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Technical work in relation to chemicals listed in the annexes to the Convention with exemptions: preparatory work for the assessment of alternatives to DDT

Background information on the assessment of alternatives to DDT

Note by the Secretariat

1. As referred to in document UNEP/POPS/POPRC.7/13, the annexes to the present note provides the following background information:

(a) Summary of information on the DDT expert group prepared by the Secretariat (annex I);

(b) Document prepared by Mr. Zachary S. Brown, an independent consultant, on developing a framework for the assessment of alternatives to DDT (annex II);

(c) Comments submitted by the World Health Organization on the document prepared by Mr. Brown (annex III).

2. The annexes have not been formally edited.

* UNEP/POPS/POPRC.7/1.

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Annex I

Summary of information on the DDT expert group

Establishment of the DDT expert group

1. In accordance with the process for the reporting on and assessment and the evaluation of the continued use of DDT for disease vector control contained in the annex to decision SC-3/2, the DDT expert group is established to assess the information on the production and use of DDT and its alternatives for the evaluation of continued need for DDT for disease vector control.

2. The DDT expert group consists of 18 experts as follows: 10 experts nominated by Parties with 2 from each of the 5 United Nations regions; 5 experts identified by WHO; and 3 experts identified by the Secretariat in consultation with UNEP Chemicals.

3. The DDT expert group:

(a) Undertakes a situational analysis on the production and use of DDT and the conditions for such use, including a review of the responses by countries to the questionnaire;

(b) Evaluates the availability, suitability and implementation of alternative products, methods and strategies to DDT;

(c) Evaluates progress in strengthening the capacity of countries to shift in a safe fashion to a reliance on suitable alternative products, methods and strategies to DDT, based on a review of the opportunities and needs in countries for sustainable transition.

Process for the evaluation of the continued need for DDT for disease vector control

4. Process followed, hitherto, for the work of the DDT expert group includes the following:

(a) Conduct a survey, every three years, on the production and use of DDT by Parties using the DDT questionnaire set out in Annex II to decision SC-3/2;

(b) Analyze the information collected through the above survey and from other published sources by a Consultant and prepare a preliminary report for the meeting of the DDT expert group;

(c) Seek inputs, observations and comments from WHO on the preliminary report ;

(d) Convene a meeting of the DDT expert group, every two years, prior to the meeting of the Conference of the Parties to review the preliminary report and develop recommendations to facilitate the evaluation of continued need of DDT for disease vector control by the Conference of the Parties at its every ordinary meeting on the basis of available scientific, technical, environmental and economic information, including:

(i) The production and use of DDT and the conditions set out in paragraph 2 of part II, Annex B to the Convention;

(ii) The availability, suitability and implementation of the alternatives to DDT; and

(iii) Progress in strengthening the capacity of countries to transfer safely to reliance on such alternatives.

Schedule for completing a cycle for the reporting, assessment and evaluation of the continue need for DDT for disease vector control

Event	Timing
*Distribute questionnaire	31 January, year 1**
*Parties complete questionnaire	30 June, year 1
Analysis of data complete	31 September, year 1
Expert group meeting	November, year 1
Complete expert group report	31 December, year 1
Translation and distribution of expert group report	February–March, year 2
Evaluation by the Conference of the Parties	May, year 2

* There is no mandatory reporting by Parties on the production and use of DDT and its alternatives prior to one out of every three evaluations undertaken by the Conference of the Parties.

** “year 1” refers to the first year of a budget biennium and “year 2” refers to the second.

Annex II

Developing a framework for the assessment of alternatives to DDT

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Glossary

CEA	Cost effectiveness analysis
CG	Corn granule (formulation of insecticides)
CV	Contingent valuation (a method in the social sciences)
DCE	Discrete choice experiment (a method in the social sciences)
DS	Decision support
DSS	Decision support system
DSSA	"Demonstrating and scaling up sustainable alternatives [to DDT]," a group of GEF-funded projects for the Stockholm Convention
EE	Expert elicitation (a method in the social sciences)
EPA	Environmental Protection Agency (in the United States government)
GEF	Global Environment Facility
GFATM	Global Fund to Fight AIDS, Tuberculosis, and Malaria
ICON®	Trade name for lambda-cyhalothrin, a pyrethroid-class insecticide used in malaria control
IRS	Indoor residual spraying
ITN	Insecticide-treated nets
KDR	Knockdown resistance (a mosquito mutation to resist insecticides)
LLIN	Long-lasting insecticidal nets
M&E	Monitoring and evaluation
OCP	OnchocerciasisControl Program
PEA	Programmatic environmental assessment
PEEM	Panel of Experts on Environmental Management for Vector Control (in WHO)
PMI	President's Malaria Initiative (within USAID)
SEA	Supplementary environomental assessment
USAID	Unites States Agency for International Development
WHOPES	World Health Organization Pesticide Evaluation Scheme
WP	Wettable powder (formulation of insecticides)
WTP	Willingness to pay

1. Introduction

1. The fifth meeting of the Conference of Parties (COP) requested the POPs Review Committee to assess the alternatives to DDT in accordance with the general guidance on considerations related to alternatives and substitutes to listed persistent organic pollutants on the basis of factual information provided by parties and observers and collected and compiled by the Secretariat. The objective of this report is to provide background information for the Committee to facilitate the development of a framework to undertake such assessment at its seventh meeting.

2. In Section 2, the report highlights important elements on the development of databases and decision analysis tools which can aid in the assessment of the conditions under which the usage of DDT and its alternatives for vector control can be justified. These findings are based on a review of the scientific literature in Sections 3,4, and 5, which address, respectively, the available vector control interventions, methods and examples of cost-effectiveness analysis (CEA) for chemical-based vector control interventions, decision support (DS) tools for vector control, and institutional barriers to implementing decision support systems.

