is extremely remote, even with frequent exposure to the low concentrations used for malaria control. Systemic toxicity has not been seen in users, except on very rare occasions when few precautions were taken during packaging of pyrethroids and the victim's whole body was subjected to repeated and often prolonged exposure through soaked clothing.

Nevertheless, if ingested, these products may produce nausea, vomiting, cough, respiratory distress, and convulsions.

The field use of pyrethroids in the recommended concentrations, accompanied by the normal precautions for insecticide use, poses little or no hazard to applicators. Skin reactions such as pruritus, tautness and reddening of the facial skin, partial facial paraesthesia, and signs of irritation in the oropharyngeal cavity or coughing, especially when combined with increased sensitivity to touch stimuli, may be signs of dermal contact or inhalative exposure. These dermal sensations are direct and transitory effects on sensory nerve endings and are not the result of a primary skin irritation. Toxicologically, these are useful characteristics, as they provide an early indication of exposure.

After breathing in the insecticide spray mist, there may be irritation of respiratory mucous membranes with coughing and sneezing.

Treatment by Medical Professional

1. **Skin decontamination.** Wash skin promptly with soap and water. If irritant or paresthesia occurs, obtain treatment by a physician. Because volatilization of pyrethroids apparently accounts for paresthesia affecting the face, strenuous measures should be taken (ventilation, protective face mask and hood) to avoid vapor contact with the face and eyes. Vitamin E oil preparations (dL-alpha tocopheryl acetate) are uniquely effective in preventing and stopping the paresthesia. They are safe to apply to the skin under field conditions. Corn oil is somewhat effective, but possible side effects with continuing use make it less suitable. Vaseline is less effective than corn oil. Zinc oxide actually makes the reaction worse.

2. **Eye contamination.** Some pyrethroid compounds can be very corrosive to the eyes. Extraordinary measures should be taken to avoid eye contamination. The eye should be treated immediately by prolonged flushing of the eye with copious amounts of clean water or saline. If irritation persists, obtain professional ophthalmologic care.

3. **Gastrointestinal decontamination.** If large amounts of pyrethroids, especially the cyano-pyrethroids, have been ingested and the patient is seen soon after exposure, consider gastrointestinal decontamination. Based on observations in laboratory animals and humans, large ingestions of allethrin, cismethrin, fluvalinate, fenvalerate, or deltamethrin would be the most likely to generate neurotoxic manifestations.

   If only small amounts of pyrethroid have been ingested, or if treatment has been delayed, oral administration of activated charcoal and cathartic probably represents optimal management. Do not give cathartic if patient has diarrhea or an ileus.

4. **Other treatments.** Several drugs are effective in relieving the pyrethroid neurotoxic manifestations observed in deliberately poisoned laboratory animals, but none has been tested in human poisonings. Therefore, neither efficacy nor safety under these circumstances is known. Furthermore, moderate neurotoxic symptoms and signs are likely to resolve spontaneously if they do occur.

5. **Seizures.** Any seizures should be treated as outlined in the general principles for management of acute poisoning.

SECTION 2: SPECIFIC TREATMENT GUIDELINES FOR NEW INSECTICIDES FOR MALARIA IVM PROGRAM.

Pyrazole

Pyrazole is a new class of pyrrole insecticides based on a natural product that is termed a pro-insecticide, where the biological activity depends on its activation to another chemical. To date chlorfenapyr is the only insecticide in this class.

Chlorfenapyr

Chlorfenapyr was discovered in 1985 following the isolation of a toxin from a Streptomyces bacterium. As a pesticide it is low in toxicity, kills pests quickly (within 1-2 hour). Residual activity of different substrates was found to be effective against adult mosquitoes up to 34 weeks therefore it is a candidate for IRS. It is very effective against pests that are resistant to organophosphates, carbamates, pyrethroids, and chitin-synthesis inhibitors. No instances of target site cross-resistance have been observed anywhere in the world. Chlorfenapyr is sold in emulsifiable concentrate and pressurized liquid forms.

Chlorfenapyr controls a variety of insects on terrestrial non-food crops, aquatic non-food industrial sites, greenhouse food and nonfood crops, outdoor residential, indoor food and non-food uses, indoor medical, and indoor residential. Chlorfenapyr is applied via aerosol can, low pressure sprayer, foam applicator, injection equipment, hand pressure sprayer, low volume sprayer, power sprayer, and pump spray bottle.

Toxicology

Chlorfenapyr is a moderate but reversible eye irritant. Studies with rabbits found that corneal opacity, iritis, and conjunctivitis were present at 48 hours after the exposure. By 72 hours, iritis was resolved. By day 6 all rabbits were normal. Eye exposure is rated as slightly toxic (III). Dermal toxicity was measured on rabbits is rated at toxicity level III (slight irritation). Slight erythema was observed at 1 hour and persisted in a rabbit at 24 hours. All signs of irritation had resolved by 48 hours. Inhalation toxicity is rated at level II. Therefore, risk via the inhalation route is a potential concern. It is slightly toxic if swallowed.

The central nervous system is the primary target of chlorfenapyr in rats and mice. Chlorfenapyr caused liver toxicity and changes in brain morphology in sub-chronic and chronic feeding studies in rodents. In the rat chronic toxicity study there were increased trends in the incidence of hepatocellular adenomas, hepatocellular adenomas and/or carcinomas combined, malignant histiocytic sarcomas and testicular interstitial cell tumors in males rats. In female rats there were significant increasing trends in endometrial stromal polyps. Significant difference is pair-wise comparison of fibroadenomas at low dose and carcinomas at the mid-dose existed for female rats.

Absorption route:

Absorption can be from the insecticide on the skin, inhaled as a spray mist or in dust, or by ingestion.

Mode of action:

It uncouples oxidative phosphorylation preventing the conversion of ADP to ATP, and the mite or insect dies from the inability to generate its own energy.

Symptoms of poisoning

As chlorfenapyr is a rather new product there are not many cases of poisonings where the symptoms were described. Five cases of poisoning attributable to chlorfenapyr can be related. One person experienced occupational exposure to his eyes while at work. The patient immediately flushed his eyes and the itchiness went away within few hours. The second case involved a patient with a history of brain surgery who developed seizures after being at home while the product was applied. The third incident involved a 52 year old female who experienced an asthma attack after a nearby office was sprayed. The only symptoms reported were respiratory effects. This case was ranked as low severity. A fourth patient first exhibited general fatigue, hyper-perspiration, nausea and vomiting. He was initially diagnosed as being dehydrated. A fifth entered the hospital due to exogenous intoxication with chlorfenapyr with suicidal purposes, initially presenting diaphoresis, headache and cough. Symptomatic management was initiated, but after seven days she presented neurological and respiratory deterioration, causing her death.

Emergency Treatment First Aid

General advice

First aid providers should wear protective equipment to prevent exposure. Remove contaminated clothing. Move person to fresh air. If person is not breathing give artificial respiration

1. If inhaled

Over-exposure by inhalation is improbable but if it occurs move the affected individual into fresh air and keep person calm. Assist in breathing if necessary.

2. If on skin

It is a mild skin irritant but not a skin sensitizer. Rinse skin immediately with plenty of water. Wash affected areas thoroughly with soap and water for 15-20 min. Remove contaminated clothing and launder before re-use.

3. If in eyes

It is not an eye irritant. If in eyes hold lids open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, and then continue rinsing.

4. If swallowed

Have person sip a glass of water if able to swallow. Do not induce vomiting unless told by a poison control center or doctor. Make every effort to prevent vomit from entering the lungs by careful placement of the patient. If he victim is unconscious or having convulsions do not induce vomiting or give anything by mouth.

Treatment by Medical Professional

As chlorfenapyr affects the central nervous system, it can be managed through supportive care and early treatment of seizure through benzodiazepine. No specific symptoms can be said for exposure by inhalation or ingestion. Possible generalized symptoms include nausea and vomiting. Prolonged contact of the skin with the concentrate may cause irritation. Eye contact may cause some discomfort if contact is prolonged. Evidence from prolonged animal studies indicates that repeated or prolonged exposure to high doses of chlorfenapyr can result in spongiform (encephalomyelopathy) and effects on the liver and kidney.

Microbial

Microbial insecticides are based on toxins identified from naturally occurring organisms such as bacteria or fungi and are also called bio-insecticides.

Spinosad

Spinosad is a bacterial product identified in 1986 from metabolites of fermented *Sacchrapolyspora spinosa*. Spinosad is a mixture of tetracyclic macrolide neurotoxins Spinosyn A and D metabolites. Spinosad is registered as a mosquito larvicide. It also is registered against moth, fly, and beetle pests of field crops, fruits, vegetables, ornamentals, and turf. Spinosad is available in suspension, gel/paste/cream, flowable concentrate, solution/ liquid (ready-to-use), aqueous concentrate, and granular/flake formulations.

Toxicology

Mammalian toxicity of spinosad is extremely low rodents. Spinosad is of low acute oral and dermal toxicity (toxicity class IV). Spinosad is slowly and poorly absorbed through the skin. It was non- irritating to the skin of rabbits and induced slight eye irritation in rabbits in one study, but was found non irritating in a second study, and was not a skin sensitizer in guinea pigs. The inhalation toxicity value is level III.

Absorption route:

Absorption into the human body can occur by contact with the active ingredient. It can also be ingested through drinking water taken from treated bodies of water.

Mode of action:

Spinosad alters the function of nicotinic- and GABA-gated ion channels of the insect nervous system. Spinosad alters the function of mosquito larva's nicotinic acetylcholine receptors in a unique action that causes continuous nervous impulses. This constant involuntary nervous stimulus causes paralysis and death.

Symptoms of poisoning

Spinosad has a very low mammalian toxicity. No data was seen on signs and symptoms of poisoning.

Emergency Treatment First Aid

General advice

First aid providers should wear personal protective equipment before giving assistance.

1. If inhaled

A single exposure to mist is not likely to cause adverse effects. Remove affected person to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

2. If on skin

A single exposure is not likely to result in the material being absorbed through the skin in harmful amounts. Prolonged exposure also is not likely to cause significant skin irrigation. It did not cause irritation or reactions when tested on guinea pigs. Remove contaminated clothing and wash affected areas of skin with soap and water. Launder contaminated clothing before reuse.

3. If in eyes

It is mildly irritating to the eyes. Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, and then continue rinsing. Call a poison control center or doctor for treatment advice.

4. If swallowed

No hazards are anticipated from swallowing small amounts incidental to normal handling operations. If large amounts are ingested call a physician or Poison Control Center immediately. Do not induce vomiting as vomiting may cause aspiration resulting in chemical pneumonia. Do not give anything by mouth to an unconscious person.

Treatment by Medical Professional

Spinosad contains petroleum distillate therefore gastric lavage is indicated if material was taken internally. Vomiting may cause aspiration pneumonia. It may affect the kidneys and liver resulting in tissue lesions. There is no specific antidote. Provide supportive care. Treatment should be based on the judgment of the physician in response to reactions of the patient.

Pyridine juvenile hormone analogue

Juvenile hormone analogues work by preventing the insect from molting and thus it never grows.

Pyriproxyfen

Pyriproxyfen is an insect growth regulator that affects the physiology of morphogenesis, reproduction and embryogenesis of insects. Pyriproxyfen is a potent insecticide and works especially well against public health insects like houseflies, mosquito larvae, and ants. It results in 95% inhibition of emergence of mosquito larvae into adults where eventually the larvae die. Its effects can last for two months after application. It has low mammalian toxicity and environmental impact. It is also effective against fleas/ticks on dogs. It is commonly formulated as an emulsifiable concentrate, granule, or water dispersible granules.

Toxicology

Pyriproxyfen functions as an insecticide by overloading the hormonal system of the target insect, ultimately affecting egg production, brood care and other social interactions, and inhibiting growth. It is active at very low dosages from 25-100 grams active ingredient per hectare. Due to its unique effect on molting insects it is unlikely to be a hazard to mammals. Therefore acute toxicity of pyriproxyfen is relatively low and transient. Minimal signs of toxicity were observed only in mammals in high oral dosages.

Absorption route:

Pyriproxyfen can enter the body during application by inhaling dust or if the product touches the skin. It can also be ingested through drinking water taken from treated bodies of water.

Mode of action:

Pyriproxyfen has a unique mode of action affecting the morphogenesis, reproduction and embryogenesis of insects. The morphogenetic effect of pyriproxyfen is primarily seen during larval-pupal transformation. Therefore death occurs at the pupal stage and adult mosquitoes fail to emerge.

Emergency Treatment First Aid

General advice

First aid providers should wear protective equipment to prevent exposure. Remove contaminated clothing. Move person to fresh air. If person is not breathing give artificial respiration

1. If inhaled

Based on an evaluation of the ingredients and/or similar products this product may be minimally toxic when inhaled. But exposure to high concentrations in the air may cause respiratory irritation. Move the patient from contaminated area to fresh air. If any signs or symptoms occur or persist, seek medical advice.

2. If on skin

Pyriproxyfen can cause brief and minor irritation to skin. It is slightly toxic when absorbed through the skin but is not expected to cause allergenic skin reactions. Rinse skin with plenty of water or shower. Remove contaminated clothing and wash skin thoroughly with soap and water. Launder contaminated clothing before re-use. Seek medical advice if irritation develops.

3. If in eyes

Pyriproxyfen can cause brief and/or minor eye irritation. The expected adverse health effects resulting from an exposure may include redness and possible swelling. Hold eyes open and rinse with plenty of water flood with water for at least 15 minutes (remove contact lenses if easily possible) then take to a doctor or and seek medical advice.

4. If swallowed

It is minimally toxic when ingested. If swallowed do not induce vomiting. Wash mouth with water. Give water to drink. Have the patient rest. Seek medical advice.

Treatment by Medical Professional

Signs and symptoms of poisoning may include, but may not be limited to, nasal discharge, sore throat, coughing and difficulty in breathing. However no symptoms were observed from studies on volunteers from oral or dermal exposure. Therefore apply basic aid and decontamination procedures. Treat symptomatically. Chronic studies with pyriproxyfen technical indicated that repeated high exposures produced changes in the liver, kidney and red blood cells but did not produce cancer in test animals.

Synergist

Synergists do not, by themself, have pesticidal properties. However, when added to insecticide mixtures (typically pyrethrin, pyrethroid, or carbamate insecticides) their potency is increased considerably.

Piperonyl Butoxide (PBO)

PBO acts as an enzyme and has no pesticidal properties but enhances the efficacy of the pesticide. PBO inhibits the ability of insects to metabolize certain insecticides. This allows products containing PBO to be equally effective with lower concentrations of insecticides. As a synergist, PBO is formulated with other insecticides, mainly pyrethroids. These are formulated as dusts, emulsifiable concentrates, fogger, paper coating, pressurized spray, solution, and wettable

powers. In the context of this study PBO is impregnated into mosquito nets with a synthetic pyrethroid such as deltamethrin.

Toxicology

PBO is minimally toxic to mammals. Hepatic changes and liver injury have been seen with large doses given to various animal species. Various anemias have been reported in animal studies from exposures. Animal studies have also shown elevated metabolic enzymes after ingestion. Acute oral or dermal exposure is unlikely to result in significant signs and symptoms of systemic toxicity or dermal irritation.

Absorption route:

Monitoring data indicate that the general population may be exposed to PBO via inhalation of dust, ingestion of food, and dermal contact with this compound or other insecticide products containing PBO

Mode of action:

PBO inhibits mixed function oxidase enzymes of the liver which metabolize pyrethrins and pyrethroids, with which they are combined.

Symptoms of poisoning

Primary sources of data are from animals which include reports of hyper-excitability, unsteadiness, coma, seizures, and brain damage in large overdoses. PBO targets the liver, but does not disrupt the metabolism of other chemicals as it does in insects. It generally has a low toxicity in humans through any route of exposure. Ingesting PBO may cause vomiting and diarrhea. Prolonged or repeated exposure may cause dizziness and headache. PBO is often combined with hydrocarbons or other insecticides that are more toxic.

Emergency Treatment First Aid

General advice

Based on data from Poison Control Centers, there appears to be a greater risk of moderate or major symptoms among those exposed to products containing pyrethrins and PBO than those exposed to pyrethrins alone.

1. If inhaled

PBO may cause respiratory tract irritation. Move the patient to fresh air after inhalation.

2. If on skin

PBO may be harmful if absorbed through skin. It may cause skin irritation, redness or swelling due to exposure. From dermal exposure remove contaminated clothing and wash exposed area thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

3. If in eyes

PBO may cause eye irritation. Irrigate exposed eyes with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persists, the patient should be seen in a health care facility. Irrigate each eye continuously with 0.9% saline (NS) during transport.

4. If swallowed

PBO may be harmful if swallowed. Never give anything by mouth to an unconscious person. Do not induce vomiting. Give the victim one or two glasses water to drink. Seek immediate medical attention.

Treatment by Medical Professional

PBO is of low toxicity on its own but is normally combined with pyrethroids making a more toxic formulation. Control any seizures first. Gastric decontamination is only indicated if there is a co-ingestant with significant toxicity such as a pyrethroid. Instructions say to consider gastric lavage after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect the patient's airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation.

Administer charcoal as a slurry (240 ml water/30 g charcoal). Usual dose: 25-100 g in adults/adolescents, 25-50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old. Monitor for respiratory distress. If a cough or difficulty breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer oxygen and assist ventilation as required. Treat bronchospasm with inhaled beta2 agonist and oral or parenteral corticosteroids.

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SECTION 3: GENERAL PRINCIPLES IN THE MANAGEMENT OF ACUTE PESTICIDE POISONINGS

Skin Decontamination

Decontamination must proceed concurrently with whatever resuscitative and antidotal measures are necessary to preserve life. Shower patient with soap and water, and shampoo hair to remove chemicals from skin and hair. If there are any indications of weakness, ataxia, or other neurologic impairment, remove the victim's clothing, have the victim lie down, and give the victim a complete bath and shampoo using copious amounts of soap and water. Check for pesticide sequestered under fingernails or in skin folds and wash these areas.

Flush contaminating chemicals from eyes with copious amounts of clean water for 10-15 minutes. If eye irritation is present after decontamination, ophthalmologic consultation is appropriate.

Persons attending the victim should avoid direct contact with heavily contaminated clothing and vomitus. Contaminated clothing should be promptly removed, bagged, and laundered before returning to the patient. Shoes and other leather items cannot usually be decontaminated and should be discarded. Note that pesticides can contaminate the inside surfaces of gloves, boots, and headgear. Decontamination should especially be considered for emergency personnel (such as ambulance drivers) at the site of a spill or contamination. Wear rubber gloves while washing pesticide from skin and hair of patient. Latex and other surgical or precautionary gloves usually do not provide adequate protection from pesticide contamination.

Airway Protection

Ensure that a clear airway exists. Suction any oral secretions using a large bore suction device if necessary. Intubate the trachea if the patient has respiratory depression or if the patient appears obtunded or otherwise neurologically impaired. Administer oxygen as necessary to maintain adequate tissue oxygenation. In severe poisonings, mechanically supporting pulmonary ventilation for several days may be necessary.

Note on Specific Pesticides: There are several special considerations with regard to certain pesticides. In **organophosphate** and **carbamate** poisoning, adequate tissue oxygenation is essential prior to administering atropine.

Gastrointestinal Decontamination

A joint position statement has recently been released by the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists on various methods of gastrointestinal decontamination. A summary of the position statement accompanies the description of each procedure.

1. **Gastric Lavage.** If the patient presents within 60 minutes of ingestion, lavage may be **considered**. Insert an orogastric tube and follow with fluid, usually normal saline. Aspirate back the fluid in an attempt to remove any toxicant. If the patient is neurologically impaired, airway protection with a cuffed endotracheal tube is indicated prior to gastric lavage. Lavage performed more than 60 minutes after ingestion has not proven to be beneficial and runs the risk of inducing bleeding, perforation, or scarring due to additional trauma to already traumatized tissues. It is almost always necessary first to control seizures before attempting gastric lavage or any other method of GI

decontamination. Studies of poison recovery have been performed mainly with solid material such as pills. There are no controlled studies of pesticide recovery by these methods. Reported recovery of material at 60 minutes in several studies was 8 percent to 32 percent. There is further evidence that lavage may propel the material into the small bowel, thus increasing absorption.

Note on Specific Pesticides: Lavage is contraindicated in hydrocarbon ingestion, a common vehicle in many pesticide formulations.

Position Statement: Gastric lavage should not be routinely used in the management of poisons. Lavage is indicated only when a patient has ingested a potentially life-threatening amount of poison and the procedure can be done within 60 minutes of ingestion. Even then, clinical benefit has not been confirmed in controlled studies.