3. The principle of this approach is to organize current scientific information on vector control insecticides within a cost-effectiveness framework. In practice, this consists of developing an information and decision analysis system which can be used by national vector control programmes (e.g. national malaria control programmes) to conduct CEAs of vector control interventions. Importantly, such a cost-effectiveness system would take into account any health and environmental risks that arise with the use of insecticides.

4. The outline for the rest of this report is to first present the major elements of the approach, before moving to a detailed summary of the literature. A note should be made here regarding on the scope of this report: The majority of this document focuses on the chemical-based control of malaria, since this is by far the most prevalent and burdensome vector-borne disease[1]. However, depending on the needs of the POPRC, future work can extend much of the present analysis to consider adopting CEA frameworks for other vector-borne diseases, conditional on the availability of the necessary scientific data.

2. Elements of a potential framework to assess DDT and its alternatives

2.1. Update and enhance existing tools for the cost-effectiveness analysis of malaria control

5. The 1993 guidelines of the WHO-convened Panel of Experts on Environmental Management (PEEM) provide the most up-to-date and suitable framework for conducting CEA of chemical-based vector control methods[2]. However, this document has not gained the traction among malaria control managers that would be required to serve as a central instrument for evaluation of chemical vector control alternatives including DDT. It is the consultant's professional opinion that the reason for this is that, while the PEEM guidelines are accurate, the document is too long and unwieldy for time and budget constrained vector control managers to use in implementing their own CEA. Without additional incentives and resources for conducting CEAs following the PEEM guidelines, there is not much reason for vector control managers to undertake such a task. As one party who was involved in the development of the PEEM guidelines put it when interviewed by the consultant: "I think the main weakness of the PEEM 3 guidelines is that it does "not speak" to [those in] the vector control community, who are … preoccupied with the technical aspects of vector control."

6. In place of a static document, the consultant recommends that an updated version of the PEEM guidelines is made available online, along with a forum for users (i.e. vector control managers and environmental ministers) to exchange advice, and downloadable software tools which automate many of the components of a CEA. The software tools should include:

(a) Standardized system for assessing intervention effectiveness using a handful of different measures (human biting rate, inoculation, incidence, prevalence) and based on computer models of malaria interventions which are validated by WHO.

(i) Since the majority of effectiveness evaluations will not be randomized controlled experiments, scientifically vetted models will be necessary for assessing the counterfactual—i.e. what would

1 WHO. Global Burden of Disease. 2004; Available from: http://apps.who.int/ghodata/.

2 Phillips, M., A. Mills, and C. Dye, Guidelines for Cost-effectiveness Analysis of Vector Control, Panel of Experts on Environmental Management (PEEM), Editor 1993, WHO/FAO.

have happened without the intervention—and if need to be the predicted impacts of the alternative interventions. The references in Section 4.1.1 provide references for the construction and rollout of such models. This effectiveness system should allow or the user to specify different assumptions about insecticide resistance becoming a problem over the course of the intervention (Section 4.4).

(b) A standardized system for assessing intervention costs, including financial, opportunity, and external costs (defined in section 4.1.2).

(i) Previous WHO-approved tools[3] and PMI-published guidance documents[4] are available for developing an automated system for assessing financial costs; see Sections 4.1.2 and 5.4. Opportunity costs could also probably be assessed through some modifications to this system—e.g. allowing user to input information on donations and volunteers' time commitments. External costs—of principal interest to POPRC—will require more care, and will need to be further addressed by scientific experts and perhaps by additional primary research, as discussed below. As with effectiveness, insecticide resistance should be considered in the cost evaluation as well.

7. In addition to the provision of these tools (comprised mostly of the synthesis of other scientific work), a panel of **experts on vector control, environmental health, and economics should be convened to update the PEEM guidelines.** Though not an exhaustive list, specific items in the PEEM guidelines requiring update, as identified by the consultant (see Section 2) are as follows:

(a) Provide updated methods for evaluating effectiveness when no counterfactual is directly observable.

(i) Updated guidelines in Chapter 2 should make reference to the role of disease modelling in assessing intervention effectiveness. An easier-to-reference list of effectiveness indicators should also be included. For example, see the effectiveness indicators profiled by The Global Fund[5]. Additional indicators—specific to vector control interventions—should be included in this list.

(b) Verify that the PEEM guidelines conform to the WHO recommendations for generalized cost-effectiveness analysis[6].

(i) For example, any discussion of using disability-adjusted life years (DALYS) as an effectiveness measure should be made consistent with the WHO's guidance on generalized cost-effectiveness analysis.

(c) Reorganize the cost evaluation chapter according to the demarcation laid out in Section 4.1.2 of this report—financial, opportunity, and external costs—with a description, instructions, and examples of how to assess each type of cost.

2.2 Synthesize existing tools to improve inter-agency coordination

8. Accounting for human health and environmental risks from insecticide usage in vector control will require coordination across agencies at the global and national levels. As detailed in Section 5, it appears that most—if not all—funding sources for vector control programmes recognize the importance of decision support (DS) and CEA in formulating vector control strategies, and the related imperative of evaluating the cost-effectiveness of different interventions (although usually the costs of insecticide risks are not included in the costing). Furthermore, major funding sources for malaria control, such as the Global Fund, WHO, UNEP, and their RBM umbrella, have all taken meaningful steps to incorporate elements of CEA into their monitoring and evaluation protocol. Indeed, most funders administer their own questionnaires and/or issue their own M&E requirements to national vector control programmes. At the same time, UNEP, WHO, and PMI also recognize the importance of conducting environmental monitoring of insecticide-based vector control interventions, as well as monitoring the global status of insecticide resistance in disease vectors. However, with the exception

3 Tan-Torres, T., Malaria Costing Tool, 2011, World Health Organization.

4 Sine, J. and A. Doherty, Indoor Residual Spraying (IRS) for Malaria Control Indefinite Quantity Contract (IQC) Task Order 1 (TO1): Analysis of 2008 Expenditures in Five IRS TO1 Countries, United States Agency for International Development, Editor 2010: Washington, DC.

5 The Global Fund, Tools for monitoring programs for malaria, in Monitoring and Evaluation Toolkit: HIV, Tuberculosis, Malaria, and Health Systems Strengthening2009.

6 Edejer, T.T.-T., et al., eds. WHO Guide to Cost Effectiveness-Analysis. 2003, World Health Organization: Geneva.

of a UNEP project underway[7] and the PEEM guidelines, little official guidance exists on how to connect the information contained in environmental assessments or vector resistance surveys to cost-effectiveness evaluations.

9. Therefore, UNEP-WHO could initiate a standardized reporting system and associated database for environmental impact assessments of vector control interventions. The Global Alliance on DDT and Alternatives may be able to provide an institutional framework for such a reporting system (see Section 5.1). Where possible, quantitative measures of human health and environmental impacts of insecticide exposure and transport should be incorporated into the database (see Recommendation 2.3.1). A first step in this work should include the integration of the POP DDT database and the WHO database on general insecticide usage in vector control: As discussed in Section 5.1, the POP DDT questionnaire is more detailed, but the WHO questionnaire enjoys better response rates. A second step would be to extend these questionnaires down to lower levels of vector control programs (as recommended by the UNEP project on DDT data collection[7]), and to link these lower-level questionnaires with programmatic environmental assessments (PEAs) mandated by other malaria control donors such as USAID's President's Malaria Initiative (PMI). The information in the PEAs for USAID (e.g. for IRS and LLINs) are increasing in quality and detail. However, these PEAs are not sufficiently standardized.

2.3 Fill gaps in existing research

10. Through a review of the literature, the consultant identified gaps in knowledge necessary to establish a cost-effectiveness framework for evaluating DDT relative to its alternatives. These gaps are listed below, with methods for addressing them.

2.3.1. More research is needed on the costs of exposing humans and the environment to insecticides through vector control interventions

11. As illustrated in Section 4.1.2, the understanding of the risks posed by human exposure to DDT and other insecticides, as well as by the diffusion of these chemicals into the environment, remains about the same as when a report was prepared for the DDT Stakeholders' Meeting in November 2008 to review the interim report for the establishment of a global partnership to develop alternatives to DDT. Moreover, due to methodological limitations, our understanding of these risks is unlikely to advance much within the next 5 years. This leaves policymakers, vector control managers, technical staff, and the households who submit to insecticide exposure to make decisions under inherent uncertainty. **It is recommended that further social science research be conducted to quantify stakeholders' perceived costs of insecticide exposure and diffusion into the environment from vector control interventions.** Such research is remarkably absent in the published academic literature; where valuation work on insecticide exposure is performed, it is usually done in the context of agriculture—not public health. This is significant, since exposure pathways vary dramatically between these contexts. Methods for conducting this kind of research, e.g. discrete choice experiments and best-worst scaling, are discussed in Section 4.3.

2.3.2. More research is needed on institutional barriers to implementing a CEA system for assessing DDT and alternative vector control strategies

12. As implicated in the quote at the beginning of Section 2, the 1993 framework advanced by PEEM did not gain traction because it was not well-targeted at its audience. **Therefore, more information is required about the constraints and motives of the audience—vector control managers and environmental ministers.** Improved knowledge is needed by the POPRC on the level of collaboration and exchange between different national-level institutions, for example Ministries of Health and Ministries of Environment. Such collaboration will be essential for the establishment of an effective CEA framework of the type that the POPRC requires. Furthermore, assessment of stakeholders' views of the objective of the Convention with regard to DDT—which is to ultimately eliminate the use of the chemical—needs to be conducted. This will allow UNEP-WHO to better calibrate their implementation to the different attitudes about POPs in vector control which prevail across institutions.

13. Section 6 addresses research on implementation barriers research in the context of malaria control, and then discusses available methods for studying these types of problems. In summary, the current portfolio of projects at the Global Environment Facility (GEF) focusing on DDT use in vector control points to the need for systematic assessments of institutional barriers and capacities. As an

7 UNEP. DSSA Establishment of Efficient and Effective Data Collection and Reporting Procedures for Evaluating the Continued Need of DDT for Disease Vector Control. GEF Project Database 2007 [cited 2011 August 30]; Available from: http://www.gefonline.org/projectDetailsSQL.cfm?projID=3349.

example, the GEF-funded project on "developing efficient and effective data collection systems" for DDT and alternatives in vector control is designed to fill an identified gap in the institutional capacity of national vector control programmes to effectively monitor DDT use. However, there is currently no clear plan disseminated by UNEP, WHO, or GEF for identifying national-level institutional barriers to implementing a CEA for evaluating DDT relative to alternatives. The execution of such a plan is necessary for a CEA system satisfying the needs of the Stockholm Convention to gain traction among NMCPs. Methods for identifying and solving institutional barriers to implementation include expert elicitation, stakeholder analysis, and ongoing review of case studies from related literature

3. DDT spraying and other interventions in disease vector control

14. DDT has been a mainstay of vector control strategies since the 1940s, due to its low cost and long-lasting effects. The chemical kills and repels a broad range of infectious disease vectors, including *Anopheles* mosquitoes (malaria vectors), *Aedes*mosquitoes (vectors for flaviviruses such as yellow fever and dengue),*Culex*mosquitoes (vectors for different types of encephalitis such as West Nile), and tsetse flies (vectors for sleeping sickness).[8]For malaria control, DDT can be used via spray applications either in so-called indoor residual spraying (IRS) or in outdoor applications. IRS for malaria control is the only method of DDT use which is currently approved by the WHO[9].WHO recommendations for IRS with DDT are to apply 1-2 g/m^2 of the chemical in a wettable powder form onto indoor surfaces at an interval of 6 months or greater. Globally, use of DDT in vector control averaged 4,429 tonnes per year between 2000 and 2009, with India being the largest user throughout the period[10].