2. **Activated Charcoal Adsorption**. Activated charcoal is an effective absorbent for many poisonings. Volunteer studies suggest that it will reduce the amount of poison absorbed if given within 60 minutes. There are insufficient data to support or exclude its use if time from ingestion is prolonged, although some poisons that are less soluble may be adsorbed beyond 60 minutes. Clinical trials with charcoal have been done with poisons other than pesticides. There is some evidence that paraquat is well adsorbed by activated charcoal. Charcoal has been anecdotally successful with other pesticides.

Dosage of Activated Charcoal:

- *Adults and children over 12 years:* 25-100 g in 300-800 mL water.
- *Children under 12 years:* 25 50 g per dose.
- *Infants and toddlers under 20 kg*: 1 g per kg body weight.

Many activated charcoal formulations come premixed with sorbitol. Avoid giving more than one dose of sorbitol as a cathartic in infants and children due to the risk of rapid shifts of intravascular fluid. Encourage the victim to swallow the adsorbent even though spontaneous vomiting continues. Antiemetic therapy may help control vomiting in adults or older children. As an alternative, activated charcoal may be administered through an orogastric tube or diluted with water and administered slowly through a nasogastric tube. Repeated administration of charcoal or other absorbent every 2-4 hours may be beneficial in both children and adults, but use of a cathartic such as sorbitol should be avoided after the first dose. Repeated doses of activated charcoal should not be administered if the gut is atonic. The use of charcoal without airway protection is contraindicated in the neurologically impaired patient.

Note on Specific Pesticides: The use of charcoal without airway protection should be used with caution in poisons such as organophosphates, carbamates, and organochlorines if they are prepared in a hydrocarbon solution.

Position Statement: Single-dose activated charcoal should not be used routinely in the management of poisoned patients. Charcoal appears to be most effective within 60 minutes of ingestion and may be considered for use for this time period. Although it may be considered 60 minutes after ingestion, there is insufficient evidence to support or deny its use for this time period. Despite improved binding of poisons within 60 minutes, only one study suggests that

there is improved clinical outcome. Activated charcoal is contraindicated in an unprotected airway, a GI tract not anatomically intact, and when charcoal therapy may increase the risk of **aspiration** of a hydrocarbon-based pesticide.

Seizures: Lorazepam is increasingly being recognized as the drug of choice for status epilepticus, although there are few reports of its use with certain pesticides. Emergency personnel must be prepared to assist ventilation with lorazepam and any other medication used to control seizures. See dosage table below. For organochlorine compounds, use of lorazepam has not been reported in the literature. Diazepam is often used for this, and is still used in other pesticide poisonings.

Dosage of Diazepam:

- *Adults*: 5-10 mg IV and repeat every 5-10 minutes to maximum of 30 mg.
- *Children*: 0.2 to 0.5 mg/kg every 5 minutes to maximum of 10 mg in children over 5 years, and maximum of 5 mg in children under 5 years.

Dosage of Lorazepam:

- Adults: 2-4 mg/dose given IV over 2-5 minutes. Repeat if necessary to a maximum of 8 mg in a 12 hour period.
- Adolescents: Same as adult dose, except maximum dose is 4 mg.
- Children under 12 years: 0.05-0.10 mg/kg IV over 2-5 minutes. Repeat if necessary .05 mg/kg 10-15 minutes after first dose, with a maximum dose of 4 mg.

Caution: Be prepared to assist pulmonary ventilation mechanically if respiration is depressed, to intubate the trachea if laryngospasm occurs, and to counteract hypotensive reactions.

Phenobarbital is an additional treatment option for seizure control. Dosage for **infants, children, and adults** is 15-20 mg/kg as an IV loading dose. An additional 5 mg/kg IV may be given every 15-30 minutes to a maximum of 30 mg/kg. The drug should be pushed no faster than 1 mg/kg/minute.

For seizure management, most patients respond well to usual management consisting of benzodiazepines, or phenytoin and phenobarbital.

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ANNEX J: CODEX MAXIMUM RESIDUE LIMITS

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
ALAPHA-CYPERMETHRIN				No MRLs established or prior MRLs revoked
BENDIOCARB				No MRLs established or prior MRLs revoked
BIFENTHRIN				Residues are not expected to exceed 0.01 mg/kg.
	Barley	0.05	(*)	
	Barley straw and fodder, Dry	0.5		
	Cattle fat	0.5		
	Cattle kidney	0.05	(*)	
	Cattle liver	0.05	(*)	
	Cattle meat	0.5	(fat)	
	Cattle milk	0.05	(*)	
	Chicken eggs	0.01	(*)	
	Chicken fat	0.05	(*)	
	Chicken meat	0.05	(*) (fat)	
	Chicken, Edible offal of	0.05	(*)	
	Grapefruit	0.05	(*)	Residues are not expected to exceed 0.01 mg/kg.
	Hops, Dry	10		
	Lemon	0.05	(*)	Residues may occur near this level.
	Maize	0.05	(*)	Residues are not expected to exceed 0.01 mg/kg.
	Maize fodder	0.2		
	Maize forage	0.05	(*)	
	Orange, Sweet	0.05	(*)	Residues may occur near this level.
	Pear	0.5		
	Potato	0.05	(*)	Residues are not

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
				expected to exceed 0.01 mg/kg.
	Strawberry	1		
	Wheat	0.5	Po	
	Wheat bran, Unprocessed	2	PoP	
	Wheat flour	0.2	PoP	
	Wheat forage (whole plant)	0.2		
	Wheat straw and fodder, Dry	0.5		
	Wheat wholemeal	0.5	PoP	
CHLORFENAPYR				No MRLs established or prior MRLs revoked
CYFLUTHRIN	Apple	0.5		
	Cattle milk	0.01	F	The MRL accommodates external animal treatment.
	Cotton seed	0.05		
	Maize	0.05		
	Peppers, Sweet	0.2		
	Rape seed	0.05		
	Tomato	0.5		
DDT	Carrot	0.2		
	Cereal grains	0.1		
	Eggs	0.1		
	Meat (from mammals other than marine mammals)	5	(fat) T	
	Milks	0.02	F	
	Poultry meat	0.3		
DELTAMETHRIN	Apple	0.2		
	Beans (dry)	1	Po	
	Brassica vegetables	0.1		
	Bulb vegetables, except fennel, bulb	0.1		
	Carrot	0.02		
	Cereal grains	2	Po	
	Citrus fruits	0.02		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information		Footnote
	Eggs	0.02	(*)		
	Field pea (dry)	1		Po	
	Flowerhead brassicas	0.1			
	Fruiting vegetables, Cucurbits	0.2			
	Grapes	0.2			
	Hazelnuts	0.02	(*)		
	Kidney of cattle, goats, pigs & sheep	0.03	(*)		
	Leafy vegetables	0.5			
	Leek	0.2			
	Legume vegetables	0.2			
	Lentil (dry)	1		Po	
	Liver of cattle, goats, pigs & sheep	0.03	(*)		
	Mandarins	0.02			
	Meat (from mammals other than marine mammals)	0.5		(fat)	The MRL accommodates external animal treatment.
	Milks	0.05		F	
	Mushrooms	0.05			
	Nectarine	0.05			
	Olives	1			
	Onion, Bulb	0.05			
	Oranges, Sweet, Sour	0.02			
	Peach	0.05			
	Plums (including prunes)	0.05			
	Potato	0.01	(*)		
	Poultry meat	0.1		(fat)	
	Poultry, Edible offal of	0.02	(*)		
	Pulses	1		Po	
	Radish	0.01	(*)		
	Stone fruits	0.05			
	Strawberry	0.2			
	Sunflower seed	0.05	(*)		
	Sweet corn (corn-on-the-cob)	0.02	(*)		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information			Footnote
	Tea, Green, Black	5				
	Tomato	0.3				
	Walnuts	0.02	(*)			
	Wheat bran, Unprocessed	5		PoP		
	Wheat flour	0.3		PoP		
	Wheat wholemeal	2		PoP		
ETOFENPROX	Pome fruits	1				
	Potato	0.01	(*)			
FENITROTHION	Cereal grains	10		Po		
	Meat (from mammals other than marine mammals)	0.05	(*)	(fat)	E	
	Milks	0.002	(*)		E	
	Rice bran, Unprocessed	20		PoP		
	Rice, Polished	1		PoP		
	Wheat bran, Processed	2		PoP		
	Wheat bran, Unprocessed	20		PoP		
	Wheat flour	2		PoP		
	Wheat wholemeal	5		PoP		
LAMBDA-CYHALOTHRIN						No MRLs established or prior MRLs revoked
MALATHION	Apple	2				
	Asparagus	1				
	Beans (dry)	2				
	Beans, except broad bean and soya bean	1				
	Blueberries	10				
	Broccoli	5				
	Cabbages, Head	8				
	Cereal grains	8		Po		
	Citrus fruits	4				
	Cucumber	0.2				
	Grapes	8				
	Mustard greens	2				
	Onion, Bulb	1				
	Peach	6				

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	Peppers	0.1		
	Raspberries, Red, Black	8		
	Root and tuber vegetables	0.5		
	Spinach	3		
	Spring onion	5		
	Strawberry	1		
	Sweet corn (corn-on-the-cob)	0.02		
	Tomato	0.5		
	Tomato juice	0.01		
	Turnip greens	5		
	Turnip, Garden	0.2		
	Wheat flour	2	PoP	
PIPERONYL BUTOXIDE	Cattle kidney	0.3		
	Cattle liver	1		
	Cattle meat	5	(fat)	
	Cattle milk	0.2		
	Cereal grains	30	Po	
	Citrus fruits	5		
	Citrus juice	0.05		
	Dried fruits	0.2	Po	
	Eggs	1		
	Fruiting vegetables, Cucurbits	1		
	Kidney of cattle goats, pigs and sheep	0.2		
	Lettuce leaf	50		
	Liver of cattle, goats, pigs and sheep	1		
	Maize oil, crude	80	PoP	
	Meat (from mammals other than marine mammals)	2	(fat)	
	Milks	0.05	F	
	Mustard greens	50		
	Pea hay or pea fodder (dry)	200	Dry wt	
	Peanut, whole	1		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	Peppers	1		
	Peppers chili, dried	10		
	Poultry meat	7	(fat)	
	Poultry, edible offal of	10		
	Pulses	0.2	Po	
	Radish leaves (including radish tops)	50		
	Root and tuber vegetables	0.5		
	Spinach	50		
	Tomato	2		
	Tomato juice	0.3		
	Wheat bran, unprocessed	80	PoP	
	Wheat flour	10	PoP	
	Wheat germ	90	PoP	
	Wheat wholemeal	30	PoP	
PIRIMIPHOS-METHYL	Apple	2		
	Brussels sprouts	2		
	Cabbages, Head	2		
	Carrot	1		
	Cauliflower	2		
	Cereal grains	10	Po	
	Cherries	2		
	Citrus fruits	2		
	Common bean (pods and/or immature seeds)	0.5		
	Cucumber	1		
	Currant, Black	1		
	Dates, Dried or dried & candied	0.5	Po	
	Dried fish	8	Po	
	Eggs	0.05	(*)	
	Gooseberry	1		
	Kiwifruit	2		
	Lettuce, Head	5		
	Meat (from mammals other than marine	0.05	(*)	

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	mammals)			
	Milks	0.05	(*)	
	Mushrooms	5		
	Olives	5		
	Peanut	2	Po	
	Peanut oil, Crude	15	PoP	
	Peanut oil, Edible	15	PoP	
	Peanut, whole	25	Po	
	Pear	2		
	Peas (pods and succulent=immature seeds)	0.05	(*)	
	Peppers	1		
	Plums (including prunes)	2		
	Potato	0.05	(*)	
	Raspberries, Red, Black	1		
	Rice bran, Unprocessed	20	PoP	
	Rice, Husked	2	PoP	
	Rice, Polished	1	PoP	
	Rye wholemeal	5	PoP	
	Spinach	5		
	Spring onion	1		
	Strawberry	1		
	Tomato	1		
	Wheat bran, Unprocessed	20	PoP	
	Wheat flour	2	PoP	
	Wheat wholemeal	5	PoP	
	White bread	0.5	PoP	
	Wholemeal bread	1	PoP	
PROPOXUR				No MRLs established or prior MRLs revoked

Larvicide	Commodity	MRL (mg/kg)	Additional Information			Footnote
METHOPRENE	Cattle milk	0.05			F	The MRL accommodates external animal treatment.
	Cereal grains	5			Po	
	Edible offal (mammalian)	0.1				
	Eggs	0.05				
	Maize oil, Edible	0.2		(*)	PoP	
	Meat (from mammals other than marine mammals)	0.2			(fat)	The MRL accommodates external animal treatment.
	Wheat bran, Unprocessed	10			PoP	
	Wheat flour	2			PoP	
	Wheat wholemeal	5			PoP	
PYRIPROXYFEN	Cattle meat	0.01	(*)	(fat)		
	Cattle, edible offal	0.01	(*)			
	Citrus fruits	0.5				
	Cotton seed	0.05				
	Cotton seed oil, crude	0.01				
	Cotton seed oil, edible	0.01				
	Goat meat	0.01	(*)	(fat)		
	Goat, edible offal o	0.01	(*)			
SPINOSAD	Almond hulls	2				
	Almonds	0.01		(*)		
	Apple	0.1				
	Brassica (Cole or Cabbage) vegetables, head cabbage, flowerhead brassicas	2				
	Cattle kidney	1				
	Cattle liver	2				
	Cattle meat	3			(fat)	
	Cattle milk	1				
	Cattle milk fat	5				
	Celery	2				
	Cereal grains	1			Po	
	Citrus fruits	0.3				
	Cotton seed	0.01	(*)			

Larvicide	Commodity	MRL (mg/kg)	Additional Information	Footnote
	Cotton seed oil, crude	0.01	(*)	
	Cotton seed oil, edible	0.01	(*)	
	Dried grapes (currants, raisins, and sultanas)	1		
	Edible offal (mammalian)	0.5		
	Eggs	0.01		
	Fruiting vegetables, cucurbits	0.2		
	Grapes	0.5		
	Kiwifruit	0.05		
	Leafy vegetables	10		
	Legume vegetables	0.3		
	Maize fodder (dry)	5		
	Meat (from mammals other than marine mammals)	2	(fat)	
	peppers	0.3		
	Pepper chili, dried	3		
	Potato	0.01	(*)	
	Poultry meat	0.2	(fat)	
	Soya bean (dry)	0.01	(*)	
	Stone fruits	0.2		
	Sweet corn (corn-on-the-cob)	0.01	(*)	
	Tomato	0.3		
	Wheat bran, unprocessed	2		
	Wheat straw and fodder, dry	1		
TEMEPHOS				No MRLs established or prior MRLs revoked

Insecticide used in LLIN	Commodity	MRL (mg/kg)	Additional Information	Footnote
PERMETHRIN	Alfalfa fodder	100		
	Almonds	0.1		
	Apple pomace, dry	50		
	Asparagus	1		
	Bean (dry)	0.1		
	Blackberries	1		

Larvicide	Commodity	MRL (mg/kg)	Additional Information	Footnote
	Broccoli	2		
	Brussels sprouts	1		
	Cabbage, savoy	5		
	Cabbage, head	5		
	Carrot	0.1		
	Cauliflower	0.5		
	Celery	2		
	Cereal grains	2	Po	
	Chinese cabbage (type pe-tsai)	5		
	Citrus fruits	0.5		
	Coffee beans	0.05	(*)	
	Common bean (pods and/or immature seeds)	1		
	Cotton seed	0.5		
	Cotton seed oil, edible	0.1		
	Cucumber	0.5		
	Currants, black, red, white	2		
	Dewberries (including boysenberry and loganberry)	1		
	Edible offal (mammalian)	0.1		
	Eggplant	1		
	Eggs	0.1		
	Gerkin	0.5		
	Gooseberry	2		
	grapes	2		
	Hopes, dry	50		
	Horseradish	0.5		
	Kale	5		
	Kiwifruit	2		
	Kohlrabi	0.1		
	Leek	0.5		
	Lettuce head	2		

Larvicide	Commodity	MRL (mg/kg)	Additional Information	Footnote
	Maize fodder (dry	100	Dry wt	
	Meat (from mammals other than marine mammals)	1	(fat)	
	Melons, except watermelon	0.1		
	Milks		F	
	Mushrooms	0.1		
	Olives	1		
	Peanut	0.1		
	Peas, shelled (succulent seeds)	0.1		
	Peppers	1		
	Peppers chili, dried	010		
	Pistachio nuts	0.5	(*)	
	Pome fruits	2		
	Potato	0.05	(*)	
	Poultry meat	0.1		
	Radish, Japanese	0.1		
	Rape seed	0.05	(*)	
	Raspberries, red, black	1		
	Sorghum straw and fodder, dry	20		
	Soya bean (dry)	0.05	(*)	
	Soya bean fodder	50	Dry wt	
	Soya bean oil, crude	0.1		
	Spinach	2		
	Spring onion	0.5		
	Squash, summer	0.5		
	Stone fruits	2		
	Strawberry	1		
	Sugar beet	0.05	(*)	
	Sunflower seed	1		
	Sunflower seed oil, edible	1		
	Sunflower seed oil, crude	1		

Larvicide	Commodity	MRL (mg/kg)	Additional Information	Footnote
	Sweet corn (corn-on-the cob)	0.1		
	Tea, green, black (black fermented and dried)	20		
	tomato	1		
	Wheat bran, unprocessed	5	PoP	
	Wheat flour	0.5	PoP	
	Wheat germ	2	PoP	
	Wheat wholemeal	2	Pop	
	Winter squash	0.5	Pop	

Key	
MRL	Maximum Residue Limit
EMRL	Extraneous Maximum Residue Limit
(*)	At or about the limit of determination.
E (only for MRLs)	The MRL based on extraneous residues.
F (for milks)	The residue is fat soluble and MRLs for milk products are derived as explained in "Codex Maximum Residue Limits/Extraneous Maximum Residue Limits for Milk and Milk Products".
(fat) (for meat)	The MRL/EMRL applies to the fat of meat.
Po	The MRL accommodates post-harvest treatment of the commodity.
PoP (for processed foods)	The MRL accommodates post-harvest treatment of the primary food commodity.
T	The MRL/EMRL is temporary, irrespective of the status of the ADI, until required information has been provided and evaluated.
V (for products of animal origin)	The MRL accommodates veterinary uses.

ANNEX K: STOCKHOLM CONVENTION QUESTIONNAIRE FOR REPORTING ON PRODUCTION AND USE OF DDT FOR DISEASE VECTOR CONTROL

Disease Vector Control

Annex III to decision SC-1/25

Format for reporting by each Party that uses DDT for disease vector control pursuant to paragraph 4 of part II of Annex B to the Stockholm Convention on Persistent Organic Pollutants and questionnaire for reporting other information relevant to the evaluation of the continued need for DDT for disease vector control

COUNTRY: _____ 3-year reporting period:_____ - _____

Name of principal reporting official	
Designation	
Agency name and address	
Fax:	
E-mail	
Signature of official	_____ Date: _____

SECTION A: PRODUCTION AND USE OF DDT

A.I. SOURCES OF DDT

In-country production

1. Is DDT produced in your country? YES ☐ NO ☐ (If NO, proceed to question # 4)

2. If YES, please list the DDT production facilities in the country:

No.	Production Facility and Location	Total production capacity (kg)	Net output/yr (kg) Yr. 1	Yr. 2	Yr. 3	Formulation (type & % of active ingredient [a.i.])	% for in-country use
i.							
ii.							
iii.							

3. For each of the production facilities listed above, provide the following:

No.	Facility	Export information				
		Destination country(s)	Quantity/yr (kg) Yr. 1	Yr. 2	Yr. 3	Formulation (type and % a.i.)
i.						
ii.						
iii.						

Import

4. Has DDT been imported into your country over the reporting period? YES ☐ NO ☐. (if NO, proceed to question 6.)

5. If DDT is imported please provide the following:

Country of export	Name of manufacturer	Total net wt of import/yr for the reporting period (kg) Yr. 1	Yr. 2	Yr. 3	Formulation (type & % of a.i.)

Stock information

6. Is DDT repackaged/reformulated in the country? YES ☐ NO ☐ (If NO, please proceed to question 8)

7. If YES, please complete the following table:

Repackaging/ reformulation agency	Description of repackaging (boxed, polythene bagged; description of labeling, etc.)	Formulation (type and % of active ingredient)	Intended end-use	Average annual amount (kg)

8. Please provide the following information on the usable stocks of DDT in your country.

Location	Total amount in storage (kg)	Formulation (type and % a.i.)	Managing authority of facility	Conditions of storage (e.g., storage capacity; access)

A.II. DDT DISPOSAL

9. Do you have obsolete DDT stocks in the country? YES ☐ NO ☐ (If NO, proceed to question 13)

10. If YES, what is the total weight of obsolete DDT stock in the country? (kg):_____
Please tick here ☐ if amount is unknown.

11. Please provide the following information on facilities where obsolete DDT is stored.

Facility and location	Total capacity of storage (kg)	Total amount (kg) of obsolete pesticides in storage at the facility	Amount (kg) and approximate age (yrs) of obsolete DDT component

12. For each storage facility storing obsolete DDT listed in question 11, please complete the following on the storage conditions.