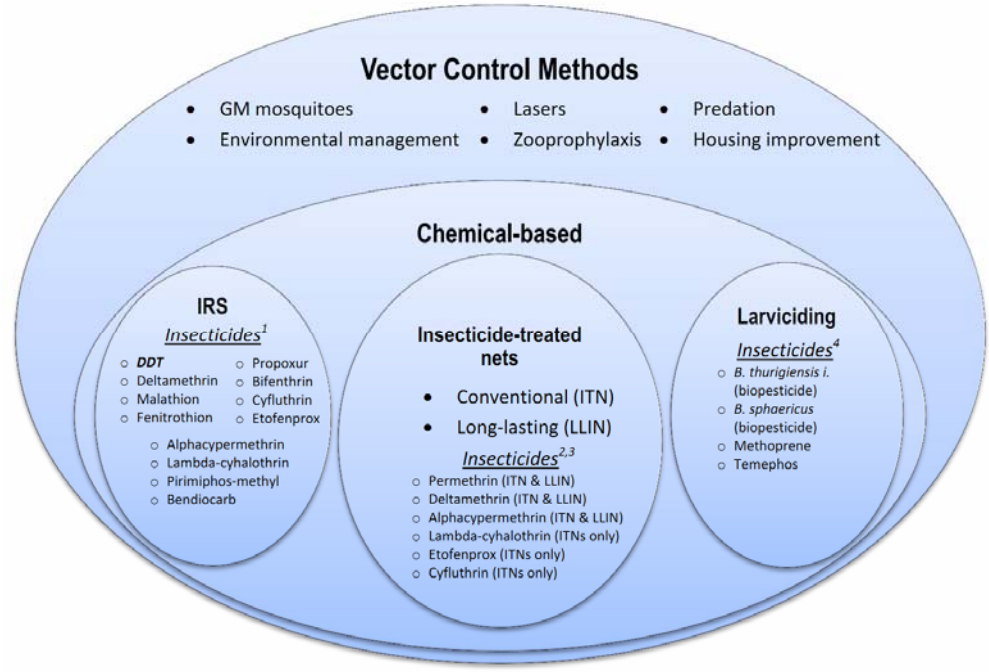

Figure 1: Classes of vector control methods. See van den Berg[11] for details on interventions.

1 WHO-approved IRS insecticides: http://www.who.int/whopes/Insecticides_IRS_Malaria_09.pdf

2 WHO-approved ITN insecticides: http://www.who.int/whopes/Insecticides_ITN_Malaria_ok3.pdf

8 DDT is also effective at killing and repelling so-called "nuisance" insects such as bedbugs and cockroaches, which do not have significant vectorial capacity but which can nonetheless affect public perceptions of DDT spray campaigns.

9 WHO, The use of DDT in malaria vector control: WHO position statement, Global Malaria Programme, Editor 2007: Geneva.

10 WHO, Global insecticide use for vector-borne disease control: a 10-year assessment (2000-2009), 2011, World Health Organization Pesticide Evaluation Scheme (WHOPES).

11 van den Berg, H., Global status of DDT and its alternatives for use in vector control to prevent disease, Stockholm Convention on Persistent Organic Pollutants, Editor 2007: Geneva, Switzerland.

3 WHO-approved LLIN insecticides: http://www.who.int/whopes/Long_lasting_insecticidal_nets_Jul_2011.pdf

4 USEPA-approved larvicides:http://mosquito.ifas.ufl.edu/Documents/Florida_Mosquito_Control_White_Paper.pdf

15. A number of other alternative interventions for controlling malaria vectors have existed for decades. A subset of these interventions includes chemical-based methods (Figure 1), which are the focus of this report.[12]

16. In addition to DDT, the WHO Pesticide Evaluation Scheme (WHOPES) recommends 11 other insecticides for IRS belonging to 3 chemical classes[13].WHOPES bases its recommendations for IRS on assessments of the efficacy and the risks associated with each chemical evaluated.[14]All insecticides in IRS are applied by mixing small sachets with water and sprayed onto indoor surfaces. The concentration and frequency of spraying required for effective vector control vary with insecticide type (Table 1).

Table 1: WHOPES-approved insecticides for IRS.*(1) CS: capsule suspension; EC = emulsifiable concentrate; SC = suspension concentrate; WG = water dispersible granule; WP = wettable powder. (2) OC = Organochlorine; OP = Organophosphate; C = Carbamates; PY = Pyrethroids. From: http://www.who.int/whopes/Insecticides_IRS_Malaria_09.pdf*

Insecticide compounds and formulations (1)	Class group (2)	Dosage (g a.i./m^2)	Mode of action	Duration of effective action (months)
DDT WP	OC	1-2	contact	>6
Malathion WP	OP	2	contact	2-3
Fenitrothion WP	OP	2	contact & airborne	3-6
Pirimiphos-methyl WP & EC	OP	1-2	contact & airborne	2-3
Bendiocarb WP	C	0.1-0.4	contact & airborne	2-6
Propoxur WP	C	1-2	contact & airborne	3-6
Alpha-cypermethrin WP & SC	PY	0.02-0.03	contact	4-6
Bifenthrin WP	PY	0.025-0.05	contact	3-6
Cyfluthrin WP	PY	0.02-0.05	contact	3-6
Deltamethrin WP, WG	PY	0.02-0.025	contact	3-6
Etofenprox WP	PY	0.1-0.3	contact	3-6
Lambda-cyhalothrin WP, CS	PY	0.02-0.03	contact	3-6