Facility	Storage conditions					
	Housed or open?	Regular inspection? (yes/no). If yes how often?	Adequate security? (yes/no)	Leaky roof? (yes/no)	DDT leaking into environment (yes/no)	Any other comment on human and environmental safety (e.g., need for repackaging)

13. Which agency is directly responsible for DDT disposal? _____

14. Is DDT disposed of in-country? YES ☐ NO ☐

15. If the answer to question 14 is NO, is the obsolete DDT exported? YES ☐ NO ☐. If exported, then indicate destination and intent of export
_____

16. If obsolete DDT is disposed of in-country, then please complete the following table:

Disposal method (Electro-chemical, incineration, etc.)	Facilities using method	Years method has been in use	Disposal capacity/yr (kg)	Amount disposed of/yr (kg)	Cost of disposal (per kg)

A.III. DDT USE

17. What is the total amount of DDT used annually for disease vector control (kg)?

Yr 1:_____ , formulation (type & % a.i.)_____

Yr 2_____ , formulation (type & % a.i.)_____

Yr 3_____, formulation (type & % a.i.)_____

18. Please complete the following table for each disease for which DDT is used:

Disease	Total national population at risk of disease	Disease burden: prevalence rate (a) & mortality rate (b)		% Total national population at risk that is covered by DDT use			Main vector species targeted	DDT resistance in target species (Yes, no)	Year resistance was first reported
		a	b	Yr1	Yr2	Yr3			

19. Complete the following table for each disease for which DDT is used (please use additional page as necessary):

Disease	Local areas where DDT is used (e.g., district)	Population size in targeted areas	Disease transmission classification in targeted areas (stable or unstable; if stable, indicate if holo-, hyper-, meso- or hypo-endemic)[a]	Coverage in targeted areas (% of houses)			Annual amount of DDT used (kg)		
				Yr1	Yr2	Yr3	Yr1	Yr2	Yr3

[a] See instructions for definitions of endemicity.

A.IV. REGULATION AND CONTROL:

20. Are there laws and/or regulations governing or restricting the purchase and/or use of DDT?

YES ☐ No ☐. If NO, go to question 29

21. If YES, please complete the following table (use additional sheets if need).

Title of relevant law or regulation on DDT	Year it was passed or enacted	List the main objectives of the law or regulation (e.g., Prohibits the use of public transport for transporting of DDT)

22. Please indicate the major limitations with the effective enforcement of existing regulations. (Tick all that apply.)

Inadequate enforcement resources/facilities	Regulations not well understood by enforcement agencies	Inadequate number of trained personnel	Other (please specify)

23. Name the overall managing authority for DDT in the country._____

24. Which agency actually authorizes the use of DDT for disease vector control purposes?
_____

25. Please clarify if the authorizing agency (check all that apply):

- ☐ is directly involved in vector control application of DDT
- ☐ performs supervisory roles
- ☐ has district offices in charge of DDT application in local areas
- ☐ trains field staff (spray operators, inspectors etc.)
- ☐ is involved in public education on safe use of pesticides

26. Please list any other agencies with specialized management roles for DDT:

Agency	Description of role in DDT management

End-use information

27. Do local municipalities use DDT for disease vector control purposes? YES ☐ NO ☐

28. Are there any other agencies (e.g., private agencies, NGOs) involved in using DDT for disease vector control purposes? YES ☐ NO ☐. (If NO, go to question 31).

29. If the answer to question 28 is YES, please complete the following table.

Name of agency	Areas where agency uses DDT (e.g., districts)	Population size covered by agency	Annual amount of DDT used (kg active ingredient)	DDT use related activities carried out by agency		
				Training of sprayers (yes/no)	Community education/ awareness?	Other (specify)

30. For the agencies listed in question 29, provide the following additional information:

Agency	DDT application budget (as % of overall vector control budget)	Total personnel & person hours expended per application cycle			Annual population coverage		
		Yr.1	Yr. 2	Yr. 3	Yr. 1	Yr. 2	Yr.3

31. What is the average cost per house sprayed with DDT (including labor and other operational costs)?
Local currency _____ current equivalent in US$_____

32. How would you rate the general acceptance / refusal of DDT for indoor-application by the households (please tick as appropriate)?

	Provide calculated rate if available	Estimated rate (if calculated rate is not available)				
		Very Low (1)	Low (2)	(3)	High (4)	Very high (5)
Refusal rate						
Re-plastering rate						

33. If the acceptability of indoor application of DDT is low, what are the reasons given for the lack of acceptance by the households (please tick all that apply)?

Inconvenient - moving furniture etc.	Unpleasant smell of DDT	Dislike for white residues on walls	Reluctance to provide access to strangers (sprayers)	Timing of spraying inappropriate	Other (specify)

34. Is DDT application limited to certain house types or households? YES: ☐ NO: ☐. If YES, please indicate the house types targeted (e.g., traditional houses, western-type houses)

_____

35. What are the criteria for selecting a geographical area or community for DDT indoor application?

_____

_____

36. Who determines the timing of DDT application at the local level?

_____

37. What factors determine the timing of the DDT application cycle? _____

_____

38. How many DDT application cycles are there in a year? ONE ☐_ TWO ☐ OTHER? _____

39. How long does an application cycle take (time – in days or hrs)? _____

Resistance monitoring

40. What bioassay test procedure(s) is used for detecting DDT resistance? _____

_____

41. Please complete the following table on vector susceptibility to DDT according to WHO susceptibility test[1].

Disease	Main vector species	Minimum mortality %	Maximum mortality %	Year last tested	Specific geographical areas associated with test, if any

42. Please provide the following information on insecticide residual efficacy according to the WHO standard bioassay test).[2] (If no information is available for the reporting period, please provide the most recent data.)

(a) DDT bioassay results by month: yr1

Month 1_____

Month 4_____

Month 8_____

Month 12_____

(b) DDT bioassay results by month: yr2

Month 1_____

Month 4_____

Month 8_____

[1] Mortality after 24-hour holding period of mosquito specimens exposed to diagnostic concentration (4 per cent DDT) for 1 hour

[2] 24-hour holding period mortality of vector strains of known DDT susceptibility exposed for 1 hour to a DDT-sprayed surface (75 per cent WP)

Month 12_____

(c) DDT bioassay results by month: yr3

Month 1_____

Month 4_____

Month 8_____

Month 12_____

43. Briefly describe the surveillance mechanism(s) in the country for monitoring DDT resistance (Include the number & location of sentinel sites, if any):

_____

_____

_____

_____

_____

_____

SECTION B: DDT ALTERNATIVES (INSECTICIDES, METHODS, AND STRATEGIES)

B.I.: DDT ALTERNATIVES

44. Please complete the following tables for DDT alternatives that are in use:

Alternative control category	Method or chemical used	Disease targeted	Annual use (kg of active ingredient or quantity as applicable)	Target population (%)	Accept-ability[a]	Annual budget (US$) (and as % of vector control)	Unit cost[b]
Biological control (e.g., bacteria)							
Chemical control & related strategies (e.g., insecticide-treated nets, pyrethroids)							
Environ-mental control (e.g., source reduction)							

[a]End-user refusal rate (Rt) and/or use rate (Ut), indicate as appropriate

[b] As appropriate. e.g., unit cost of ITN or cost of chemical application per house

45. Complete the following table on sources of the alternative options listed above, as applicable:

Alternative category	Biological or chemical product used	Source (Import/local)	Formulations (as applicable)	Annual import (kg active ingredient)	Managing authority
Biological control					
Chemical control					

46. Complete the following table on the disposal relating to the alternative options listed:

Alternative category	Biological or chemical product used	Total national stock (kg or quantity, as applicable)	Total obsolete stock (kg or quantity, as applicable)	Disposal method used	Annual disposal cost (US$)	Agency responsible for disposal
Biological control						
Chemical control						

47. Provide information on vector resistance to any of the insecticides listed previously as DDT alternatives in use:

Disease	Vector species	Insecticide tolerance or resistance reported in the country (indicate region/area of country associated with report)	Year of first report

48. Complete the table on other DDT alternative(s) that have been considered for use or have been used in the country in the past but are not used any more:

Alternative control category	Method or product used & mode of application	Disease targeted	Reason why the use of the method/product was rejected or stopped
Biological control			
Chemical control & related strategies (e.g., insecticide-treated nets)			
Environmental control			

Main vector(s) susceptibility to insecticide (DDT alternatives listed)

49. For the alternative insecticides in use, please indicate for the targeted vector species, the minimum & maximum mortality rates using the standard (discriminating/diagnostic) insecticide concentration.

Disease	Vector species	Insecticide 1: …… ……		Insecticide 2: …… ……		Insecticide 3 ……		Insecticide 4: …… ……		Insecticide 5: …… ……	
		Mortality		Mortality		Mortality		Mortality		Mortality	
		Min %	Max %	Min %	Max %	Min %	Max %	Min %	Max %	Min %	Max %
Year last tested											

Insecticide residual efficacy (for each insecticide listed above) Please provide information on insecticide residual efficacy according to the WHO bioassay test.[3] (If no information is available for the reporting period, please provide the most recent data.)

50. Insecticide name: _____

Please provide the following information on insecticide efficacy:

(a) Insecticide bioassay results by month: yr1

Month 1_____

Month 4_____

Month 8_____

Month 12_____

[3] 24-hour holding period mortality of vector strains of known susceptibility exposed for 1 hour to an insecticide-sprayed surface.

(b) Insecticide bioassay results by month: yr2

Month 1_____

Month 4_____

Month 8_____

Month 12_____

(c) Insecticide bioassay results by month: yr3

Month 1_____

Month 4_____

Month 8_____

Month 12_____

B.II. DISEASE MANAGEMENT STRATEGIES

51. Is there a national vector control policy? YES ☐ NO ☐

52. Is the country implementing an integrated vector management (IVM) strategy? YES ☐ NO ☐

53. If yes, please list the component parts of the IVM for the diseases listed in this report:

Disease	Annual budget (US$)	Vector control component	% of overall budget	Major limitation to implementation

54. Please indicate the vector resistance management strategy employed. _____
_____
_____

55. Provide any information on the entomology laboratories available in country. For each laboratory, indicate if it is adequately equipped to carry out insect resistance testing and related functions. If not, please indicate (quantify if possible) the limitations faced. _____
_____
_____

56. Is there research into the development of locally appropriate alternative intervention options to DDT?
YES ☐ NO ☐

57. If the answer to question 56 is YES, please complete the following table

Type of research on DDT alternative	Institution leading the research	Year initiated

SECTION C: GENERAL HUMAN AND ENVIRONMENTAL SAFETY ISSUES

58. Has there been any insecticide incident(s) in relation to vector control with generalized human exposure &/or environmental release of INSECTICIDES in the country (e.g., road accidents, spills)? YES ☐ NO ☐

59. If the answer to question 58 is yes, please complete the following table:

Incident Number	Insecticide (DDT & other)	Details of exposure or environmental release			
		Date	Place	Quantity released	Estimated number of people exposed
I					
ii					
iii					
iv					

60. Please complete the following table for the incidents listed in question 59.

Incident number (Question 59)	Details of exposure or environmental release			
	Caused of incident (e.g., Road accident during transport)	Remedial actions taken	Agency undertaking remedial action	Safeguards employed to prevent future incidents
i				
ii				
iii				
iv				

61. Which agency(ies) is(are) responsible for assessing the risks posed by the use of insecticides for public health?

_____

_____

62. Is there a program to raise awareness among communities and households on safety issues relating to insecticide use in disease vector control? YES ☐ NO ☐

63. If YES, who implements the program and what public education method(s) are used?

_____

_____

SECTION D: SYSTEMS STRENGTHENING IN DISEASE VECTOR CONTROL

64. Targets for relevant trained personnel in the national disease vector control program (by category):

Category of personnel	Level of training (PhD, Master, Bachelor)	Present staffing levels (number)	Targeted staffing level
Technical (e.g., management, planners)			
Operational (e.g., sprayers, sanitarians, mosquito collectors)			
Other (please list)			

65. What is the overall budget for disease vector control_____ (US$). Also indicate as a percentage of the national health budget_____

66. What is the budget shortfall (US$) for vector control (percentage)? Yr.1_____ Yr. 2_____ Yr. 3_____

67. Give the proportion of the annual budget mobilized in-country _____and externally_____.

68. List the facilities in the country providing training in disease vector control.

Training facility	Specialization (vector biology, entomology etc.)	Training level provided (degree or other)	Annual output

69. Provide details on the in-service training programs available, especially at the regional and district levels.

_____
_____
_____

70. Do formal mechanisms exist for inter-sectoral collaboration in disease vector control?
YES ☐ NO ☐

If the answer is YES, please complete the following table (tick as appropriate).

Policy on inter-sectoral collaboration	Inter-sectoral committee/board at national level	Inter-sectoral committee at district level	Joint planning (indicate if national, provincial, district etc.)	Joint implementation of activities

71. If the answer to question 70 is NO, what are the limitations to developing such mechanisms?

_____
_____
_____
_____

72. What are the limitations to the monitoring and evaluation of vector control programs?

_____
_____
_____

and how can they be best overcome?

_____
_____
_____
_____

73. Please provide any other general information relevant to your country's situation with regards to vector borne diseases and their control:

_____
_____
_____

ANNEX L. ENVIRONMENTAL MITIGATION AND MONITORING PLAN (EMMP)

ALL ACTIVITIES

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Upsurge of malaria transmission in unstable malaria transmission areas from changes to land use from agricultural development.	Consider larval source management methods (LSM) like environmental management to minimize larvae habitat. Monitor the incidence of malaria and adjust the interventions to account for increases in malaria cases.	Continuous	• Increase in Malaria cases	PMI program and country USAID Missions, Implementing partner
Changes in inter-annual variability of malaria incidence and altitudinal malaria distribution as influenced by climate change.	Monitor the incidence of malaria and adjust the boundaries and control methods accordingly.	Continuous	• Increase in Malaria cases	PMI program and country USAID Missions, Implementing partner
Potential increase in pesticide resistance due to diversion of public health pesticides to other sectors (including *agricultural applications and private pest control enterprises).*	Identify and implement best management practices to prevent public health pesticides from being used for agriculture applications and by private pest control enterprises. Conduct resistance monitoring in areas where large quantities of	Continuous	• Increase in Malaria cases	PMI program and country USAID Missions, Implementing partner

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
	pesticides are used for agricultural crops and are targeted for malaria vector control to help develop strategies tailored to the area.			
Inadequate implementation of a sustainable malaria vector control program due to the lack of training and capacity building.	Include different types of training and capacity building for the various levels needed, including program managers and other partners involved in USAID-supported malaria vector control interventions; local, regional or national level government staff; local and/or regional counterparts; and local implementing staff such as sprayer, driver, store managers, etc.	Continuous	• Increase in Malaria cases	PMI program and country USAID Missions, Implementing partner

I) IRS ACTIVITIES

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
High and moderate risk for human and environmental impacts from certain pesticides used in IRS.	DDT, etofenprox, fenitrothion, pirimiphos-methyl, propoxur and chlorfenapyr should be used with caution in accordance with strict best management practices	Continuous	• Increase health complaints from workers and beneficiaries,	PMI program and USAID Mission
Driver and/or community exposure, or environmental contamination due to improper transport of pesticide	Driver training according to FAO recommendations Provision of appropriate equipment (reliable vehicle with side walls capable of negotiating rugged roads, tie-downs, packing materials, tarps, spill clean-up kit) Cautious driving while transporting chemicals Checking for and repairing leaks from spray equipment prior to transport In case of accident, completion of accident and corrective action report	Once prior to campaign, reinforcement as needed Continuous	• Procedures being followed • Demonstrated knowledge • Existence of training materials • Absence of vehicle accidents • Vehicle condition • Absence of spills during insecticide transport	Drivers, Implementing partners, Pesticide distributors, spray team leaders
Environmental contamination due to improper siting or construction of storage and wash facilities	Use site qualification checklist. Locate storage and wash facilities on high ground, above floodplains, away from sensitive receptors (water bodies, birds, bees, fish, children, etc.). Use appropriate construction materials as specified in FAO recommendations	Once prior to campaign	• Storage and wash facilities outside of floodplain and away from sensitive receptors (birds, bees fish, children, etc.) • Constructed of suitable material • Adequately ventilated • Adequate storage space	District Environmental Officers, Implementing partner
Storekeeper and/or community exposure or	Provision of secure storage facilities	Once prior to	• Dedicated and trained storekeeper who	Storekeeper, spray team supervisors, spray team

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
environmental contamination due to improper storage or pilferage (Cont.) Storekeeper and/or community exposure or environmental contamination due to improper storage or pilferage	Training of storekeepers, team leaders and supervisors according to FAO recommendations Daily tracking of insecticide sachets issued, used, and returned Storage procedures according to BMPs Storekeepers trained to not issue pesticides for agricultural or any other unauthorized use	campaign Continuous	demonstrates knowledge and uses correct procedures • Stock records up-to-date • Stocks orderly, rotation system in place • Expiration dates observed • Empty sachets collected, counted and reconciled with amounts issued • Ratio of structures sprayed to sachets issued • Storehouse temperature measured and recorded • No leaks or spills evident • Insecticides not stored in same room with food, or medicine, or in inhabited spaces • Facility physically secure, padlocked and guarded when not in use • No fire, flame, smoking or eating allowed in storage areas	leaders, Implementing partners
Personnel handling OPs or carbamates experience cholinesterase inhibition (CI) due to exposure. (Symptoms include tiredness, weakness, dizziness, nausea and blurred vision, headache, sweating, tearing, drooling, vomiting, tunnel vision, and	For all pesticides, all storage, spray, and wash teams receive training in recognizing effects of pesticide poisoning, remain alert to symptoms amongst their co-workers and respond appropriately. PMI will evaluate various approaches to monitoring sprayer exposure to	Training: Included in pre-campaign orientation, and in training for new personnel. PMI will use the protocols developed to inform the	• Demonstrated knowledge of symptoms of poisoning, emergency treatment, and referral protocol by supervisors, team leaders, SWS members • Antidotes available at	MOH, District Health Officers, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
twitching, abdominal cramps, muscular tremors, staggering gait)	organophosphate (OP) pesticides and will develop protocols, based on these evaluations, for a monitoring program.	implementation of PMI program monitoring for organophosphate pesticides.	health facilities	
			•	
Acute effects of pesticide toxicity go untreated (Symptoms include tiredness, weakness, dizziness, nausea, blurred vision, headache, sweating, tearing, drooling, vomiting, tunnel vision, twitching, abdominal cramps, muscular tremors, staggering gait)	Employ CI testing as needed Team leaders, storekeepers trained to recognize symptoms and enforce treatment Ensure treatment medicines are available at District health centers. If skin itches after re-entrance into home, wash with soap and water, for eye irritation, flush eyes with water. For respiratory irritation, leave the home for fresh air. For ingestion, or if symptoms persist, contact program staff or go to nearest health facility.	Training on symptoms and responses prior to each campaign Continuous observation, reinforcement and enforcement of treatment protocols	• Demonstrated knowledge of signs and symptoms of poisoning, emergency treatment, and referral protocol by supervisors, team leaders, storekeepers, spray operators, washpersons (SSW), and residents • CI test results • Antidotes and treatment medicines available at health facilities	Spray team supervisors, spray team leaders. District health officials, and Implementing partners
Exposure of SSW members and/or community during spray operations due to improper spray procedures Failure to realize/receive the benefits of IRS due to improper spray procedures	Training of SSW members, team leaders supervisors, and health workers according to MOH and WHOPES recommendations Proper assembly and calibration of spray equipment Proper spray patterns Proper cleanup and equipment storage procedures Discipline SSW members that do not follow proper procedure in all aspects of operations (handling, spraying, hygiene, cleanup)	Once prior to campaign Continuous	• Spray operators, team leaders supervisors and health workers display knowledge by following procedures at all times • Frequently agitate spray can • Hold pump such that compression gage can be seen • Stands parallel to wall being sprayed • Stands 45 cm from wall	Spray team supervisors, spray team leaders, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
			• 1m/2.5 sec spray rate • 75 cm swatch width and 5 cm overlap • All eaves and interior surfaces sprayed except dedicated kitchens	
SSW member or community exposure, or environmental contamination due to equipment or PPE issues	Use of sprayers manufactured and maintained according to WHOPES specifications Proper assembly and calibration of spray equipment Procurement and proper use of PPE by all persons in contact with pesticides Additional PPE may be required for persons in contact with DDT and pirimiphos-methyl. Additional PPE may include face masks, gloves, boots, helmets with visors, neck protection and overalls treated with water repellent to reduce the permeability of the fabric.	Continuous PMI will evaluate various approaches to monitoring sprayer exposure to organophosphate (OP) pesticides and will develop protocols, based on these evaluations, for a monitoring program. PMI will use the protocols developed to inform the implementation of PMI program monitoring for organophosphate pesticides.	• All PPE as specified in WHOPES recommendations in good condition and worn by all personnel in contact with pesticides • Condition of spray equipment • Spray nozzle not dripping during spraying or transportation • CI levels	Spray team supervisors, spray team leaders, Implementing partners
Residential Exposure from contaminated household goods	Training of spray operators to refuse to spray houses that are not properly prepared IEC Campaign, instruct residents to: • Clear homes of mats or rugs, furniture, cooking implements and foodstuffs prior to spraying • If furniture cannot be moved out of the home, then move it to the center of the room and cover with	Training and communication program prior to campaign, Spray operators require household goods removal prior to spraying domicile	• IEC materials developed and include specific instructions • IEC materials delivered in appropriate fashion • Residents outside house during spraying • Food and goods outside house during spraying	District Environment Office, NEMA, EPA, Implementing partners USAID

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Residential Exposure from contaminated household goods (cont.)	drop cloth • Stay outside the home during spraying and for two to four hours after spraying • Move and keep (tie-up or cage) all animals outside the home during spraying, and for four hours after spraying • Sweep up any insects killed from the spraying or any residual insecticide and drop waste in latrine pits		• Furniture covered during spraying • Residents stay outside for four hours after spraying • Residents sweep floor and dispose of waste properly • Occurrence of skin/eye/throat irritation • Houses not sprayed for lack of preparation	
Failure to realize benefits of spraying due to post-spray behavior change	Train residents to continue using bed nets for protection against malaria, and to refrain from re-plastering or painting over the sprayed walls after spraying, re-plaster prior to spraying if necessary	Prior to each campaign	• Continued bed net use • Walls not plastered after spraying	Village and district leaders
Staff and community exposure in vehicle used to transport spray team and/or pesticides	Frequent washing interior and exterior of program vehicles after pesticide transport using soap and water and PPE	Continuous	• Vehicle condition	Cooper, Spray team supervisors, spray team leaders, Implementing partners
SSW personnel exposure due to poor personal hygiene	Training and enforcement in good personal hygiene, daily washing of protective clothes and cleaning of equipment Prohibition of eating, drinking and smoking during travel, work or before decontamination Discipline SSW personnel that do not follow proper procedures in all aspects of operations (handling, spraying, hygiene, cleanup)	Training once prior to campaign, continuous reinforcement and enforcement of good personal hygiene	• Two uniforms and PPE issued to each spray operator and one set cleaned each day • No eating, drinking or smoking witnessed during operations or prior to washing • Adequate numbers of shower/bathing facilities available • Shower or bath taken,	Spray team supervisors, spray team leaders, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
			face/neck and hands washed with soap and water.	
Worker exposure from spills occurring during pesticide preparation. If spills in the vicinity of homes being sprayed for IRS are not properly cleaned up, subsequent resident exposures may also be of concern	Implement BMPs to minimize worker and resident exposures to pesticides from spills. Preparation of pesticides in a location outside of the homes being sprayed, and proper maintenance of tanks, lines, and nozzles to minimize dripping during application, are appropriate precautions for reducing exposures due to leaks and spills.	Continuous	• Health complaints from workers and beneficiaries • Visual observed spills	Implementing partners, spray operators supervisors
SSW personnel and/or community exposure due to poor waste management procedures	Procurement of barrels for progressive rinse, and wash-tubs for personal hygiene; inscription of equipment as District Health Office property to deter sale and domestic use in event of pilferage Collection, counting, and comparing number of empty sachets to disbursement records Collection of worn/torn gloves and masks Shipment of all wastes to authorized incinerator, destruction witnessed by Ministry of Health Official	Once prior to campaign Continuous	• Purchase records, inspection reports, waste disposal records from incinerator	District health officials, Implementing partners
Exposure of residents needing physical assistance during spray operations	Communities establish system to assist the elderly and disabled in removing self and goods from the household. Spray operators enforce removal of household goods	Train operators once prior to campaign Continuous enforcement	• IEC campaign adequately addresses issues surrounding the elderly and disabled	District, County, Parish, and Village leaders
Fetal/Infant Exposure due to maternal exposure on spray team Fetal Exposure – Pregnant	Training of stockroom, spray, and wash, (SSW) teams. Pregnancy tests as eligibility criteria for SSW teams;	Once prior to campaign, during campaign as necessary	• Pregnancy test results • Written confirmation from all female SWS workers that they are not	Spray team supervisors, spray team leaders, District heath officials, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
women in contact with pesticides	Prohibition of breastfeeding women on SSW teams; Education of women regarding risks of exposure Completion of consent forms Assign pregnant women to tasks that have no occupational exposure to insecticides.		breastfeeding • Signed consent forms from all female SSW workers • Number of females reassigned	
Exposure of aged, infirm, pregnant women or fetus, due to inability to leave the home during spraying	Prohibition of spraying in homes where seriously infirm or immobile persons, or pregnant women are living who cannot move outside the home *and* stay outside the home during, and 4 hours after spraying	Continuous	• Residents outside house during spraying • Residents stay outside for four hours after spraying Number of houses not sprayed due to resident immobility	Spray team leaders and supervisors, residents, spray personnel
Unacceptable risk to residents from exposure to IRS residual of pirimiphos-methyl on wall surfaces.	Apply pirimiphos-methyl with caution in accordance with strict best management practices as outlined in the Best Management Practices Manual for IRS. Collect samples of surface material from sprayed walls to refine the results the post-IRS resident exposure risk assessment. Consider collecting samples of floor sweepings to determine whether incidental ingestion and/or dermal absorption of IRS pesticides from residual pesticide on floors may be a significant contributor to overall post-IRS resident exposure.	Continuous	• Excess spray causing dripping on floor or on other surfaces	Implementing partner and supervisors
Significant risks to households from IRS with	1. *Do not conduct IRS with DDT in such households*	During next round of IRS.	• Site visits to households before spraying DDT to	Implementing partner, supervisors

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
DDT from eating home raised chicken	2. *Monitor DDT levels in home raised chickens* 3. *Consider monitoring DDT levels in chicken meat and eggs where chicken range in and around sprayed homes.*		observe home raised chickens • Continuous monitoring during DDT spraying program	
Significant risks to nursing infants from IRS with DDT from such households.	1. *Do not spray DDT in homes with pregnant or nursing women.* 2. *Use alternative chemical in IRS in such households.* 3. *Consider monitoring nursing infants.*	Continuous	• Continuous monitoring during DDT spraying program	Implementing partner, supervisors
Pesticide contamination of water resources, (groundwater, rivers, streams, lakes) Groundwater contamination from pesticide disposal in soak pits.	Do not spray any residences within 100 meters of principle water resources (other interventions should be implemented such as LLINs or wall lining) Do not dispose of any pesticides anywhere other than IRS triple rinse wash system Appropriately locate soak pits Avoid sandy soils and ensure water sources are not directly down gradient from soak pits. Dilute pesticides before disposal in soak pits. Dispose of DDT effluent in designated evaporation tanks only.	Continuous	• Evidence of environmental contamination (fish, bird, or bee kills), discoloration or turbidity of water	Spray team leaders, supervisors, district environmental officers, Implementing partners environmental compliance officer
Loss of biodiversity due to pesticide contamination	Do not spray or wash near sensitive areas or critical habitat (sensitive areas and critical habitats must be	Continuous	• Individual organism fatalities or impairment	Spray team leaders, supervisors, district environmental officers, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
	identified before activities commence)			environmental compliance officer
Farm, aquaculture or apiary contamination	Train farmers, fish farmers and beekeepers in target areas to guard against contamination of agri/aquaculture or apiary equipment, and to ensure sweeping and disposal of floor residue and dead after IRS in pit latrines prior to storing equipment in home. Train SSW workers on the dangers of pesticides to food, fish, birds, and bees	Once prior to campaign	• Number of post-spraying complaints from agri-aquaculture or apiary practitioners in target area • Reports of fish or bee kills	Spray team leaders and supervisors, spray personnel, Implementing partners
Spray operations have no/reduced impact on vector due to pesticide quality	Collect insecticide samples and test to ensure quality control Supervise and monitor pesticide make-up procedures	Periodic spot sampling Continuous monitoring by spray team leaders and supervisors	• Pesticide meets specifications • Spray operator usage reports reflect proper house/sachet ratio	Implementing partners, team leaders and supervisors
Loss of efficacy of pesticides due to continuous or inappropriate use	Use pesticide rotation or mosaicing protocol to minimize development of resistance to insecticides. Avoid agricultural use of health-based pesticides. Identify and implement best management practices to avoid public health pesticides being used for agriculture purposes. Resistance monitoring should be conducted in areas where large quantities of pesticides are used	Continuously re-assess pesticide to be used based on entomological monitoring The potential adverse economic impacts of the diversion of public health pesticides to the private sector must be addressed through monitoring and mitigation activities in the program. Conduct capacity building among	• Protocol developed	Implementing partners.

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
		MOAs, Ministries of Health (MOHs) and the Department of Agriculture		
Vector develops resistance to insecticide used	Change pesticide used Integrate the monitoring of mosquito resistance to pesticides into malaria and mosquito control programs during the planning and development stage, Conduct resistance monitoring in areas where large quantities of pesticides are used for agricultural crops and are targeted for malaria vector control to help develop strategies tailored to the area Manage resistance using these suggested approaches: • Use of non-chemical control methods, either alone or as a supplementary measure, in the seasons or areas in which they are applicable and cost-effective. • Limitation of pesticide use to areas with high levels of disease transmission. • Use of adulticides rather then larvicides resulting in approximately half the selection pressure for resistance. • Rotation among unrelated insecticides according to a pre-	Monitoring resistance before, during, and after each campaign. Once Periodically according to best practices.	• Monitoring results presented in end-of-round report • Planning and development documents must include mosquito resistance monitoring plans. • Periodic review of monitoring results	Implementing partners MEO

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
	arranged plan based on knowledge of the likelihood of resistance developing to each compound. • Choice of a compound that has been found by experience to select for a narrow spectrum of resistance rather than a broad one. • Use of mixtures or mosaic treatment with unrelated compounds.			
SSW worker or community exposure, or environmental contamination due to negligence	Take disciplinary action against SSW workers that do not follow proper procedure in all aspects of operations (handling, spraying, hygiene, cleanup) up to and including discharge from duties	Continuous monitoring throughout campaign, immediate action upon discovery of non-conformance with procedures	• Good hiring and management practices • Adequate supervisor to team leader to spray operator ratio • Number and severity of incidents reported	Spray team supervisors, spray team leaders, Implementing partners, District Officials
Community exposure, or environmental contamination post- campaign due to inadequate de-mobilization	Spray equipment, uniforms, PPE, wash equipment get a final cleaning at end of campaign and are securely stored Check expiration dates on all leftover pesticide. Transfer any unused pesticide to District secured warehouse for disposal if expired, or use in subsequent spray round(s).	Once at end of campaign	• Presence of adequate facilities for end of campaign cleaning and storage • Visual observance of proper de-mobilization • All equipment cleaned and properly stored	District health teams, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Community exposure due to residuals in vehicles used for pesticide transport	End-of-program cleaning/decontamination of interior and exterior of vehicles	Once after campaign	• Interiors and exteriors of vehicles cleaned	Drivers/Rental company

2) LLIN ACTIVITIES

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Driver and/or community exposure, or environmental contamination due to improper transport of LLINs	Driver training according to FAO recommendations Provision of appropriate equipment (reliable vehicle with side walls capable of negotiating rugged roads, tie-downs, packing materials, tarps) Cautious driving while transporting LLINs In case of accident, completion of accident and corrective action report	Once prior to campaign, reinforcement as needed Continuous	• Procedures being followed • Demonstrated knowledge • Existence of training materials • Absence of vehicle accidents • Vehicle condition	Drivers, Implementing partners
Environmental Contamination due to improper siting or construction of storage facilities	Use site qualification checklist. Locate storage facilities on high ground, above floodplains, away from sensitive receptors Use appropriate construction materials as specified in FAO recommendations	Once prior to campaign	• Storage facilities outside of floodplain and away from sensitive receptors • Constructed of suitable material • Adequately ventilated • Adequate storage space	District Environmental Officers, Implementing partner
Storekeeper and/or community exposure or environmental contamination due to improper storage or pilferage	Provision of secure storage facilities Training of storekeepers, team leaders and supervisors according to FAO recommendations	Once prior to campaign Continuous	• Dedicated and trained storekeeper • Stock records up-to-date • temperature measured and recorded	Storekeeper, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
			• Facility physically secure, padlocked and guarded when not in use • No fire, flame, smoking or eating allowed in storage areas	
Acute effects of pesticide toxicity go untreated	If skin itches , wash with soap and water, for eye irritation, flush eyes with water. For respiratory irritation, leave the home for fresh air. For ingestion, or if symptoms persist, contact program staff or go to nearest health facility.	Training on symptoms and responses prior to each campaign Complaints from households	• Demonstrated knowledge of signs and symptoms of poisoning, emergency treatment, and referral protocol by supervisors, • Antidotes and treatment medicines available at health facilities	District health officials, and Implementing partners
Residential Exposure from contaminated household goods, food crops, and fish	Training of household on proper use of the LLIN IEC Campaign, instruct residents to: • How to properly hang and use the LLIN • Proper maintenance (washing and mending) of the LLIN • Options for proper use of LLIN once it has lost its efficacy (after 3 years, or cannot be properly mended) such as for window screens, eave screens, etc.	Training and communication program prior to campaign,	• IEC materials developed and include specific instructions • IEC materials delivered in appropriate fashion • LLINs are being used appropriately • No observed or reported misuse	District Environment Office, NEMA, EPA, Implementing partners, USAID
Failure to realize benefits of LLIN/ behavior change	Train residents to continue using bed nets for protection against malaria,	Prior to each campaign	• Continued bed net use	Village and district leaders
Community and environmental exposure due to poor waste management procedures	Collection of non-viable LLINs Shipment of all wastes to authorized incinerator, destruction witnessed by Ministry of Health Official *(There is no information on the quantity of net material that will*	Once prior to campaign Continuous Monitor the amount of waste accumulating three	• Purchase records, inspection reports, waste disposal records from incinerator	District health officials, Implementing partners PMI will work with international organization to develop a strategy/system to manage net waste

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
	eventually need to be collected and disposed of. WHO is currently conducting a study to identify the proportion of overall plastic waste that will occur after the nets lose their efficacy.)	years after net distribution PMI will work with international organizations to develop a strategy/system to manage net waste.		
Infant exposure to LLIN pesticides (oral and dermal)	Training of households to not allow infants to suckle or chew on LLINs Education of women regarding risks of exposure	Once prior to campaign, during campaign as necessary	• No complaints of rashes on infants, or signs of illness	District heath officials, Implementing partners
Adverse impact on biodiversity in aquatic ecosystems through removal of important juvenile fish and other aquatic species from fishing with LLIN/ITNs. Pesticide contamination of water resources, (groundwater, rivers, streams, lakes)	Monitor how the LLIN/ITNs are being used. Include an educational program on appropriate use during distribution campaigns. Label nets appropriately with use and care instructions. Train household on proper wash methods Train households on proper use of LLIN (no fishing, etc.)	Continuous	• Evidence of environmental contamination (fish, bird, or bee kills), discoloration or turbidity of water	District environmental officers, Implementing partners environmental compliance officer
Loss of biodiversity due to pesticide contamination For surface waters with a volume greater than 100,000 liters (i.e small pond one meter deep with area of 100 square meters), minimal impact. For surface water with a	Do not dispose of wash water near sensitive areas or critical habitat (sensitive areas and critical habitats must be identified before activities commence) Train households on proper use of LLIN (no fishing, etc.)	Continuous	• Individual organism fatalities or impairment	District environmental officers, Implementing partners environmental compliance officer

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
volume less than 100,000 liters, acute toxicity to sensitive aquatic species.				
Pesticide contamination via washing of or fishing with LLINs directly in surface water. (Adverse impact on biodiversity in aquatic ecosystems through removal of important juvenile fish and other aquatic species from fishing with LLIN/ITNs)	Monitor how the LLIN/ITNs are being used. Include an educational program on appropriate use during distribution campaigns. Label nets appropriately with use and care instructions Perform ecological habitat review to determine if the water body is suitable habitat for susceptible aquatic species. 1) If the habitat is highly disturbed and does not support suitable habitat, then the concerns for lethality do not exist. 2) If, however, the ecosystem is healthy, then the risk of adverse impacts from LLIN/ITN washing/fishing may be an issue and the nature of the habitat should be observed (including data on the species present in the surface water, the volume of surface water, and the flow rate, if not a closed system).	Continuous	• Individual organism fatalities or impairment	District environmental officers, Implementing partners environmental compliance officer
Farm, aquaculture or apiary contamination	Train farmers, fish farmers and beekeepers in target areas to guard against contamination of agri/aquaculture or apiary equipment by not coming in contact with LLIN Train households on the dangers of pesticides to food, fish, birds, and bees Provide information to net users on unintended uses of nets that reflect the local environment	Once prior to campaign	• Number of complaints from agri-aquaculture or apiary practitioners in target area • Reports of fish or bee kills	Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Malaria vector develops resistance to insecticide used for LLINs. Pyrethroids are the only pesticide presently used for LLINs, (Pyrethroid resistance already exists in some major malaria vectors, especially in Africa.)	Use new variations of LLINs proposed by manufacturers to address the resistance issues. Use existing LLINs with pyrethroids and monitor efficacy	Monitoring resistance before, during, and after each campaign. Monitor potential impact of resistance on net efficacy.	• Monitoring results presented	Implementing partners, USAID
Community exposure due to residuals in vehicles used for LLIN transport	End-of-program distribution cleaning/decontamination of interior and exterior of vehicles	Once after campaign	• Interiors and exteriors of vehicles cleaned	Drivers/Rental company

3) LARVICIDING ACTIVITIES

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Driver and/or community exposure, or environmental contamination due to improper transport of larvicide agent	Driver training according to FAO recommendations Provision of appropriate equipment (reliable vehicle with side walls capable of negotiating rugged roads, tie-downs, packing materials, tarps, spill clean-up kit) Cautious driving while transporting chemicals Checking for and repairing leaks from spray equipment prior to transport In case of accident, completion of accident and corrective action report	Once prior to campaign, reinforcement as needed Continuous	• Procedures being followed • Demonstrated knowledge • Existence of training materials • Absence of vehicle accidents • Vehicle condition • Absence of spills during insecticide transport	Drivers, Implementing partners, Pesticide distributors, team leaders