17. In addition to IRS, chemical-based vector control methods include the distribution and promotion of insecticide-treated nets, both conventional (ITNs) and long-lasting (LLINs), as well as the reduction of vector recruitment via application of larvicides onto breeding habitat. Both ITNs and LLINs provide protection against vector-borne disease by providing a physical barrier with an insecticide treatment which repels and kills vectors in the vicinity of the net. In the case of ITNS, this treatment wears off after 1 year, requiring manual retreatment with insecticides. In the case of LLINs, the netting material is impregnated with pyrethroids during manufacture so that the insecticidal effects last for the life of the product, usually 3 years. Due to the extended insecticidal effect of LLINs relative to ITNs, the WHO position is to obtain full coverage with LLINs of at-risk populations[15]. The WHOPES-approved for LLINs are a subset of the WHOPES-approved IRS insecticides, with exception of permethrin which is only approved for use in LLINs.

18. As opposed to IRS and LLINs, which target adult vectors, larviciding targets *Anopheles* larvae and/or pupae to limit the emergence of new vectors. Consequently, modern larviciding operations utilize a distinct set of chemicals specially designed for this purpose. The most favored of these are the microbial biopesticides *Bacillus thurigiensisisraelensis (Bti)* and *Bacillus sphaericus (Bs).Bti* and *B*sare highly potent toxins to mosquito and blackfly larvae but have no known effects on other

12 More detailed descriptions of non-chemical methods are provided in another report by Henk van den Berg (2007) to the Convention's DDT Review Committee.

13 WHO. WHO recommended insecticides for indoor residual spraying against malaria vectors. 2009 [cited 2011 August 9]; Available from: http://www.who.int/whopes/Insecticides_IRS_Malaria_09.pdf

14 The guidelines for both the risk and efficacy assessment scan be found at: http://www.who.int/whopes/guidelines/en/

15 WHO. Insecticide-Treated Mosquito Nets: A WHO Position Statement. 2009 [cited 2011 August 10]; Available from: http://www.who.int/malaria/publications/atoz/itnspospaperfinal.pdf.

organisms. Both *Bti* and *Bs* are produced for larviciding in 2 forms: a water dispersible granule (WDG) that is applied with knapsack sprayers, and corn granules (CG) which are spread by hand. While *Bti* is usually cheaper to purchase than *Bs*, it is less effective in polluted water (e.g. latrines) and needs to be applied more frequently to maintain toxic action on mosquito larvae[16].

19. Trends over the past 10 years for insecticides used in vector control are reported in a recent WHOPES publication[10]. Between 2000 and 2009, registered usage of DDT has increased in Africa and Southeast Asia. Pyrethroid use has also grown dramatically worldwide, and remains the dominant insecticide for use in vector control spray operations (Figure 1). The use of larvicides remains negligible relative to the four insecticide classes shown in this figure, and hence are not reported.

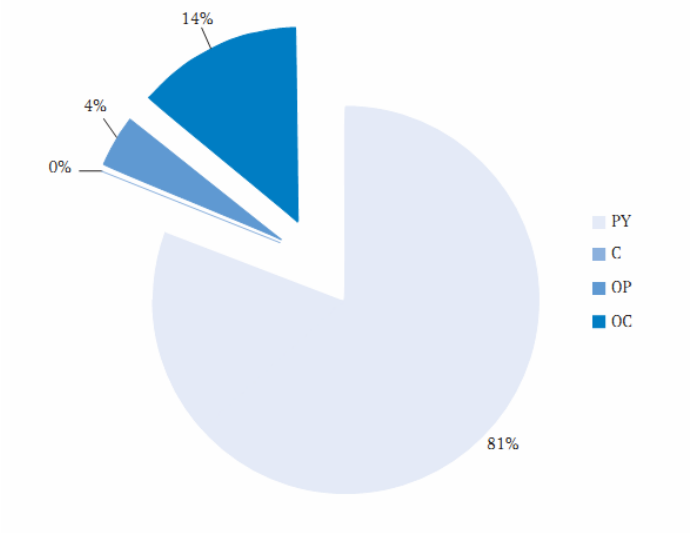

Figure 1: Proportional usage of insecticides in vector control worldwide. *PY = Pyrethroids, C = Carbamates, OP = Organophosphates, OC = organochlorine (DDT). Reproduced with permission from WHO*[10].

4. Cost-effectiveness analysis of vector control interventions

4.1. Methods for cost-effectiveness analysis of vector control alternatives

20. Cost-effectiveness analysis (CEA) is the most widely used framework for integrating disparate quantitative indicators into a single decision-analysis framework. In order to provide a foundation for a review of CEAs for various vector control activities, this section summarizes the purpose and ingredients for conducting a CEA of a set of alternative vector control programs.

21. In general, there are 3 possible objectives of a CEA: Provide updated methods for evaluating effectiveness when no counterfactual is directly observable.

(a) To calculate the amount of some impact that can be achieved given a fixed budget.

(i) For example, given a vector control budget of $10 per household per year, what kind of reduction in malaria incidence could we achieve over a period of 10 years with an IRS program spraying 90% of households using DDT as frequently as our budget allows, versus an IRS program with the same budget and population using bendiocarb?

(b) To calculate the costs of achieving a predefined policy objective.

(i) For example, how much would it cost to achieve a 90% reduction in malaria incidence over 5 years using DDT-based IRS versus bendiocarb-based IRS?

(c) To calculate the average or marginal cost per unit gain in our indicator of interest.

(i) For example, what is the average cost per malaria case avoided for IRS using DDT covering 90% of the population once a year for 10 years, versus a 10-year

16 Connelly, C.R. and D.B. Carlson, Florida Mosquito Control: The state of the mission as defined by mosquito controllers, regulators, and environmental managers, Florida Coordinating Council on Mosquito Control, Editor 2009, University of Florida, Institute of Food and Agricultural Sciences, Florida Medical Entomology Laboratory.

LLIN distribution and education campaign that distributes LLINs to all members in households with children under 5 and pregnant women and then provides conditional cash transfers (CCTs) for confirmed use of the nets?

22. Note that all 3 objectives are related but distinct. Objective (c) is the most commonly sought, as evidenced by the frequent use of cost-effectiveness ratios (i.e. total cost divided by total impacts) in programmatic reports. This is because such measures allow decision makers to evaluate the relative cost-effectiveness of programs with different budgets and different magnitudes of impact. However, it is often assumed in CEAs of type (c) that the cost-effectiveness ratio will remain constant regardless of the scale of intervention. For example, we might imagine that a large-scale larviciding program would achieve more cases avoided per dollar spent than a small-scale program. For this reason, it is important when interpreting cost-effectiveness ratios to be aware of the scale of each alternative—i.e. the absolute amount of expenditure and/or impacts—and to utilize cost-effectiveness ratios for the purpose of decision makingonly when the proposed alternatives are similar in scale.

23. Obviously, the most critical steps in a CEA are measuring the impact (i.e. effectiveness) and costs of a given intervention. Phillips, Mills, et al.[2] provide an in-depth set of guidelines for conducting a CEA for alternative vector control policies, with an emphasis on measurement. These guidelines are for most part as valid and relevant today as they were at the time of their publication: The basic ingredients of a CEA have not changed much over the last several decades. The critical points of that document are reviewed below, with additional information incorporated where necessary.

4.1.1. Assessing the effectiveness of vector control activities

24. How do program managers define success for vector programs? Is it measured by the fraction of the at-risk population that the program covers? Is it defined by decreased abundance of disease vectors, or the number of infection opportunities (e.g. mosquito bites) between vectors and humans? Or is it defined as a decline in the incidence of vector-borne disease?

25. In order to compare alternative vector control strategies using a CEA, a common measure of effectiveness—i.e. program impact—must be adopted. For vector control interventions, defining such a measure requires care, since the epidemiology of vector-borne diseases is complex. The more that factors other than the intervention affect some measure of effectiveness, the more difficult it will be to evaluate the effectiveness of an intervention using that measure. For example, the prevalence of malaria in a given community with an IRS program is also affected by the level of healthcare in that community, the quality of housing, and the average level of acquired immunity to malaria.

26. In general, there is a trade off between choosing an effectiveness measure which is common to many alternative interventions and one which can be easily identified with available data. Phillips, Mills, et al.[2] recommend taking a decision analytic approach, by constructing an influence diagram which follows the causal pathways from a given intervention activity to the final outcome it is intended to affect, in this case the human burden of disease.

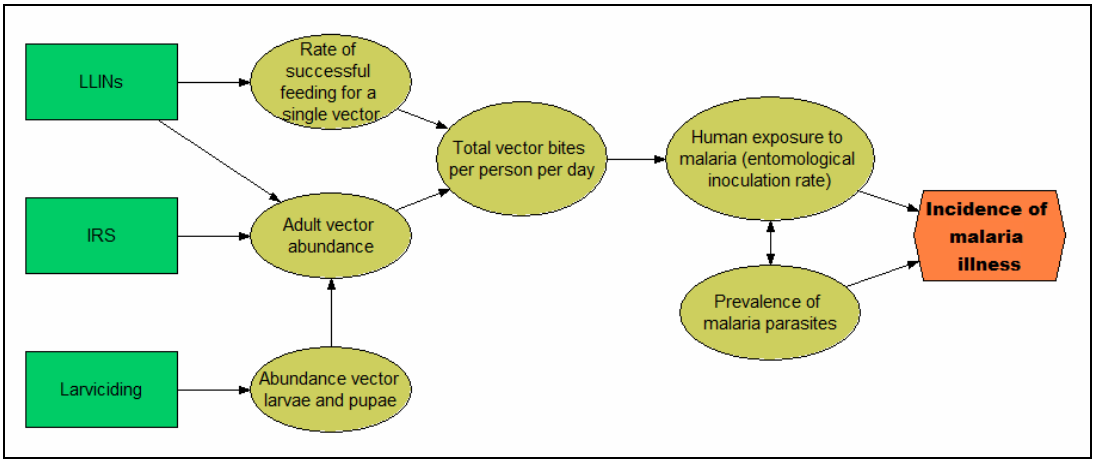

Figure 3: Example influence diagram for vector control activities. Influence diagrams are graphical representations of a decision problem. The green boxes are decision nodes, i.e. variables determined by the policymaker. The ovals are chance nodes, i.e. variables that are uncertain and are instrumental in translating decisions into impacts. The hexagon is an objective node, i.e. the variable which the policymaker seeks to control in the decision problem. The arrows illustrate how each of these nodes influences other nodes.

27. Figure 3 presents an influence diagram for how LLIN, IRS, and larviciding affects malaria incidence. As can be seen here, each of these interventions affects different aspects of vector populations. Therefore, using adult vector abundance as a measure of intervention effectiveness would be inappropriate since LLINs also affect the ability of single vectors to bite humans. Malaria incidence, on the other hand, provides a common measure of effectiveness among all interventions. However, as shown in the influence diagram there are a number of intermediate variables that add to the uncertainty in this measure of effectiveness. A sound principle for CEA is to choose a measure of effectiveness which captures all avenues of prevention for each intervention (e.g. captures mosquito mortality and repellency), is least removed from the direct effects of the intervention, and can be reliably evaluated using current methods. In Figure 3, the total number of vector bites per person per day is good candidate measure. If this cannot be reliably measured in a given area, then the intensity of malaria transmission should determine the outcome measure: In high transmission settings, the EIR can be most reliably estimated and thus is a candidate measure. In low transmission settings, the EIR is difficult to measure, and the analyst might consider using the incidence of malaria illness (e.g. at health clinics) as the primary measure of program effectiveness.