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Environmental Contamination due to improper siting or construction of storage and wash facilities	Use site qualification checklist. Locate storage and wash facilities on high ground, above floodplains, away from sensitive receptors (water bodies, birds, bees, fish, children, etc.). Use appropriate construction materials as specified in FAO recommendations	Once prior to campaign	• Storage and wash facilities for larvicide equipment outside of floodplain and away from sensitive receptors (birds, bees fish, children, etc.) • Constructed of suitable material • Adequately ventilated • Adequate storage space	District Environmental Officers, Implementing partner
Storekeeper and/or community exposure or environmental contamination due to improper storage or pilferage (Cont.) Storekeeper and/or community exposure or environmental contamination due to improper storage or pilferage	Provision of secure storage facilities Training of storekeepers, team leaders and supervisors according to FAO recommendations Tracking of larvicide agents issued, used, and returned Storekeepers trained to not issue larvicides for any unauthorized use	Once prior to campaign Continuous	• Dedicated and trained storekeeper who demonstrates knowledge and uses correct procedures • Stock records up-to-date • Stocks orderly, rotation system in place • Expiration dates observed • Empty larvicide containers collected, counted and reconciled with amounts issued • Storehouse temperature measured and recorded • No leaks or spills evident • Insecticides not stored in same room with food, or medicine, or in inhabited spaces • Facility physically secure, padlocked and guarded when not in use	Storekeeper, supervisors, team leaders, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
			• No fire, flame, smoking or eating allowed in storage areas	
Personnel handling organophosphate pesticides (OPs) (Temephos) experience cholinesterase inhibition (CI) due to exposure. (Symptoms include tiredness, weakness, dizziness, nausea and blurred vision, headache, sweating, tearing, drooling, vomiting, tunnel vision, and twitching, abdominal cramps, muscular tremors, staggering gait)	For all larvicides, all storage, application equipment (sprayers and granule spreaders, etc.) and wash teams receive training in recognizing effects of pesticide poisoning, remain alert to symptoms amongst their co-workers and respond appropriately. PMI will evaluate various approaches to monitoring sprayer exposure to organophosphate pesticides and will develop protocols, based on these evaluations, for a monitoring program.	Training: Included in pre-campaign orientation, and in training for new personnel. PMI will use the protocols developed to inform the implementation of PMI program monitoring for organophosphate pesticides.	• Demonstrated knowledge of symptoms of poisoning, emergency treatment, and referral protocol by supervisors, team leaders • Antidotes available at health facilities	MOH, District Health Officers, Implementing partners
Acute effects of pesticide toxicity go untreated (Symptoms include tiredness, weakness, dizziness, nausea, blurred vision, headache, sweating, tearing, drooling, vomiting, tunnel vision, twitching, abdominal cramps, muscular tremors, staggering gait)	Employ CI testing as needed Team leaders, storekeepers trained to recognize symptoms and enforce treatment Ensure treatment medicines are available at District health centers. If skin itches, wash with soap and water, for eye irritation, flush eyes with water. For respiratory irritation, breath fresh air. For ingestion, or if symptoms persist, contact program staff or go to nearest health facility.	Training on symptoms and responses prior to each campaign Continuous observation, reinforcement and enforcement of treatment protocols	• Demonstrated knowledge of signs and symptoms of poisoning, emergency treatment, and referral protocol by supervisors, team leaders, storekeepers, larvicide applicators and residents • CI test results • Antidotes and treatment medicines available at health facilities	Team supervisors, team leaders. District health officials, and Implementing partners
Exposure of workers and/or community during application (spray or granule spreaders) due to improper application procedures	Training of team leaders supervisors, and health workers according to MOH and WHOPES recommendations Proper assembly and calibration of	Once prior to campaign	• Spray operators, team leaders supervisors and health workers display knowledge by following procedures at all times	Team supervisors, spray team leaders, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Failure to realize/receive the benefits of larviciding due to improper application procedures	spray equipment, granule spreaders Proper cleanup and equipment storage procedures Discipline workers that do not follow proper procedure in all aspects of operations (handling, spraying, hygiene, cleanup)	Continuous		
Workers or community exposure, or environmental contamination due to equipment or PPE issues	Use of sprayers and other larvicide equipment maintained according to WHOPES specifications Proper assembly and calibration of equipment Procurement and proper use of PPE by all persons in contact with pesticides PPE should include facemask, gloves, and overalls.	Continuous	• All PPE as specified in WHOPES recommendations in good condition and worn by all personnel in contact with pesticides • Condition of equipment	Team supervisors, team leaders, Implementing partners
Staff and community exposure in vehicle used to transport workers and/or larvicides	Frequent washing interior and exterior of program vehicles after larvicide transport using soap and water and PPE	Continuous	• Vehicle condition	Cooper, team supervisors, team leaders, Implementing partners
Larviciding personnel exposure due to poor personal hygiene	Training and enforcement in good personal hygiene, daily washing of protective clothes and cleaning of equipment Prohibition of eating, drinking and smoking during travel, work or before decontamination Discipline personnel that do not follow proper procedures in all aspects of operations (handling, spraying, hygiene, cleanup)	Training once prior to campaign, continuous reinforcement and enforcement of good personal hygiene	• PPE issued to each person applying larvicide agent • No eating, drinking or smoking witnessed during operations or prior to washing • Adequate numbers of shower/bathing facilities available • Shower or bath taken, face/neck and hands	Team supervisors, team leaders, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
			washed with soap and water.	
Larviciding personnel and/or community exposure due to poor waste management procedures	Procurement of barrels for progressive rinse, and wash-tubs for personal hygiene; inscription of equipment as District Health Office property to deter sale and domestic use in event of pilferage Collection, counting, and comparing number of empty larvicide containers to disbursement records Collection of worn/torn gloves and masks Shipment of all wastes to authorized incinerator, destruction witnessed by Ministry of Health Official	Once prior to campaign Continuous	• Purchase records, inspection reports, waste disposal records from incinerator	District health officials, Implementing partners
Fetal/Infant Exposure due to maternal exposure on team Fetal Exposure – Pregnant women in contact with larvicides	Training of stockroom, spray, and wash, teams. Pregnancy tests as eligibility criteria for larviciding teams; Prohibition of breastfeeding women on teams; Education of women regarding risks of exposure Completion of consent forms Assign pregnant women to tasks that have no occupational exposure to insecticides.	Once prior to campaign, during campaign as necessary	• Pregnancy test results • Written confirmation from all female workers that they are not breastfeeding • Signed consent forms from all female workers • Number of females reassigned	Team supervisors, spray team leaders, District heath officials, Implementing partners
Pesticide contamination of water resources, (groundwater, rivers, streams, lakes)	Use appropriate larvicide for the type of mosquito habitat and at recommended amount Monitor weather forecasts and do not apply larvicides before or during rain events	Continuous Weekly	• Evidence of environmental contamination (fish, bird, or bee kills), discoloration or turbidity of water • Monitor water quality of	Team leaders, supervisors, district environmental officers, Implementing partners environmental compliance officer

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
			potable water located near larvicide applications • Reports of fish or other non-target kills	
Loss of biodiversity due to pesticide contamination	Do not apply larvicide agents near sensitive areas or critical habitat (sensitive areas and critical habitats must be identified before activities commence) Do not apply larvicide agents to water bodies with volumes smaller than 13,000 liters and with habitat for sensitive non-target aquatic species. Use appropriate pesticide for the type of mosquito habitat and at recommended amount. Perform ecological habitat review to determine if the water body is suitable habitat for susceptible aquatic species. 1) If the habitat is highly disturbed and does not support suitable habitat, then the concerns for lethality do not exist. 2) If, however, the ecosystem is healthy, then the risk of adverse impacts from larvaciding may be an issue and the nature of the habitat should be observed (including data on the species present in the surface water, the volume of surface water, and the flow rate, if not a closed system).	Continuous	• Individual organism fatalities or impairment	Team leaders, supervisors, district environmental officers, Implementing partners environmental compliance officer

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Farm, aquaculture or apiary contamination	Use appropriate larvicide for the type of mosquito habitat and at recommended amount Monitor weather forecasts and do not apply larvicides before or during rain events	Continuous	• Number of post-spraying complaints from agri-aquaculture or apiary practitioners in target area • Reports of fish or other non-target kills	Team leaders and supervisors, personnel, Implementing partners
Spray operations have no/reduced impact on vector due to larvicide quality	Collect insecticide samples and test to ensure quality control Supervise and monitor larviciding procedures	Periodic spot sampling Continuous monitoring by spray team leaders and supervisors	• Pesticide meets specifications • Spray operator usage reports reflect proper house/sachet ratio	Implementing partners, team leaders and supervisors
Loss of efficacy of pesticides due to continuous or inappropriate use	Use appropriate larvicide for the type of mosquito habitat and at recommended amount	Continuously re-assess larvicide to be used based on entomological monitoring	• Protocol developed	Implementing partners.
Vector develops resistance to larvicide used	Use appropriate larvicide for the type of mosquito habitat and at recommended amount	Monitoring resistance before, during, and after each campaign.	• Monitoring results presented in end-of-round report	Implementing partners
Worker or community exposure, or environmental contamination due to negligence	Take disciplinary action against workers that do not follow proper procedure in all aspects of operations (handling, spraying, hygiene, cleanup) up to and including discharge from duties	Continuous monitoring throughout campaign, immediate action upon discovery of non-conformance with procedures	• Good hiring and management practices • Adequate supervisor to team leader to operator ratio • Number and severity of incidents reported	Team supervisors, spray team leaders, Implementing partners, District Officials
Community exposure, or environmental contamination post- campaign due to inadequate de-mobilization	Spray equipment, uniforms, PPE, wash equipment, , etc. get a final cleaning at end of campaign and are securely stored Check expiration dates on all leftover larvicide. Transfer any unused pesticide to District secured warehouse for disposal if expired, or	Once at end of campaign	• Presence of adequate facilities for end of campaign cleaning and storage • Visual observance of proper de-mobilization • All equipment cleaned	District health teams, Implementing partners

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
	use in subsequent larviciding campaigns.		and properly stored	
Community exposure due to residuals in vehicles used for larvicide transport	End-of-program cleaning/decontamination of interior and exterior of vehicles	Once after campaign	• Interiors and exteriors of vehicles cleaned	Drivers/Rental company

4) ENVIRONMENTAL MANAGEMENT METHODS ACTIVITIES

The following is a partial mitigation and monitoring plan for environmental management methods, more specific measures should be included that are method and site specific

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Community exposure or environmental contamination due to use of machinery	Properly maintain machinery Proper location identified for storage of machinery	Continuous	• No oil or gas spillage • No impact to surrounding areas	District environmental officers, Implementing partners environmental compliance officer
Contamination of water resources, (groundwater, rivers, streams, lakes)	Do not fill sites that are water resources (e.g. impoundment construction) Intercept and control water runoff from disturbed sites Re-grade and re-vegetate disturbed and bare soil Do not flood water resources with salt water (i.e. salt water flooding)	At the beginning of the site selection Continuous	• Evidence of environmental contamination (fish, bird, or bee kills), discoloration or turbidity of water • Lack of water for agriculture or personal use	District environmental officers, Implementing partners environmental compliance officer
Produce areas of bare soil that cause erosion, siltation, changes in natural water flow and damage to aquatic ecosystems	Minimize disturbance to only mosquito habitat areas. Clear without destroying large plants and other native species that can be transplanted and used to re-vegetate the impacted area.	Continuous	• Siltation in water courses • Appearance of gulleys • Drying of important, not targeted wetlands	District environmental officers, Implementing partners environmental compliance officer

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
	Move earth and vegetation only during dry periods. Store topsoil for re-spreading.			
Block water courses	Re-grade to allow natural water flow Avoid impoundment construction	At the end of a method that involved changes to the topography	• Water backed up and flooding • Runoff into fields and homes	Implementing partners
Loss of biodiversity due to poorly implemented method or improper identification of project sites	Do not fill in sensitive areas or critical habitat (sensitive areas and critical habitats must be identified before activities commence) Do not introduce non-native larvivorous fish in water bodies with habitat for sensitive species Take special precaution to prevent dumping of debris, oil, fuel, cement and similar harmful materials	At the beginning of the site selection Continuous	• Individual organism fatalities or impairment	District environmental officers, Implementing partners environmental compliance officer
Change of ecosystem compositions or loss of habitats	Proper identification of sites to receive management method Do not conduct salt water flooding		• Individual organism fatalities or impairment Polluted water • Loss of available water	
Decrease ground water and surface water quality availability	Minimize impact to important wetlands Proper identification of sites to receive management method Minimize impoundment construction Do not conduct salt water flooding			District environmental officers, Implementing partners environmental compliance officer
Increase risk of flooding	Minimize impact to important wetlands Proper identification of sites to receive management method			District environmental officers, Implementing partners environmental compliance officer
Loss of beneficial aquatic	Do not use invasive fish for vector	At the beginning of	• Individual organism	District environmental

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
species and fish	control (i.e. larvivorous fish), or only use in a contained site Conduct site specific surveys to identify affected plant and animal species to determine if selected approach is appropriate or outweighs risks.	the site selection	fatalities or impairment	officers, Implementing partners environmental compliance officer
Farm, aquaculture or apiary contamination	Proper identification of sites to receive management method	At the beginning of the site selection	• Number complaints from agri-aquaculture or apiary practitioners in target area • Reports of fish or bee kills	district environmental officers, Implementing partners environmental compliance officer

5) WALL LINING ACTIVITIES

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Driver and/or community exposure, or environmental contamination due to improper transport of wall lining	Driver training according to FAO recommendations Provision of appropriate equipment (reliable vehicle with side walls capable of negotiating rugged roads, tie-downs, packing materials, tarps) Cautious driving while transporting wall lining In case of accident, completion of accident and corrective action report	Once prior to campaign, reinforcement as needed Continuous	• Procedures being followed • Demonstrated knowledge • Existence of training materials • Absence of vehicle accidents • Vehicle condition	Drivers, Implementing partners
Environmental Contamination due to improper siting or construction of storage facilities	Use site qualification checklist. Locate storage facilities on high ground, above floodplains, away from sensitive receptors Use appropriate construction materials	Once prior to campaign	• Storage facilities outside of floodplain and away from sensitive receptors • Constructed of suitable material	District Environmental Officers, Implementing partner

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
	as specified in FAO recommendations		• Adequately ventilated • Adequate storage space	
Storekeeper and/or community exposure or environmental contamination due to improper storage or pilferage	Provision of secure storage facilities Training of storekeepers, team leaders and supervisors according to FAO recommendations	Once prior to campaign Continuous	• Dedicated and trained storekeeper • Stock records up-to-date • temperature measured and recorded • Facility physically secure, padlocked and guarded when not in use • No fire, flame, smoking or eating allowed in storage areas	Storekeeper, Implementing partners
Exposure of workers and/or community during wall lining installation operations due to improper procedures Failure to realize/receive the benefits of wall lining due to improper installation	Training of installers, team leaders supervisors, and health workers according to MOH and WHOPES recommendations Proper installation of wall lining Proper use of PPE (gloves) Discipline installers that do not follow proper procedure in all aspects of operations (handling, hygiene, cleanup)	Once prior to campaign Continuous	• Installers, team leaders supervisors and health workers display knowledge by following procedures at all times • Proper installation of wall lining as per manufacturers recommendations	Exposure of SSW members and/or community during spray operations due to improper spray procedures Failure to realize/receive the benefits of wall lining due to improper installation
Acute effects of pesticide toxicity go untreated	If skin itches , wash with soap and water, for eye irritation, flush eyes with water. For respiratory irritation, leave the home for fresh air. For ingestion, or if symptoms persist, contact program staff or go to nearest health facility.	Training on symptoms and responses prior to each campaign Complaints from households	• Demonstrated knowledge of signs and symptoms of poisoning, emergency treatment, and referral protocol by supervisors, • Antidotes and treatment medicines available at health facilities	District health officials, and Implementing partners
Residential Exposure from contaminated household	Training of household on proper use of	Training and communication	• IEC materials developed and include specific	District Environment Office, NEMA, EPA, Implementing

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
goods, food crops, and fish	the wall lining IEC Campaign, instruct residents to: • How to properly hang the wall lining • Proper maintenance (washing and mending) of the wall lining	program prior to campaign,	instructions • IEC materials delivered in appropriate fashion • Wall linings are being used appropriately • No observed or reported misuse	partners, USAID
Community and environmental exposure due to poor waste management procedures	Collection of non-viable wall lining Shipment of all wastes to authorized incinerator, destruction witnessed by Ministry of Health Official Monitor amount of waste accumulating three years after distribution.	Once prior to campaign Continuous	• Purchase records, inspection reports, waste disposal records from incinerator	District health officials, Implementing partners
Infant exposure to wall lining pesticides (oral and dermal)	Training of households to not allow infants to suckle or chew on wall lining Education of women regarding risks of exposure	Once prior to campaign, during campaign as necessary	• No complaints of rashes on infants, or signs of illness	District heath officials, Implementing partners
Pesticide contamination of water resources, (groundwater, rivers, streams, lakes)	Train household on proper wash methods Train households on proper use of wall lining(no fishing, etc.)	Continuous	• Evidence of environmental contamination (fish, bird, or bee kills), discoloration or turbidity of water	District environmental officers, Implementing partners environmental compliance officer
Loss of biodiversity due to pesticide contamination	Do not dispose of wash water near sensitive areas or critical habitat Train households on proper use of wall lining	Continuous	• Individual organism fatalities or impairment	District environmental officers, Implementing partners environmental compliance officer

Negative Impact	Mitigation Activities	Monitoring Frequency	Monitoring Indicators	Implementation Responsibility
Farm, aquaculture or apiary contamination	Train farmers, fish farmers and beekeepers in target areas to guard against contamination of agri/aquaculture or apiary equipment by not coming in contact with wall lining Train households on the dangers of pesticides to food, fish, birds, and bees	Once prior to campaign	• Number of complaints from agri-aquaculture or apiary practitioners in target area • Reports of fish or bee kills	Implementing partners
Vector develops resistance to insecticide used	Pyrethroids are the only pesticide presently used for wall lining	Monitoring resistance before, during, and after each campaign. Monitor efficacy of wall lining as resistance changes.	• Monitoring results presented	Implementing partners, USAID
Community exposure due to residuals in vehicles used for wall lining transport	End-of-program distribution cleaning/decontamination of interior and exterior of vehicles	Once after campaign	• Interiors and exteriors of vehicles cleaned	Drivers/Rental company

ANNEX M. PUBLIC REVIEW COMMENTS

The following are comments that were received during the 30-day public review process of the Draft PEA. Comments that were provided through "track changes" in a copy of the document have not been included in this Annex, but were considered when revising the PEA.

Jason D. Clark
Public Health and Forestry Business Unit
Valent BioSciences Corporation

August 31, 2011

Steve Krause asked that I follow-up with you regarding the issues/completeness associated with the 2011 draft PEA. Our Regulatory Affairs and Development staff is currently reviewing the document in detail and we should have a formal response to you within a week. However, we want to outline some key issues upfront that caught our immediate attention:

- Omission of *Bacillus thuringiensis* subsp. *israelensis* (Bti) and *Bacillus sphaericus* (Bs) from all key larvicide sections in this document outside a cursory definition of these bacterial larvicides.
- Claim that Spinosad does not affect non-target aquatic organisms. As I am sure you are already aware, Spinosad is used in the agricultural sector and it is well documented that this biochemical affects a broader range of arthropods and aquatic non-targets than other larvicides, specifically bacterial larvicides.
- Claim that Spinosad is a "bacterial larvicide". To clarify, the metabolites that make up the Spinosad active ingredient are more simply biochemicals produced through fermentation and then isolated. Bti and Bs are fermented and all "solids and solubles" from the fermentation are utilized in Bti and Bs larvicide products. As such, Bti and Bs represent the more classic definition of a "bacterial larvicide".
- Claim that larvicides affect non-target aquatic organisms and this is of concern. This statement is of course more relevant if Bti and Bs are not included in the discussion, if more broad-spectrum larvicides such as temephos, oils/MMFs and spinosad are what define "larvicides". However, the target specificity of bacterial larvicides (Bti - select insects in the order Diptera; Bs - mosquitoes only) clearly need to be considered when making envinronmental assessment statements about the LSM approach.
- Methoprene has the safest profile in container applications. Again, this statement is more relevant if Bti and Bs are not included in the discussion. However, Bti is recognized as holding the lowest risk profile of all larvicides that are WHOPES approved for direct applications to containers to control Dengue vectors.

I have attached a brief outline of the utility of Bti and Bs for control of malaria vectors and suppression of malaria transmission along with a references cited list. In addition, I have attached the USAID cost analysis report on the large-scale use of Larval Source Management in malaria control published in 2007. Hopefully these two documents will help pave the way for any follow-up dialogue we may have once our technical team provides their edits/comments to the PEA document.

We look forward to collaborating with your team on refining the LSM section.

Utility of the microbial mosquito larvicides *Bacillus thuringiensis israeliensis* strain AM65-52 (*Bti* AM65-52) and *Bacillus sphaericus 2362* strain ABTS-1743 (*Bs* ABTS-1743) for control of malaria vectors and suppression of malaria transmission.

Discovery, Activity, Target Specificity and Risk Profile

Bacillus thuringiensis israeliensis serotype H-14 (*Bti*), was isolated from mosquito larval habitats in Israel in 1976 and was found to have high larvicidal activity against *Aedes, Culex,* and *Anopheles spp.* mosquitoes (Goldberg 1977). Mosquitocidal strains of *Bacillus sphaericus* (*Bs*) have been isolated from various environmental substrates, and found to be very active against *Culex* and *Anopheles spp.* larvae (Singer 1990). Owing to their efficacy against vector and nuisance-fly species in the Order Diptera, Sub-Order Nematocera, *Bti* and *Bs* have become well established for control of nuisance and vector mosquito species world wide (Becker 1998, Lacey 2007). Due to their target specificity, *Bti* and *Bs* present very little risk to human health or the environment (Merritt 2005, Stark 2005, WHO 1999).

Development of *Bti* AM65-52 for Vector Control

VectoBac® formulations based on fermentation products of *Bacillus thuringiensis israeliensis* strain AM65-52 (*Bti* AM65-52) have been developed by Valent BioSciences Corporation (formerly Abbott Laboratories) for use by vector control professionals in a variety of settings around the world. Fermentation is carried out in an FDA inspected facility, and formulation of the products is carried out under strict ISO manufacturing guidelines. Formulations include aqueous suspension (AS), water dispersible granules (WG) and granules (G/GR). These products have been found to be highly effective for control vectors of onchocerciasis, dengue, West Nile virus, and malaria. *Bti* AM65-52 is the only *Bti* strain to have completed review under the WHOPES program, and VectoBac® WG is the only *Bti* formulation to have established manufacturing standards under WHOPES (WHO 2004, 2007).

Efficacy and Utility of *Bti* AM65-52 for Malaria Vector Control

Efficacy of VectoBac® mosquito larvicides for control of African malaria vectors has been demonstrated by several authors (Majori 1986, Mukiama 1989, Karch 1991&1992, Romi 1993, Shililu 2003, Fillinger 2004, WHO 2004, and Majambere 2007). A program based on weekly application of VectoBac® resulted in >92% suppression of adult malaria vectors and reduction in malaria EIR during a one-year period in the town of Mbita Point, Kenya (Fillinger 2006). Reduction in density and EIR of *An. funestus* was demonstrated in Ivory Coast (Tchicaya 2009).