28. In cases where a new intervention is being proposed, there may be inadequate resources or time to scientifically test the impact of a given vector control intervention on vector biting rates, malaria exposure, and/or prevalence. For these situations, a number of mathematical models have been developed to evaluate the predicted effectiveness of a number of vector control interventions, including IRS with DDT and pyrethroids and the distribution of LLINs[17,18].These models are based on a number of peer-reviewed studies of malaria epidemiology and the effectiveness of IRS and LLINs, and are being continually refined to make them suitable for a variety of malaria contexts.

4.1.2. Assessing the costs of vector control interventions

29. Evaluating the costs of a vector control intervention consists of evaluating the economic costs. Such costs include:

(a) **Financial costs.** These consist of all expenditures directly associated with the intervention, across all contributors.

Examples of what to include in this category:

- Cost of insecticides purchased for an IRS operation.
- Construction costs of warehouses built for housing equipment for a larviciding operation.
- Wages for intervention personnel.

Documents and data useful for assessing these costs:

- For completed and ongoing interventions, expenditure, budget, and inventory records for the intervention from the ministry of health (MOH), the national malaria control programme (NMCP), or the national institute of medical research (NIMR).
- For future proposed interventions, projections of prices and quantities of inputs for the intervention, including projected wages and man-hours for labor inputs.
- Local purchase orders (LPOs) for capital equipment such as vehicles or warehouses.

(b) **Opportunity costs.** These consist of the value of resources that were donated, loaned, or already available within the organization overseeing the intervention program. The value of such resources is defined as the value they would generate if employed for their next best use. In practice, the value of these resources is assessed using price of purchasing these resources.

Examples of what to include in this category:

- The value of time village leaders spends assisting with sensitizing communities to a larviciding operation.
- The value of a household's time spent collecting water and removing household goods from homes to prepare for an IRS visitation.

17 Chitnis, N., et al., Comparing the effectiveness of malaria vector-control interventions through a mathematical model. American Journal of Tropical Medicine and Hygiene, 2010. 83(2): p. 230-240.

18 Griffin, J.T., et al., Reducing Plasmodium falciparum Malaria Transmission in Africa: A Model-Based Evaluation of Intervention Strategies. PLoS Med, 2010. 7(8): p. e1000324.

- The value of knapsack sprayers donated or loaned to a larviciding intervention.
- The value of salaried employees' time devoted to planning and budgeting for the intervention.
- The value of space used for equipment storage in pre-existing warehouse facilities.

Documents and data useful for assessing these costs:

- National employment surveys for detailed wage estimates for valuing volunteer labor.
- Price quotes for loaned or donated recurring inputs and capital equipment.

(c) **External costs.** These consist of the costs (and benefits) of intervention "side-effects," i.e. impacts that are unrelated to disease reduction. Assessing the value of these impacts consists of estimating the shadow prices associated with the impact. *Shadow prices* provide a measure of the economic value on some good or service for which there is no market price, for instance the economic value of good water quality. *Nonmarket valuation methods* provide estimates of these shadow prices, and are discussed below.

Examples of what to include in this category:

- The value of reductions in non-vector pests in and around the home as a result of IRS (being a benefit, this should be assessed as a negative cost).
- The value of any expected loss in water quality as a result of groundwater contamination from IRS.
- The value of any expected loss in profit resulting from crop exports no longer receiving organic certification due to widespread IRS use.
- The costs of expired-LLINs, either their disposal costs or their impact on the environment when disposed of improperly.
- The costs of lost future efficacy of IRS due to accumulating insecticide resistance in vector populations.

Documents and data useful for assessing these costs:

- Peer-reviewed epidemiological and toxicological studies of the impact of chemical-based vector control on human health and the environment.
- Expert-elicitation of the risks and economic costs associated of chemical-exposure from IRS, LLINs, or larviciding[19].
- Population surveys for the valuation of a given external impact, e.g. discrete choice experiments (DCEs) or contingent valuation (CV) surveys of households' perceived costs of an increased risk of cognitive impairments due to prenatal DDT exposure[20].
- Evaluations of household behaviors with regard to LLIN disposal.
- Reports to funding agencies, such as programmatic environmental assessments (PEAs) of specific vector control activities.

30. When compiling intervention cost data into a spreadsheet or database, it is recommended that one sheet or database field is maintained to record inputs for each contributor to the intervention and to keep detailed information about the timing of the intervention and the currencies that inputs were purchased in. Figure 4 provides an example of a cost record arranged in a spreadsheet format.

31. To perform a CEA using such a database, a single measure of costs over the life of the intervention must be calculated from the disaggregated data. This can be done in a number of ways, depending on the availability of exchange rate data between USD and local currency, inflation data, and how policymakers value future costs relative to current costs, i.e. discounting. The basic approach is as follows: First, convert each cost to a common currency using exchange rates and convert these costs in each year to a common base year using inflation rate data. Second, set a fixed discount rate

19 USEPA, Expert Elicitation Task Force White Paper, USEPA Science Policy Council, Editor 2009: Washington, DC, USA.

20 Ryan, M., K. Gerard, and M. Amaya-Amaya, eds. Using Discrete Choice Experiments to Value Health and Health Care. The Economics of Non-Market Goods and Resources2010, Springer. 276.