Impacts of *Bti* AM65-52 Use on Malaria Transmission

Recent publications have indicated a very high potential for Larval Source Management (LSM) programs utilizing *Bti* to contribute to malaria control. Reduction in transmission of malaria in addition to that realized by deployment of ITN was demonstrated in the Kenya Highlands with routine VectoBac® treatments (Fillinger 2009). The Dar es Salaam Urban Malaria Control Program effectively reduced the risk of malaria transmission with routine VectoBac® treatments (Geissbühler 2009). VectoBac® applications by the Singapore Ministry of Defense contributed to elimination of malaria risk on a tropical island (Lee 2010).

Development of *Bs* ABTS-1743 for Vector Control

VectoLex® formulations based on *Bacillus sphaericus 2362* strain ABTS-17 (*Bs* ABTS-1743) have also been developed by Valent BioSciences Corporation (formerly Abbott Laboratories) for use by vector control professionals in a variety of settings around the world. Fermentation is carried out in an FDA inspected facility, and formulation of these products is carried out under strict ISO manufacturing guidelines. Formulations include granules (G/CG) and water dispersible granules (WDG). These products have been found to be highly effective for control of West Nile virus vectors in North America, and malaria vectors in Latin America.

Efficacy and Utility of *Bs* ABTS-1743 for Malaria Vector Control

Efficacy of VectoLex ® mosquito larvicides for control of key malaria vectors in Latin America has been demonstrated by several researchers (Suarez 1999, Berrocal 2000, Berti 2002, 2004, Moreno 2010). Residual efficacy ranging from 14 days to >45 days has been observed by these authors. Control of African malaria vectors has been demonstrated as well (Karch 1991, 1992, Barbazan 1997, Fillinger 2003, Shililu 2003 and Majambere 2007). In Maroua, Cameroon (Africa), routine treatments with VectoLex® larvicide was followed by a reduction in the Anopheles population and malaria cases at health centers (Barbazan 1998)

Cost of LSM Malaria Vector Control Programs Based on *Bti* and *Bs*

USAID commissioned an extensive economic evaluation of LSM based on the use of microbial larvicides in three different African settings. Results of this evaluation demonstrated that LSM with *Bti* AM65-52 in these settings will be comparable to that of ITN (Worral 2007)

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USAID Bureau for Europe and Eurasia

August 31, 2011

Europe and Eurasia Bureau Environmental Office Comments on Draft Updated Programmatic Environmental Assessment (PEA) for the Integrated Vector Management Programs for Malaria Vector Control

Section, Page	Text	Comment
5. Pesticide Procedures and Human Health and Environmental Consequences, 109-110	Table 5-28 Ranking of Environmental Management Interventions from Low Impact to High Impact	This table does not appear to be referenced in the text. Such reference is needed and should include a description of the methodology that was used to rank the interventions. Perhaps this methodology information is contained in the 2007 PEA, but there should be at least a couple sentence description here as well. Potential negative impacts in Table 5-28 do correlate closely with Table 6-5.

Section, Page	Text	Comment
		However, there does not appear to be a similar rationale for deciding which potential negative impacts for IRS, LLIN, and Larviciding are worthy of being addressed in Tables 6-1, 6-3, and 6-4. A description of this rationale would be helpful.
6. Mitigation and Monitoring, 137-138	The Recommended Mitigation Measures section should provide detailed descriptions of how mitigation measures should be planned for, implemented, monitored, and evaluated, and what action should be taken when mitigation activities are poorly implemented or fail. The section should also make evident the links between identified potential human health and environmental impacts and mitigation activities. SEAs should also include the appropriate elements of the EMMP and the mitigation measures that are relevant to the malaria control intervention(s) that have been selected for that particular country program. It is also important to factor in the reporting and monitoring activities and costs required by the Stockholm Convention if DDT is used in an IRS program. A comprehensive EMMP is included in Annex L.	It is not obvious what "Recommended Mitigation Measures" section is being referenced. Is it section 6.1.2. Mitigation Recommendations (note the different titles)? Also, should there be a higher fidelity correlation between the Negative Impacts in the Tables (e.g., 6-1, 6-3, 6-4, and 6-5) and the EMMPs in Annex L? If the reader should not expect there to be high correlation, some explanation of the reason why this expectation will not be met would be useful.
Annex L, L-7, L-11, L-17	Negative impact: Loss of biodiversity due to pesticide contamination Mitigation: Do not spray or wash near sensitive areas or critical habitat Indicator: Species die-off	Several issues: 1. This statement appears to assume that sensitive areas and critical habitat will be identified before spraying or washing, but there is no provision for that in the M&M Plan; 2. Instead of "species die-off" we think they mean "individual organism fatalities or impairment." At the next higher level it would be "population die-off", even then the indicator seems to only indicate complete failure. We cannot imagine a case where the indicator would be "die-off of the entire species." In any of these cases, there would need to be some analysis to attribute loss of individuals or species to the pesticide spraying/washing. Also, perhaps a there should be a recommendation in Sections 11.1 Planning or 11.2 SEA Guidelines that sensitive areas and critical habitat need to be identified before spraying or washing activities are initiated.
Annex L, L-7	Negative impact: Pesticide contamination of water resources, (groundwater, rivers, streams, lakes)	Is not spraying residences within 100 m of water resources a feasible mitigation. Will not these residences be some of the highest risk? Will not

Section, Page	Text	Comment
	Mitigation: Do not spray any residences within 100 meters of water resources	these residences serve as reservoir for the malaria vector?
Annex L, L-19	Negative impact: Loss of biodiversity due to poorly implemented method or improper identification of project sites Mitigation: Do not fill in sensitive areas or critical habitat and take special precaution to prevent dumping of debris, oil, fuel, cement and similar harmful materials Indicator: Species die-off	Comments similar to those for Annex L, L-7, L-11, L-17 above
Annex L, L-19	Negative impact: Change of ecosystem compositions or loss of habitats Indicator: Species die-off	Suggest indicator be "individual organism fatalities or impairment" or something similar (see comments above)
Annex L, L-19	Negative impact: Loose of beneficial aquatic species and fish Indicator: Species die-off	Change "loose" to "loss" and suggest indicator be "individual organism fatalities or impairment" or something similar (see above comments)
Annex L, L-22	Negative impact: Loss of biodiversity due to pesticide contamination Indicator: Species die-off	Suggest indicator be "individual organism fatalities or impairment" or something similar (see comments above)

Dr. Tom McLean
Chief Operating Officer
IVCC

September 5, 2011

Please find attached a response to the draft PEA from IVCC.

The PEA considers the role of biomonitoring in the use of Actellic CS.

As you may be aware IVCC supported the development of Actellic CS in our role as a PDP focused on bringing resistance breaking insecticides to market.

As part of our due diligence in this process IVCC undertook an independent assessment of the toxicity issues that should be considered for this product. I hope that you may find the observations made by our independent advisor on toxicity and risk assessment helpful in considering the draft PEA.

I will be happy to discuss this with you and expand on IVCC s role as an independent Not For Profit Charity.

RESPONSE TO THE DRAFT PEA REPORT (USAID, 2011) CONCERNING THE RISK ASSESSMENT OF PIRIMIPHOS-METHYL FOR INDOOR RESIDUAL SPRAYING

Introduction

The Draft Updated Programmatic Environmental Assessment (PEA) for the Integrated Vector Management Programs for Malaria Vector Control is available for public review and comment (USAID, 2011).1 The approaches for assessing the human health and environmental risks of vector control products are supported. Where additional data on hazard or exposure are available these should be used to replace the default values in order to further refine the estimated risks. It is in this context that the following response has been prepared with regard to the human health risk assessment of pirimiphos-methyl.

1) USAID (2011). Integrated Vector Management Programs For Malaria Vector Control Programmatic Environmental Assessment Update, Draft, August 2011
2) WHO (2011). Generic risk assessment model for indoor and outdoor space spraying of insecticides. WHO/HTM/NTD/WHOPES/2010.6 rev 1

The report notes that exposures of operators and residents to pirimiphos-methyl from indoor residual spraying (IRS) results in unacceptable levels of risk using updated parameters in the exposure assessment models. Among the mitigation measures considered the report notes that cholinesterase activity must be tested in personnel exposed to organophosphates, which includes pirimiphos-methyl, for health impact monitoring.

There are various factors that need to be considered in the risk assessment of pirimiphos-methyl and the purpose of this response is to show that pirimiphos-methyl is expected to result in acceptable risks to operators or residents from its application in IRS. Furthermore, on this basis it is considered that cholinesterase monitoring should not be a mandatory requirement for pirimiphos-methyl.

Pirimiphos-methyl risk assessment

Pirimiphos-methyl has relatively low toxicity compared with many other organophosphates. It is a WHOPES approved insecticide for IRS with an established history of safe use. The registrant (Syngenta) has recently developed a long lasting IRS capsule suspension (CS) formulation of pirimiphos-methyl and the company submitted a risk assessment to the WHOPES which considered both the US models and the recent WHOPES generic risk assessment model.2 The risk assessment showed that pirimiphos-methyl presented no undue risks to operators or residents and it was accepted by WHOPES. The approach to the risk assessment was reviewed and commented on by the External Scientific Advisory Committee of the Innovative Vector Control Consortium (IVCC) and it is in this context that the following comments are made with respect to the PEA assessment.

The current draft PEA report incorporates some refinements to the PEA 2007 assessment which documented screening level risk assessments that were intended to produce conservative estimates of risk. The risk estimates in the current PEA report still retain some conservatism as a variety of assumptions relating to hazard and exposure usually incorporate a level of protection.

The reference doses used for risk assessment of pirmiphos-methyl in the draft PEA report are based on cholinesterase endpoints in animal toxicity studies using conservative uncertainty factors. The FAO/WHO derived an ADI based on acute and short term human volunteer studies in which no inhibition of erythrocyte cholinesterase activity was observed. The human studies are considered to be appropriate to derive the reference doses for risk assessment of pirimiphos-methyl in IRS. This was the approach taken by Syngenta in the risk assessment submitted to the WHO. The reference doses in the PEA report are considered to be unnecessarily conservative.

Assessments of dermal exposure in the PEA report assumed by default that 100% of the dose in contact with the skin would be absorbed. However, Syngenta has shown that less than 1% and 10% of pirimiphos-methyl is absorbed from an emulsifiable concentrate (EC) formulation and the diluted spray, respectively. The dermal route is the principal route of exposure to pirimiphos-methyl in IRS and a 10-100 fold reduction in the estimate of the absorbed dose will produce a marked improvement in the risk assessment. The PEA report notes that the pirimiphos-methyl hazard quotients (HQs) for operators were up to 50 (mid range HQ) for IRS application using personal protective equipment. Calculated child and adult HQs following dermal exposure to residual pirmiphos-methyl following IRS were 8 and 6, respectively. In all cases the HQs are likely to be lower than 1 if refined dermal absorption estimates are used, thus demonstrating acceptable levels of risk. Relatively low HQs above 1 are unlikely to represent a risk in practice given the inherent conservatism retained in the risk assessment models.

Syngenta further refined the exposure model for residential exposure by measuring dislodgeable residues of pirimiphos-methyl from a variety of wall substrates previously sprayed with the IRS formulation. The recommendations contained in the WHO guidelines and in the USAID Best Management Practices (BMP) Manual for IRS with regard to the wearing of appropriate personal protective equipment are fully supported. The pirimiphos-methyl IRS products are deemed safe to use in accordance with safety instructions on the product label or the material safety data sheet (MSDS).

Cholinesterase monitoring

According to the WHO, measurement of cholinesterase activity in personnel applying organophosphates approved for vector control is only mandated for the application of fenitrithion and diazinon.3 This is because of associated toxicological concerns. Pirimiphos-methyl is not one of the more toxic organophosphates and since a refined risk assessment produced by Syngenta demonstrates that pirimiphos-methyl can be used safely for IRS, it is considered that mandatory cholinesterase monitoring is unnecessary. Although cholinesterase monitoring may be useful under certain circumstances it is not specific to an individual organophosphate and professional applicators may have experienced exposure to more than one organophosphate insecticide.

3) WHO (2006). Pesticides and Their Application For the control of vectors and pests of public health importance. Sixth edition.

Conclusions and recommendations

It has been shown above that refinements to the pirimiphos-methyl IRS risk assessment are likely to have a major impact on the levels of risk currently reported in the draft PEA assessment. The refined risk assessment produced by Syngenta for WHOPES demonstrates acceptable risks to operators and residents and the PEA is encouraged to consider this information before finalising the report.

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September 6, 2011

Further to our previous communications I would like to provide a formal response to the draft PEA. We welcome the opportunity to comment and hope that our guidance will be considered to ensure that the vector control programs have clear recommendations based on the latest scientific evaluations and best practice. I have taken the liberty of copying the wider Stateside team on this mail given the recent communications regarding organophosphate / Actellic use in IRS for pyrethroid resistance management.

Firstly there are some general points I would like to address:

1. Syngenta is currently the sole holder of a WHO specification for pirimiphos-methyl active ingredient and formulated product (500g/L EC) specifications. The PEA mentions a wettable powder (WP) formulation of pirimiphos-methyl. We suggest that this should be withdrawn from the PEA as it is no longer supported by a valid WHO specification. We do not supply WHO specification active ingredient to any third party formulation producers. Syngenta was the former holder of the WHO specification for pirimiphos-methyl WP and this was withdrawn given this product's inherent chemical instability.
2. All Syngenta labels require that personal protective equipment be used as per WHO recommendations for IRS.

There are two specific areas that we would like to address with regards to organophosphate use in Indoor residual Spraying (IRS), particularly as it relates to pirimiphos-methyl and Syngenta's Actellic branded products:

1. Risk assessment for operators and residents
2. Blood acetylcholinesterase monitoring

1. Operator and residential risk assessment

Reference document attached: 'Actellic CS – IRS Residential Risk Assessment for WHOv2.pdf'

Syngenta has conducted an internal risk assessment in support of the World Health Organization Pesticide Evaluation Scheme evaluation of the new micro-encapsulated formulation of pirimiphos-methyl, Actellic 300CS. I have attached a copy for your reference. The assessment was based on our recommended application rate for Actellic 300CS of 1gai/m2 (one gram of active ingredient per square meter). In support of the assessment, Syngenta also conducted a specific dislodgeable residue study to refine the assumptions in the model.

The summary conclusions were as follows:

1(a) For operators

- The risk to trained professional operators from mixing, loading and application of ACTELLIC CS was assessed for the target application rate of 1 g ai/m^2.
- Occupational exposure for trained operators was demonstrated to be acceptable as long as a single layer of clothing and gloves are worn (3 – 12% of the AOEL). A single layer of clothing and gloves is an entirely realistic scenario given that we have had no instances of unclothed spraying documented. Indeed all Actellic products are labeled with due regard to appropriate personal protective equipment being worn during an IRS program as per WHO guidelines. PMI IRS programs would therefore at the very least meet but likely normally exceed the protective scenario described in our risk assessment.

1(b) For residents:

- Based on our assumptions, estimated long-term residential exposure to adults is below the AOEL for all scenarios considered.
- For applications of Actellic CS to porous substrates (e.g. breeze-block, wood, mud) estimated long-term residential exposure to children is also below the AOEL (32% AOEL).
- For applications to less-porous substrates estimated long-term residential exposure to children exceeds the AOEL. Although exposure to residues from less-porous substrates could exceed the AOEL, this still allows for 5x margin of safety. The AOEL is 10 fold lower than a dose level in adults which produces no clinical symptoms & no clear plasma cholinesterase inhibition. On this basis, even allowing for the potential for children to be more sensitive than adults, it is highly unlikely that exposure of a child to 212% of the AOEL would result in any symptoms.
- In any case, this worst case modeled exposure level is unlikely to be achieved due to the highly conservative model and the limited use of non-porous surfaces in target populations.
- Taking the above factors into account we consider the use of Actellic 300CS at the proposed rate in indoor residual spraying acceptable.

2. Acetylcholinesterase monitoring and the safe use of Actellic in IRS programs

Reference document attached: 'Vector Control with Actellic insecticides_safe use.pdf'

The key conclusions are as follows:

- None of the organophosphates recommended by the WHO for IRS are subject to the concerns relating to long term nervous system effects linked to highly toxic organophosphates
- Due to its safety profile, we do not recommend routine cholinesterase monitoring for Actellic use in vector control, including IRS programs; indeed, conducting monitoring risks generating equivocal data with (a) no clear cause / effect relationship and (b) no clear and actionable outcome for the IRS program and as such would represent highly questionable value for money

The Syngenta team welcome any additional questions you may have regarding this guidance and the associated assessments. Please do not hesitate to contact me if we can be of further assistance. I would appreciate it if you could confirm receipt of this message to ensure that it is included in the evaluation process.

RESPONSE TO THE DRAFT PEA REPORT (USAID, 2011) CONCERNING THE HUMAN RISK ASSESSMENT OF PIRIMIPHOS-METHYL FOR INDOOR RESIDUAL SPRAYING

The purpose of this document is to provide Syngenta's position on statements made within the USAID 'Integrated Vector Management Programs For Malaria Vector Control - Programatic Environmental Assessment Update' draft document[1] with regards to human risk assessment of pirimiphos-methyl for indoor residual spraying.

The approach taken in the PEA report is similar to that taken by the WHO in their generic risk assessment model[2], with some inputs altered to take account of the PEA's own survey results[3]. Estimated external values for worker and resident-dermal exposure generated in the PEA approach are similar to those generated by the WHO and Syngenta approaches. Syngenta have study data which can be used to further refine the estimated exposure, outlined below and detailed within the Syngenta risk assessment document provided.

Reference Doses

The reference doses used in the PEA risk assessments are taken from the EPA study data on rats. Syngenta considers that data generated in a short-term human volunteer study are more appropriate to derive reference doses for indoor residual application (details within Syngenta's risk assessment).

Worker exposure assessment

In the PEA's assessment of worker exposure, 100% dermal absorption is assumed. Since the reference dose to which the estimated systemic exposure is compared is derived from an oral study, it is appropriate to incorporate dermal absorption when calculating systemic exposure. Syngenta have study data to demonstrate that for an EC formulation the dermal absorption of the concentrate is 0.56% and

[1] USAID (2011) : Integrated Vector Management Programs for Malaria vector control – Programatic Environmental Assessmet Update – draft (Aug 2011)
[2] WHO (2011) : generic risk assessment model for indoor residual spraying of insecticides. WHO/HTM/NTD/WHOPES/2010.5
[3] PEA update draft (Aug 2011) - Annex F

for the spray diltion is 8.5% (details within Syngenta's risk assessment). Incorporating this absorption factor to the exposure calculations results in a pragmatic reduction in systemic exposure.

Residential Exposure assessment – dermal exposure from contact with surfaces.

The PEA assessment of dermal exposure to residents living in treated dwellings assumes that all available active ingredient on the treated surface is actually transferred to the skin during contact with surfaces. Syngenta have performed a study to quantify the amount of active ingredient which is dislodged from a treated surface upon contact (referred to as dislodgeable residue) which demonstrates that when applied to porous surfaces such as mud or breezeblock, less than 1% of the applied dose is actually transferred upon contact (details within Syngenta's risk assessment). These data can be used to refine the dermal exposure components of the risk assessments for residents. Additionally, the PEA assessment of dermal exposure to residents incorporates a 10% dermal absorption factor as a default. The dermal absorption data generated for the concentrate (0.56%) is considered appropriate for a dried surface deposit, and can be used as a refinement when considering the dermal absorption of any contacted material.

Conclusions

Syngenta has demonstrated acceptable exposure to operators and residents through refinement of exposure calculations using study data for dermal absorption and dislodgeable residues. The WHO have evaluated Actellic 300CS (pirimiphos-methyl) according to their generic risk assessment approach[1] and concluded that 'when used for IRS as instructed, Actellic 300CS does not pose undue hazards to spray operators or resident'.

Louise Blake

Product Safety, Jealott's Hill
5th September 2011

Karen J. Larson
Director, Global Registrations
Clarke

September 7, 2011

I begin by thanking you and the EMCAB team in your efforts to expand the scope of the PEA to include new pesticides and updated programmatic elements. This is a considerable undertaking, and we applaud the work presented in the draft. Thank you, as well, for the opportunity to provide comment. On behalf of Clarke, I've attached brief comments I hope will be helpful to the team in completing the final document. Please do not hesitate to contact me directly if you should have any questions about the attached.

I look forward to the Final PEA.

Subject: Public Comment: Draft Updated Programmatic Environmental Assessment (PEA) for the Integrated Vector Management Programs for Malaria Vector Control

Dear Ms. Anderson:

Clarke is pleased to submit comments to the Draft Updated Programmatic Environmental Assessment (PEA) for the Integrated Vector Management Programs for Malaria Vector Control.

We also would like to extend our appreciation to the EMCAB team and the USAID Bureau Environmental Officer in their efforts to expand the scope of the PEA to include new pesticides and programmatic changes. This is a large undertaking and you have done an excellent job.

Clarke is the developer, formulator, and global registrant of Natular® (Spinosad) products for control of the immature stages of mosquitoes. Clarke is very interested in this PEA and welcomes the opportunity to comment. We hope our comments will be helpful in completing the final document.
We address first a material inaccuracy in the discussion in the PEA concerning the lack of aquatic toxicity of Spinosad [PEA page references XXII, 156 - 157]. While it is certain that the use and application of Spinosad in integrated malaria vector management programs, as described in the PEA and in the literature and by product labeling, is not expected to pose hazard of toxicity to aquatic species, it is not accurate to describe Spinosad as "not toxic" in this environment. Indeed, some free-swimming and sediment-dwelling aquatic invertebrates may be sensitive to long-term exposure to spinosad. This sensitivity is mitigated by extremely low rates of application, rapid dissipation from the water column as well as sorption and binding of that portion of residues which becomes associated with the sediment. Results of key ecotoxicity studies for aquatic non-target organisms are summarized below [i].

Common Name	Scientific Name	Effect Level(s)
Rainbow Trout	*Oncorhynchus mykiss*	96-hr Acute LC50 30 mg/L
Bluegill Sunfish	*Lepomis macrochirus*	96-hr Acute LC50 5.9 mg/L
Sheepshead Minnow	*Cyprinodon variegates*	96-hr Acute LC50 7.9 mg/L
Common Carp	*Cyprinus carpio*	96-hr Acute LC50 5.0 mg/L
Water Flea	*Daphnia magna*	48-hr Acute EC50 1.5-14.0 mg/L21-d NOEC 0.001-0.007 mg/L
Grass Shrimp	*Palaemonetes pugio*	48-hr LC50 > 9.7 mg/L
Mysid Shrimp	*Americamysis bahia*	48-hr LC50 > 7.9 mg/L
Eastern Oyster	*Crassostrea virginica*	96-hr EC50 0.3 mg/L

Even considering the laboratory evaluations of aquatic toxicity, the conclusions of the PEA concerning larviciding, including the use of Spinosad, in malaria vector control remain the same: *"There is potential for adverse effects to sensitive non-target aquatic species to water bodies treated with larvicides.* (p. 156).

The Recommendation in the PEA concerning non-target aquatic species, however, may inappropriately limit the effectiveness of strategic and tactical larval control efforts in residential areas.
Recent studies of the larval and pupal stages of *An. gambiae* s.l. have demonstrated that the formation and maintenance of productive habitats is limited in space and time: while *An. gambiae* s.l. may be found in a range of habitats, the vast majority of adult mosquitoes are produced from man-made habitats that are located near human dwellings and are capable of holding water for several weeks [ii]. This finding implies that specific bodies of water that are likely to be productive for adult mosquitoes can be targeted effectively. These bodies of water, and above all the smaller bodies, are less likely to be significant habitat

to sensitive species, and are particularly suitable for certain larval control methods described further in the comments below. Limiting applications of larval control agents to bodies of water greater than 13,000 L in volume, regardless of the presence or absence of sensitive non-target aquatic species, may be inappropriately limiting. We suggest a revision to the recommendation on page 156 of the PEA concerning non-target aquatic impacts is warranted to consider the presence or absence of sensitive non-target species instead of a reference to water volume alone.

Lastly, Clarke would like to impress upon the authors the growing interest in the feasibility of controlling malaria by targeting the immature stages [iii, iv] . While IRS and ITNs sharply reduce malaria transmission, they cannot eliminate it entirely. Additional and complimentary tools are urgently needed, in particular ones that target other stages and resources required by these mosquitoes, and when implemented synergize with IRS or ITNs in their effects in reducing vector density and vectorial capacity. Shifts to vector species that are less likely to enter and feed indoors may result after the introduction of ITNs or IRS [v], limiting the impact of these interventions. Furthermore, the mode of action of most larvicides is completely independent of those of most adulticides and therefore may become an essential tool to manage insecticide resistance.

Significant impacts on adult mosquitoes and malaria transmission have been achieved in western Kenya using the larvicide *Bti* [vi vii viii.] However, a pilot study in Rarieda District showed little or no impact on vector populations (Bayoh et al., unpublished data). There were many potential explanations for the failure of larval control in these sites but one issue was the short duration of *Bti* which necessitated frequent visits to the same habitats. Newer insecticides and insecticide formulations may last for up to a month or more and would allow larval control operators to be more efficient and cover a larger area.

Natular T30 and **Natular G30** formulations are spinosad based larvicide formulations that were developed for control of *Culex* species in permanent natural and manmade habitats. Both of these formulations employ award-winning [ix] slow release technologies that maintain a level of spinosad concentration that kill neonate and 1st instar *Culex* larvae [x]. Natular T30 is a solid, tablet formulation designed for direct application to shallow surface water. Natular G30 is a coated granule providing extended release of spinosad upon application to water. Both formulations provide 30 days control in water. The tablet formulation will withstand periods of dry-down and rewetting. Research field studies in Kenya demonstrate that these formulations are effective against *Anopheles* species that vector human malaria. Both Natular T30 and Natular G30 formulations can be applied prior to the start of a rain event. Both formulations are registered for use in the United States by the US EPA [xi] and are currently in the WHOPES larvicide evaluation scheme. The PEA considers two very effective singlebrood, or short-term, spinosad formulations: G and EC. We respectfully submit these two additional formulations for consideration in the PEA as well (Tablet and Coated Granule, or "CG").

Again, we thank you for the opportunity to provide our comment to the Draft Updated PEA and hope our comments are accepted with the sincerity they are provided. Please feel free to contact either of us at the contact information provided below.

Sincerely,

Karen J. Larson
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[i] Spinosad Technical Bulletin© 2001 Dow AgroSciences Y45-00-0006 (06/02)
[ii] Mutuku, et al. 2006. Pupal habitat productivity for *Anopheles gambiae* s.l. mosquitoes in a village in western Kenya. *American Journal of Tropical Medicine and Hygiene* 74: 54-61.
[iii] Killeen, et al. 2002. Eradication of *Anopheles gambiae* from Brazil: lessons for malaria control in Africa? *Lancet Infectious Diseases* 2: 618-627.
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[v] Bayoh, et al. 2010. *Anopheles gambiae*: historical population decline associated with regional distribution of insecticide-treated bed nets in western Nyanza Province, Kenya. *Malaria Journal* 9: 62.
[vi] Fillinger et al. 2003. Efficacy and efficiency of new Bacillus thuringiensis var *israelensis* and *Bacillus sphaericus* formulations against Afrotropical anophelines in Western Kenya. Tropical *Medicine & International Health* 8 (1): 37-47.
[vii] Fillinger, U. and Lindsay, SW 2006. Suppression of exposure to malaria vectors by an order of magnitude using microbial larvicides in rural Kenya. *Tropical Medicine in International Health* 11: 1629.
[viii] Fillinger et al. 2009. Integrated malaria vector control with microbial larvicides and insecticide-treated nets in western Kenya: a controlled trial. *Bulletin of World Health Organization* 87: 655-665.
[ix] 2010 U.S. Presidential Green Chemistry Challenge Award: http://www.epa.gov/greenchemistry/pubs/pgcc/winners/dgca10.html
[x] Bayoh, M.N. 2010. Evaluation of extended release formulations of spinosad for Anopheles control in Western Kenya. American Mosquito Control Association Annual Meeting, New Products Symposium.
[xi] Natular T30 U.S. EPA Registration No. 8329-85; Natular G30 U.S. EPA Registration No. 8329-83

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September 8, 2011

We appreciate you taking the time to review the draft PEA and providing us with your comments. We also appreciate you providing spelling and grammar corrections, along with your content recommendations. All comments will be taken into consideration when we revise the PEA to ensure the document provides comprehensive and accurate information.

Comments were provided through track changes in the PEA document

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September 8, 2011

I have recently been passed the final draft of above document (http://www.irgltd.com/Our_Work/Projects/EMCAB%20Drafts/Updated%20PEA_25Aug.pdf), the deadline for comment on which, I believe is tomorrow?

With short notice to look through this extensive document I have not had the opportunity to pass it to my IRAC Public Health team colleagues for their input, however, I would like to make a couple of comments relating to the [Insecticide] Resistance Management conclusions on page 149 -.

Whilst implied in other parts of the document, I believe the conclusions miss-out one of the most important steps in managing insecticide resistance, namely to use insecticides the target insects are susceptible to. As such I think it would be valuable to explicitly state this. Can I therefore suggest the addition of another point in the conclusions based on the following text:

- "Rotation among insecticides from different Mode of Action (MoA) classes according to a program based on knowledge of the insecticide susceptibility status of the vector mosquito species present."

I would also like to draw your attention to the inclusion of the point "use of adulticides rather than larvicides resulting in approximately half the selection pressure for resistance". There are a number of larvicides with different modes of action to the available adulticides. Whilst it is true that both larvae and adults from a mosquito population should never be exposed to insecticides from the same mode of action class, it should not be implied that larvicides cannot be used for insecticide resistance management where adulticides are also being used. The use of larvicides to control anopheline mosquitoes can be challenging, but where feasible, and with a different MoA class insecticide to the adulticides, they can play an important role in both mosquito control, and insecticide resistance management. Taking these conclusions, without reading the rest of the document, may falsely suggest that larvicides are to be excluded from vector control programmes. Can I therefore suggest some additional text to reflect this, such as:

- "Use of larvicides with a different mode of action to available adulticides, in addition to adulticides where feasible and cost effective."

I apologise for the lateness of these comments, and thank you for your consideration.

Dr. Helen Pates Jamet

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September 8, 2011

Please find attached my comments on the PEA document. Unfortunately I did not have time to go through with a fine tooth comb, but please let me know if you have any questions.

Comments were provided through track changes in the PEA document

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Jessica M. Rockwood

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September 8, 2011

On behalf of BASF – The Chemical Company, I would like to provide you with comments and suggested edits/deletions/additions to USAID's Draft PEA.

Based on Susan's email, we are attaching the word document provided to us with tracked changes and also attaching the extracted tracked changes in a separate document as requested. Please note that while extracting, the process changes the index based on edits, comments, etc. so please disregard the new page numbers other than as they correlate to the extracted track changes.

Additionally, we would like to provide you with comments to the section labeled **Profile Chlorfenapyr in Annex E** provided by two colleagues below and not in a separate document.

1- Some of the parameters in the equations given are not fully clear. Specifically, there is a difference between USAID assessments and WHO common practice, and also BASF in house measurements:
   - USAID considers a higher application rate: 400 mg/m2 compared to 150 to 250 mg/m2 in our assessment > this inflates results by 2x
   - USAID is applying an additional uncertainty factor (safety factor) of 10 as they use 1000 compared to the 100 recommended by WHO > this inflates results by 10x
   - USAID averages the exposure for workers over the spraying cycle (42 days = 1.25 cycle) when WHO averages over the whole year (365 days) > again inflating results by 10x

2- Other comments:

   - Page E-25 1st paragraph, "..kills pests..": Maybe be better to state, CFP rate of intoxication is species specific with a range that covers minutes to days depending on formulation, duration of exposure and target pest.
   - Page E-25 3rd paragraph. Add to last sentence: Chlorfenapyr is a slow action non-repellant insecticide.
   - Page E-26 1st paragraph regarding Phantom 21.5% EC: This should state SC. There is no EC formulation.
   - Page E-27 1st paragraph "Because of it persistence..". Comment: this is speculative and contrary to actual BASF field data. BASF requests that this be removed.
   - Page E-31 1st paragraph last sentence: We believe this to be speculative and not based on data at hand, which includes WHO, USEPA Pesticide Fact Sheet and other dossier information. BASF requests that this sentence be deleted.

I did notice one thing before sending this. Page 24 of the main document: the following should be edited to reflect that microencapsulated formulations are only used in LLIN field retreatment.
"Microencapsulated formulations have improved washing resistance and handling safety (WHO 2001)"

Lastly, we caught a significant typo on page E-61 regarding the profile for Etofenprox. In the Chronic Exposure Conclusions, it refers to Permethrin not Etofenprox.

Kindly let us know if you have any questions or comments.

Best regards,

Jessica Rockwood and Bob Farlow on behalf of BASF – The Chemical Company

Comments were also provided through track changes in the PEA document

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ANNEX N: INDEPENDENT CONSULTANT ORGANOPHOSPHATE BIOMONITORING REVIEW

Final USAID Cadmus 2012 May 2 2012 (wfisher copy edits 7may12)

To: Teresa Bernhard

From: Bob Krieger

Re: Malaria vector control PEA review: OP Biomonitoring in IRS

The objectives of this paper are 1) to review the need to biomonitor urine or blood during Organophosphate IRS operations, and 2) to assess potential methods of biomonitoring to achieve the required protection of human health as well as to advance the understanding of Organophosphate exposure during IRS.

Recent advances in the malaria vector control program have been accomplished through increases in the use of long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS). Both of these measures depend upon insecticides to repel, kill or reduce the lifespan of female mosquitoes. Each strategy includes pesticide use practices that inevitably results in human exposure at some level. The overall chemical safety of the IRS program in malaria vector control rests on minimizing human pesticide exposures.

The organophosphorus insecticides fenitrothion, malathion and pirimiphos-methyl are among the 12 insecticides recommended for use in IRS. Herein these 3 insecticides are designated OPs (organophosphates). The application of OPs in IRS presents an opportunity for evaluation of use practices since the environmental fate and human disposition of these insecticides are well known.

This memorandum addresses the use of these OPs by spray operators in IRS. The following topics are included in this memorandum:

- WHO Guidance for Worker Health and Safety for OP Use in IRS Programs

- Biomonitoring Spray Operator OP Exposures During IRS
  - Blood Cholinesterase Activity of Spray Operators Using OPs
  - Urine Biomonitoring of Spray Operators Using OPs

I. WHO Guidance for Worker Health and Safety for OP Use in IRS Programs

WHO's Global Malaria Programme (WHO 2006) recommends IRS as a major means of malaria vector control to reduce and eliminate malaria transmission (WHO Indoor Residual Spraying, Position Statement, 2006). The choice of insecticide is to be informed by consideration of (1) insecticide susceptibility and vector behavior; (2) safety for humans and the environment, and, (3) efficacy and cost-effectiveness. Insecticides recommended by WHO are classified as safe for public health use under the recommended conditions of use in the *IRS WHO Pesticide Evaluation Scheme* (WHOPES). Safety for humans and the environment are particularly important operational considerations accompanying the use of OPs in IRS.

The pesticides recommended by USAID for IRS have been fully evaluated by the WHOPES and can be used for malaria control in safe and effective quantities by sprayer operators who are adequately protected from their potential toxic effects. Safety supervisors, entomologists, and medical specialists should be aware of the:

- Mode of action of the pesticide
- Significance of diagnostic measures
- Signs and symptoms of toxic effects; and
- Facilities required for treatment of cases of poisoning (WHO, 2006)

This awareness places a very high level of responsibility on those assigned to manage persons using pesticides in IRS, and when in force they will administratively minimize risk.

To assure minimum risk of pesticide poisoning, any USAID-sponsored IRS program must assure appropriate safety standards for handling, storing, and disposing of pesticides. Najera and Zaim (2003) acknowledged the importance of clothing and PPE "appropriate to the insecticide used and the climate under which it is being used, hats, face wraps, goggles, gloves and boots, and have two sets of working clothes" to minimize potential exposure, i.e. "to prevent unnecessary contamination." They also note the importance of regulating the duration of the working day "to ensure that the exposure of spraymen to the insecticide remains within the limits allowed by the safety requirements." End-of-shift showers are also considered generally important for pesticide applicators and "particularly important" when operators have been working with OPs. Those authorities also recognized that special attention is required for more toxic insecticides such as fenitrothion (Najera and Zaim 2003).

In accordance with WHO health and safety regulations, all persons working on IRS must be adequately protected against potential harm due to exposure from pesticides (WHO 2006). All persons with potential direct contact or exposure to pesticides during handling, transportation, storage, use and cleaning of pesticides or pesticide

contaminated materials must wear appropriate personal protective clothing in accordance with the safety instructions on the product label or material safety data sheet (MSDS). Responsibility for compliance of workers to wear personal protective equipment (PPE) is assigned to the supervisor. The rationale for use of PPE results from the ever-present need to minimize worker exposure.

The Best Management Practices for Indoor Residual Spraying includes *Section 2: Worker and Resident Health and Safety* (USAID 2010; BMP). *Section 2* addresses acceptable safety standards and practices for the handling, storage, transportation and use of pesticides for IRS in the PMI program **"to minimize the risk for human exposure.** [emphasis added]**"** The BMP health and safety guidelines reflect the collective knowledge and experience of WHO (2002) and FAO (1990). All of the measures described in detail in *Section 2* cite the *Integrated Vector Management Programs for Malaria Vector Control Programmatic Environmental Assessment* (2007) and represent actions to prevent pesticide over-exposure. The PPE listed in the BMP 2010 for spray operators performing IRS includes the following:

- Filter masks – as identified in the Material Safety Data Sheets (MSDS) for the pesticide being used, nitrile rubber, neoprene, PVC or butyl rubber gloves,
- Face shield or goggles (face shield preferable -protects face and eyes against spray fall-out)
- 2 or 3 cotton long-sleeved overalls per spray operator (keep overalls outside of boots)
- Rubber boots or heavy canvas boots that are unlined and can be easily rinsed
- Broad-rimmed helmet (protects head, face and neck from spray droplets)
- Neck protection such as a spray sock

BMP 2010 also includes specific notation of the importance of personal hygiene as a means to minimize insecticide exposure. The directives include the following statement:

> *"During spray operations, scrupulous attention to personal hygiene is essential for the safe use of pesticides. For spray staff, safety precautions will depend largely on personal hygiene, including washing and changing clothes."*

Specific measures for the conduct of IRS and for the reduction of occupational exposures during IRS are enumerated in the 2007 and 2011 PEA (Table 6-1 IRS Recommendations):

- Training of spray operators, team leaders, and supervisors according to best practices, including recognition of insecticide-poisoning symptoms.
- Procurement and proper use of PPE by spray operators, team leaders, and supervisors
- Training of health workers in insecticide-poisoning treatment
- Procurement and distribution of treatment medicines for insecticide exposure
- Daily on-site personal washing (after spraying)

- Reprimand of spray operators who do not follow proper procedure in all aspects of operations (handling, spraying, hygiene, cleanup)
- Hiring of commercial laundry or local wash persons (can be spray operators) for proper washing of overalls
- Frequent washing of overalls (after spraying)
- Procurement and wearing of PPE by wash person (chemical apron, rubber boots, rubber gloves) if a wash person is hired to clean spray operator PPE
- Procurement and distribution of barrels for progressive rinse of PPE, and wash-tubs for overall washing and personal hygiene
- Progressive rinse of sprayers
- **Development and implementation of a human health monitoring plan to determine pesticide impacts on spray operators and residents, particularly when using organophosphates**.(emphasis added)

These operational practices are intended to reduce the likelihood of overexposure. However, it is imperative that all personnel involved in administering the IRS program are aware that <u>any</u> use of a pesticide will result in some level of exposure. The recommendation for baseline cholinesterase testing is unambiguous (WHO 2006):

> *"When organophosphates are used, cholinesterase activity must be tested prior to the start of spraying and once per week during the spray campaign for all personnel exposed to the insecticide. Spray operators should cease their participation in the spray campaign if their cholinesterase activity decreases to 50% or more of their baseline cholinesterase activity (WHO, 2006 and in PEA 2007)."*

Monitoring the cholinesterase status (a biomarker of effect) of spray operators and others in IRS is a long-standing WHO recommendation. Campaigns using these OPs should monitor the cholinesterase status of spray operators and handlers until it is demonstrated that work is being safely performed (Najera and Zaim 2003). For fenitrothion, the most hazardous of the OPs authorized for use in IRS, it may be necessary to demonstrate compliance with weekly cholinesterase monitoring during the spray season.

Najera and Zaim (2003) also state the following related to routine monitoring of operator exposure: *"The routine monitoring of exposure may not be necessary in operational programs with established safety practices.* ***For most organophosphates, however, it will be necessary to monitor the level of acetyl cholinesterase in any worker who may have been exposed to contamination. Spray operators will need to be monitored at regular intervals*** [emphasis added]**.**"

The experience and recommendations of the extensive evaluations of pesticides offered by WHOPES in the determination of safe use practices for insecticides in IRS is acknowledged and accepted. Means to demonstrate safe use outside of those carefully measured and supervised trials performed during the WHOPES program is limited. The

role of operator safety in current IRS should be monitored with levels of care and resources similar to those applied in the assessment of the entomological status of malaria vectors and the determination of environmental impacts of pesticide use.

The benchmark dosages for noncancer and cancer endpoints are described for each exposure route and duration in Annex E (IVM 2007). Discussion of those endpoints is outside the scope of this overview which focuses specifically on the role of biomonitoring to preserve and protect the health and safety of spray operators in IRS.

When best management practices (BMP 2010) are followed, workers will be closely monitored for acute symptoms of excessive OP exposure. Absent symptoms of poisoning, there will always be some level of exposure when insecticides are used in the IRS program. Exposures will be measurable using cholinesterase monitoring, and with even greater sensitivity, urine chemical biomarker monitoring, so that symptoms are much less likely to occur. With respect to the health and safety of persons using OPs in IRS, the routine monitoring of exposure may not be necessary in operational programs with established safety practices (Najera and Zaim 2003). Demonstration that operational programs do not require blood cholinesterase biomonitoring seems to be a worthwhile operational objective, but initially both biomonitoring methods (blood and urine) should be used concurrently.

Selected references on WHO Guidance for Worker Health and Safety for OP Use in IRS Programs are provided at the end of this paper.

II. Biomonitoring Spray Operator OP Exposures During IRS

The goal of biomonitoring (either blood or urine) is to prevent over-exposures and adverse effects. Biomonitoring also offers feedback about the effectiveness of PPE and inter-individual differences in exposure. Occupational exposures to OP insecticides are measurable using blood cholinesterases and urinary excretion of chemical biomarkers. The value of these measurements of effect and absorbed dose is limited to individual or workforce assessments of exposure in most cases rather than representing clinically diagnostic conditions. The earliest uses of biomonitoring applied the two strategies concomitantly as part of medical supervision of workers using OPs such as ethyl parathion, the highly toxic insecticide that preceded introduction of the much less hazardous OPs proposed for use in contemporary IRS. The potential health effects of OP use in IRS will depend upon the route of exposure (i.e. ingestion, inhalation, and dermal), the frequency and duration of exposure, the inherent toxicity of the insecticide, and the sensitivity of the exposed spraymen or other handlers. Each of the OPs are relatively rapidly absorbed, metabolized by competing pathways that form both more toxic oxons and more water soluble products that are rapidly excreted in urine (Chambers and Levi 1992). The common adverse effect of the OPs is excessive acetylcholinesterase inhibition (Wilson, 2010), the response which serves as the foundation for measurement of blood cholinesterase activity (Cocker et al. 2002).

Regardless, the biomonitoring strategies remain the same but the immediate goal is minimizing exposure to develop safe use practices rather than identifying exposures of immediate health significance. Nevertheless, individual and workforce baseline cholinesterase measurements can be used to evaluate worker hygiene and compliance with approved work practices. Such measurements have immediate application under existing field conditions, while exposure assessments based upon urine metabolites require additional research on the relationship between exposure and clinical or benchmark endpoints of concern. Cholinesterase measurements, while important, do not satisfy the need for contemporary risk characterization or for estimates of daily worker exposure based on urine biomonitoring which could and should be developed.

II.A. Blood Cholinesterase Activity of Spray Operators Using Ops

Blood cholinesterase activities have been extensively used to monitor occupational exposures to OPs Biological monitoring is essential in evaluating the extent of spray operator exposure. In 1967 blood cholinesterase measurements were advocated as biological effect monitoring (WHO 1967). This involved determination of plasma (or serum) cholinesterase (ChE) and red blood cell (RBC; erythrocyte) acetylcholinesterase (AChE) in persons exposed to insecticides that inhibited those blood enzymes as surrogates for AChE in neural tissue and neuromuscular junctions (Cocker et al. 2002). Physiological variations in blood-ChE levels occur in a healthy person and within populations. It has been estimated that the coefficient of variation for AChE activity in samples from an individual is 8 - 11%, and that a decrease of 23% below pre-exposure level may be considered significant. If the average of several pre-exposure values were available, then a decrease of 17% would be significant (WHO 1986). Plasma ChE accounts for about 10% of whole blood cholinesterase activity (Worek et al. 1999). The relationship between *RBC AChE Inhibition and Actions to Prevent Further Exposure* are presented in Table 1 after WHO (1986) and Lotti (1995).

Table 1. Clinical RBC AChE Inhibition and Actions to Prevent Further Exposure

Percent Inhibition Re: Pre-exposure	**Significance**	**Action**
20-29%	Evidence of exposure	Improve hygiene conditions
30-50%	Hazardous to health	Remove worker from exposures and evaluate/improve hygiene conditions
>50%	Poisoning	Admit worker to hospital

WHO, 1986. Organophosphorus Insecticides: A General Introduction. Environmental Health Criteria 63 Geneva: 181s.

Blood cholinesterase measurements used in previous evaluations of OP exposures in IRS

The best suited testing procedure for measurement of blood cholinesterase must be determined. The following examples illustrate how tintometric (staining) blood

cholinesterase measurements or alternative procedures have been used to produce timely estimates of blood cholinesterase activity in spray operators using the OP insecticides recommended for use in IRS.

Malathion formulations contaminated with a highly toxic derivative combined with poor work practices triggered a major poisoning in Pakistan in 1976. It should be noted that improper storage of malathion at temperatures >40 °C can produce byproducts in situ that greatly synergize AChE inhibition. Cholinesterase measurements were important features of the epidemiological investigation of poisoning among malaria control field workers. Depressed cholinesterase was attributed to work practices that resulted in excessive dermal exposure combined with use of contaminated formulations of malathion. Cholinesterase activities declined during the work week reflecting the cumulative effect of OP exposure (Baker et al. 1978).

Previous field trials to evaluate malathion for vector control in Uganda and Nigeria under WHO supervision revealed “little evidence of human toxicity.”
In Haiti, the cholinesterase activity of malathion spraymen was unchanged following 6 weeks of spraying (Warren et al. 1985a). Although the levels of urinary metabolites of malathion found following head lice treatment or use of malathion dusts in the date industry (Krieger and Dinoff 2000) were higher than those commonly found in occupational studies, there was no depression in blood cholinesterase activity. Time and dose dependent inhibition of cholinesterase have been demonstrated in spray applicators who applied malathion (Baker et al. 1978) although relatively high occupational exposures may not produce cholinesterase inhibition when individual levels of activity are judged against clinical reference values (Krieger and Dinoff 2000).

Pirimiphos-methyl was applied in two WHOPES IRS spray programs. A total of 35 trained personnel participated and none showed any ill-effects attributable to pesticide poisoning. At the termination of one program three of the 12 spraymen showed plasma cholinesterase activities which were 70-75% of the mean of two pre-exposure values.

In a second study, spraymen applied pirimiphos-methyl in unoccupied dwellings for mosquito control. Spray workers in one group wore normal clothing and those in the second group wore additional, protective clothing (cotton overalls, caps, canvas shoes and safety glasses, and cotton masks). Mixer-loaders wore rubber boots, gloves, caps, cotton jackets, cotton masks and safety glasses. Cholinesterase (blood and plasma) was measured on three consecutive days prior to spraying; then at lunchtime and the evening on the days of spraying. Measurements were also taken on days one, two, three and ten post-spraying. General medical examinations were performed with emphasis on gastrointestinal, neuromuscular, cardiorespiratory, visual and psychological effects and peripheral and central nervous systems prior to, during, and subsequent to spraying. Cholinesterase depression occurred on a group basis in all groups over the spray period, with full recovery within 24 hour post-dosing. Ten of the 24 exposed individuals showed > 15% depression of erythrocyte cholinesterase, the maximum depression being 23%. Levels of plasma cholinesterase inhibition were

inconsistent, and less than those seen for erythrocyte cholinesterase inhibition. There were no clinical manifestations of toxicity (Chester & Hart, 1986).

Fenitrothion has also been evaluated by WHOPES in several field investigations. The organophosphate was sprayed in an early WHO supervised trial in Kenya (WHO, 1973). The trial included four rounds of spraying at approximately three-monthly intervals. Protective clothing included overalls, broad-brimmed hats, tennis shoes and gauze surgical masks. All protective clothing was washed daily. Each worker washed their hands and face after each pump charge and was instructed to shower at the end of the work-day. Slight to moderate depression of cholinesterase was observed in most workers toward the end of the spraying rounds. Two were removed from spraying. In the fourth spray round, lesser cholinesterase inhibition was observed, attributed to stricter attention to safety precautions and improved supervision. Symptoms of overexposure were limited to a single individual in over 2000 man-days of spraying. The Committee advised cholinesterase determination should be performed weekly whenever the spraying operation was longer than four weeks or was any six weeks within a two-month period (WHO 1973).

Fenitrothion use was also evaluated in a program that featured intensive training and supervision as well as careful monitoring of cholinesterase levels in workers in a malaria control program in Haiti (Warren et al. 1985a). Depressed blood cholinesterase activity was associated with faulty PPE (gloves and hat) and failure of supervisors to enforce recommended safe work practices. Warren et al. (1985a) credited close monitoring of cholinesterase with prevention of worker illness due to overexposure. They utilized daily fingerprick blood specimens and the tintometer procedure for colorimetric determination of cholinesterase activity (Watson and Edson 1964). Complaints of weakness, headache, and increased sweating “were common in workers with enzyme activities of 50% or less.”

Later, three of 28 fenitrothion applicators in Haiti had reduced cholinesterase activity after a week’s work that rebounded during a weekend of no exposure (Warren et al. 1985b). Urine levels of p-nitrocresol, the specific chemical fenitrothion biomarker (Table 2), were measured concurrently. Weighers and supervisors with minimal fenitrothion contact had cholinesterase levels greater than or equal to 75% of the control value and lower urine biomarker levels than spraymen. Similar exposure assessments using malathion revealed unchanged cholinesterase activity and low level malathion monocarboxylic acid levels (the malathion specific biomarker, Table 2) in urine. Warren et al. (1985b) noted the importance of safety training and cholinesterase monitoring when fenitrothion and malathion are used in IRS. Warren et al. (1985b) emphasized that “such precautions were particularly needed when the relatively more toxic compound, fenitrothion, was in use.”

Conclusion: When OPs have been applied in IRS, blood cholinesterase measurements have revealed the importance of training, protective clothing, and supervision to protect against over-exposure and possible adverse effects. The use of blood cholinesterase

measurement after occupational exposure is an invasive procedure and is of limited practical use, unless an overexposure has occurred or symptoms of intoxication appear.

II.B. Potential for Urine biomonitoring of Spray Operators Using OPs

The OPs that may be used in IRS are dimethylphosphorothionates that represent a much larger group of OP insecticides that comprise an even larger family of pesticides that have been used in global crop protection, structural pest control, medicine and public health since the 1950s. As a result their environmental fate and transport and their disposition in humans is well known and described in the literature of pesticide science (Annex E, PEA 2011). The majority of economically important OPs is structurally related pentavalent phosphorus acid esters, and share acetylcholinesterase inhibition as a common mechanism of action (the basis of their suitability for cholinesterase monitoring above) (Chambers et al., 2010).

Following OP insecticide exposures, relatively rapid absorption, metabolism, and excretion of more hydrophilic metabolites occurs in animals and humans (Chambers and Levi, 1992). The metabolites excreted in urine can be convenient chemical biomarkers of occupational exposure since they represent internal or absorbed dose and require fewer measurements to reliably estimate worker exposure (Ross et al., 2008). Both specific and generic OP urine biomarkers are available for the quantitative characterization of fenitrothion, malathion, and pirimiphos-methyl exposure of humans (Table 2).

Analytical methods and techniques are available for quantitative analysis of these human chemical biomarkers (Table 2) of exposure in blood and urine in amounts well below toxic levels signaled by high levels of cholinesterase inhibition (Sudakin and Stone, 2011).

Where history of use in IRS is available, an estimate of absorbed daily dose (mg/kg-day) may be obtained in post-shift urine samples self-collected at the end of a period of occupational exposure. The chemical biomarkers are relatively stable in urine and when used to estimate exposure, estimates of absorbed dose have quantitative usefulness that cannot be obtained with cholinesterase measurements.

Table 2. Organophosphate Insecticides Recommended For Use in IRS and Their Specific and Generic Urine Chemical Biomarkers of Exposure

Insecticide	Specific urine metabolite	Generic urine metabolites
fenitrothion	3-methyl-4-nitrophenol (p-nitrocresol)	Dimethyl phosphate (DMP) Dimethyl thiophosphate (DMTP) Dimethyldithiophosphate (DMDTP)
malathion	malathion monocarboxylic	

	acid, malathion dicarboxylic acid	
pirimiphos-methyl	2-(diethylamino)-6-methylpyrimidin-4-ol/one	

Spot or convenience end-of-shift urine specimens following week-long work periods could be considered to provide either an index of worker OP exposure, or refined to serve as an estimate of absorbed dose.

Measurements of either specific or generic urine biomarkers of spray operators could be used to assess the range and extent of worker exposure during IRS. End-of-shift spot urine specimens could reasonably be stipulated to represent a pseudo-steady state excretion of biomarker. In this example, urine excretion is assumed to represent total absorbed dose. Volume correction could be made using a creatinine measurement on the same sample to reduce variability. An ***index of daily operator OP exposure (µg/day)*** could be derived from measurement of either specific or generic biomarkers as follows:

Where BM = chemical biomarker in µg/ml urine

Cn = urine creatinine in g/ml

MW = molecular weight of BM

1.7 g/day = creatinine excretion per day

Then, X = µg biomarker/day where X is either the µg Specific Biomarker or the reported µg levels of the 3 Generic Biomarkers

MW_{OP}=molecular weight of parent OP insecticide in µg used in IRS

OP_{index} = µg OP absorbed per day

BM_{urine}/Cn_{urine} *x* 1.7 g/day = µg biomarker/day

µg/MW = µmoles biomarker/day

OP_{index} = MW_{OP} *x* µmoles biomarker/day

At either the individual or the workforce level, the OP_{index} would be more representative of actual absorbed dose than corresponding data representing cholinesterase status. This may be desirable since contemporary risk assessments concerning possible health

impacts of human pesticide exposure during IRS require an estimate of absorbed dose. The OP_{index} would have to be refined by knowledge of the relationship between urine biomarker excretion resulting from dermal (and inhalation) exposure. A relatively complete database exists for biomonitoring occupational malathion exposures (Bouchard et al. 2003 and 2006). Although chemical urine biomarkers of fenitrothion and pirimiphos-methyl have been used in studies of occupational exposure during IRS, they are less studied in occupational settings than malathion.

Advantages of urine metabolite testing versus blood cholinesterase monitoring are subjective at this time due to the limited amount of urine data available. Urine collections are non-invasive and specimens can be collected by the workers themselves. Urine sampling does not subject the personnel responsible for sample handling to blood-borne diseases such as HIV or hepatitis contracted inadvertently from needle sticks. The analytical methods are sensitive and specific, with reporting levels below those likely to be associated with inhibition of cholinesterases. Biomarker analysis could more readily permit quantitative evaluation of specific risk mitigation strategies that cannot be established using cholinesterase analyses. Finally, urinary biomonitoring results are not subject to “false positives” induced by contamination with dermal OP that can influence blood levels when drawn with fingerpricks.

A disadvantage of urine biomonitoring is the general lack of biological occupational exposure limits in contrast to those available for blood cholinesterases (above). A recent review notes the lack of a relationship between urine dialkyl phosphate levels and adverse effects (Sudakin and Stone 2011). In part this results from the sensitivity of methods available for chemical urine biomarker analysis and their persistence in the environment, particularly the diet. When biomarkers can be quantitatively measured and associated with history of exposure, such as in IRS, they provide a means to make important estimates of absorbed dose and the effectiveness of exposure mitigation strategies.

Notwithstanding the lack of generally accepted diagnostic guidelines like those existing for cholinesterase surveillance, guidelines for interpreting urine biomonitoring data resulting from occupational exposures have been offered by Workcover NSWales, Australia (*Chemical Analysis Branch Handbook 7th Edition*; www.testsafe.com.au). They have been considered here as an exercise to demonstrate how biomarker data from IRS spray operators might be utilized. Their diagnostic standards were based upon excretion of the Generic Biomarkers of OPs rather than the Specific Biomarkers (Table 2). The concept is useful and the estimates of urine biomarkers from Australia Work Safe likely have general usefulness, particularly when combined with knowledge of worker exposure history (and cholinesterase status of exposed persons in studies to evaluate or validate the diagnostic value of the chemical urine biomarkers).

Table 3. Guidelines for interpreting urine dialkylphosphates biomonitoring data resulting from occupational OP exposures

Level of dialkyl phosphates in urine	µmol/mol creatinine	µg/ g Cn[1]	Daily µg/day @ 1.7 g Cn-d[2]	Daily µg/L @ µmol/1.5 L[3]	Significance
1	below 100	3	5	3.3	low occupational exposure and equivalent to a high non-occupational
2	between 100 and 1000	3 - 30	5-50	3-33	occupational exposure to organophosphates and therefore work practices may need to be reviewed to attempt to reduce exposure levels
3	above 1000	>30	>50	>33	high occupational exposure to organophosphates and may be associated with a drop in the blood cholinesterase level

[1] µg dimethylphosphates assuming average molecular weight 322 (DMTP) based upon estimate of urinary umol/mol creatinine. Level 1 above: 322 µg/umol)/113 g/mol

[2] Daily dimethylphosphate level assumes 3 µg/g adjusted to daily excretion of 1.7 g Cn (the total urine level for adult males): 3 x 1.7

[3] Daily dimethylphosphate level assumes daily urine of 1.5 L (mean total urine level for adult males): 5/1.5

Concentrations of generic biomarker that might be measured at levels of concern compare favorably with estimates of OP dosage. In Table 4 estimates of specific chemical urine biomarkers are made under the screening conditions proposed in the PEA 2011. The unit exposure in Table 4 is derived from the dermal route of exposure. A range of conditions were used to represent possible biomarker excretion.

Table 4. Spray Operator Subchronic Dermal Exposure from PEA 2011

$$\text{Dose (mg/kg-day)} = \frac{\text{Unit exp* FAspray*Application* Area treated* Houses per day*Exposure frequency* Spray cycles}}{\text{PPE * Body Weight * Averaging time}}$$

Algorithm Factor	Fenitrothion	Malathion	Pirimiphos-

			methyl
Unit exposure (airless applicator), mg/kg Backpack not available	170	170	170
FA_{spray}	1 (0.2)	1 (0.2)	1 (0.2)
Application kg/m^2	0.002	0.002	0.001-0.002
Area treated per house, m^2	35.8	35.8	35.8
Houses treated per day	9-14 (12)	9-14	9-14
Number of days per spray cycle	33-44 (39)	33-44	33-44
Number of spray cycles per year	1-2	1-2	1-2
PPE exposure reduction factor	43	43	43
Body weight	60	60	60
Averaging time	39-51 (45)	39-51	39-51
Low dose (mg/kg-day) (170)(0.002)(35.8)(9)(33)(1)]/43(60(51 d)	0.027		
High dose (mg/kg-day) 39d	0.15		
Average dose (mg/kg-day) using mean of all ranges above and FA_{spray} of 0.2 for dermal absorption for 2 cycles per year	0.02		

If a Specific Urine Biomarker represented as little as 20% of an average dose of 0.02 mg/kg-day of an OP and it was excreted in 1 litre of urine during a spray cycle, the analyte (chemical specific biomarker) would represent up to 0.36 ug/mL (see calculation below). This level would be well within the detection (LOD) and reporting limits (LOQ) of available analytical methods for the respective Specific or Non-Specific Urine Biomarkers.

20% x (60 kgx0.02 mg/kg/1L/day) = 0.24 mg/L = 0.24 µg/mL = 0.75 µmol/L assuming MW = 322

The resulting default exposure estimate falls into Category 1 (low occupational exposure) of Australia's Work Safe criteria (Table 3).

In conclusion, urine biomonitoring does not provide the rapid feedback offered by cholinesterase monitoring, but there are several factors including false positives, blood sampling safety, self-collection and sensitivity that make urinary monitoring desirable. In contrast, analysis of chemical biomarkers in urine allows monitoring of malathion, fenpropathrin, and pirimiphos-methyl exposure well before AChE inhibition occurs and potentially allows prevention of health hazards before they become significant. Additionally, data derived from urine biomonitoring may have an important place in the future development and evaluation of recommendations of pesticide use practices. These data can be related to existing guidelines for safety (e.g., Australia's Work Safe)

and can be related to cholinesterase monitoring if conducted concurrently. At this time very limited urinary biomonitoring data are available, in spite of the fact that quantitative exposure measurements are a staple of contemporary exposure assessment and risk characterization, relevant to all uses of pesticides in malaria control programs. Again, the role of operator safety in current IRS should be monitored with levels of care and resources similar to those applied in the assessment of the entomological status of malaria vectors and the determination of environmental impacts of pesticide use.

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