(e.g. 3% per year) and calculate the total present value (TPV) costs of the intervention or to calculate the annualized costs of the intervention. The TPV measure is equivalent to calculating the cost of paying for the entire intervention upfront, whereas the annualized cost measure is the same as calculating a constant amount per year that would be necessary to fund the intervention over its lifetime. See Phillips, Mills, et al.[2] for details on recordkeeping and on calculating total costs from disaggregated cost data.

32. The above discussion illustrates the many different potential costs involved in a given intervention. It is often the case that the analyst lacks price data with which they can obtain a monetary value for opportunity costs and external costs. For example, how does one obtain a quantitative measurement of any health costs associated with chemical exposure? In such situations, it is necessary to employ methods in *nonmarket valuation*.

	A	B	C	D	E	F	G	H	I	J
1	USD = United States Dollar									
2	LC = Local Currency									
3				2001					2002	
4		Quantity	USD	LC	Total (USD)	Total (LC)	Quantity	USD	LC	Total (USD)
5	**FINANCIAL COSTS**									
6	*CAPITAL EQUIPMENT*									
7	Knapsack sprayers	10	$50		$500					
8	100 m2 warehouse	1	$10,000		$10,000					
9	Spray team uniforms	10	$30		$300					
10	Spray team helmets	10	$50		$500					
11	Training booklets	11		UGX 25,000		UGX 275,000				
12	*RECURRING COSTS*									
13	Spray team wages (per man-hour)	8100		UGX 20,000.0		UGX 162,000,000	8100		UGX 22,000.0	
14	Bendiocarb (kg)	50	$3		$150		50	$3		$158
15										
16	**OPPORTUNITY COSTS**									
17	*CAPITAL EQUIPMENT*									
18	Warehouse rents (25% of floor area)	0.25	$300		$75		0.25	$315		$78.8
19	*RECURRING COSTS*									
20	Village leader guidance (per man-hour)	810		UGX 25,000		UGX 20,250,000	810		UGX 27,500	
21										
22	**EXTERNAL COSTS**									
23	*RECURRING COSTS*									
24	Health costs of insecticide (kg per person exposed per year)	0.05	$1,000		$50		0.05	$1,000		$50.00
25	Lost profits from forefeture of organic crop certification (USD per farm)	10	$250		$2,500		10	$265		$2,650
26										
27										

Figure 4: A mock record keeping system for costs. Such a system should, for each expenditure, (A) specify the units/quantity of the input used where appropriate, (B) record the amount spent per unit and the total amount spent for each year of the intervention, (C) record the expenditure in the currency in which the transaction took place, (C) classify the expenditure according to whether it is a financial, opportunity, or external cost AND whether it is a capital or recurring expense, and (D) where possible specify which entity contributed that input, by compiling a separate spreadsheet for each contributor. Some judgment should be used in specifying the "contributor" for opportunity and external costs. These may be specified as separate sheets for these types of costs. Such a system permits the most flexibility in calculating the total economic costs of the intervention for use in a cost-effectiveness analysis.

4.2. Reviewing the effectiveness of DDT and alternatives in reducing malaria

33. In order to conduct a CEA of using DDT and alternatives in vector control, some quantitative measure of effectiveness is required. In general, effectiveness will vary from one location and context to the next. However, it is useful to have some understanding of how much a policymaker can expect a disease to be reduced from a given intervention in a given context. A number of randomized controlled trials(RCTs) and quasi-experimental studies of IRS and ITNs/LLINs have demonstrated significant effects of these interventions on reducing human exposure to malaria and the incidence of illness. However, these studies vary widely in their results. Two recent reviews[21,22] were found which evaluate the effectiveness of IRS in relation to LLINs. The review by Skaukat, Bremanet al. also identifies a study of source reduction. Additionally, a working paper by Kim, D. et al. [23] performs a formal meta-analysis of IRS studies, examining the relative importance of insecticide type, transmission context, and other factors contributing to the effectiveness of IRS in a range of studies. Finally, Chitnis N. et al [17]and Griffin J.T. et al.,[18]in their model-based analysis of intervention

21 Shaukat, A.M., J.G. Breman, and F.E. McKenzie, Using the entomological inoculation rate to assess the impact of vector control on malaria parasite transmission and elimination. Malaria Journal, 2010. 9(122).

22 Pluess, B., et al., Indoor residual spraying for preventing malaria (Review). The Cochrane Library, 2010(4).

23 Kim, D., K. Pfau, and R. Kramer, Prevalence reduction of malaria by indoor residual spraying: a meta-regression analysis, in Working paper.2011, Duke University: Nicholas School of the Environment.

effectiveness, report results from computer simulations comparing IRS, LLINs, and other malaria control interventions. The main findings of these 5syntheses are summarized here.

34. Pluess, Tanser et al.—hereafter referred to as PTLS—focus on 6 studies in their review of IRS effectiveness.[24]Of these 6 studies, 3 were characterized by unstable (i.e. epidemic) malaria transmission, and the other 3 were stable (i.e. *endemic*) settings. *A. gambiae* was the primary vector in 2 of the sites. Insecticide resistance was indicated in one site based on the WHO vector susceptibility test. Four of studies evaluated the effectiveness of pyrethroid-based IRS (deltamethrin in 2 cases, alphacypermethrin in 1 case, and ICON® in 1 case), and the other 2 studies focused on carbamate effectiveness (one on propoxur and the other on bendiocarb).

35. Based on their review, PTLS conclude: "Historical and programme documentation has clearly established the impact of IRS. However, the number of high-quality trials is too few to quantify the size of the effect in different transmission settings. The evidence from randomized comparisons of IRS versus no IRS confirms that IRS reduces malaria incidence in unstable malaria settings, but randomized trial data from stable malaria settings is very limited. Some limited data suggest that ITN give better protection than IRS in unstable areas, but more trials are needed to compare the effects of ITNs with IRS, as well as to quantify their combined effects."

36. Among the 6 studies reviewed in detail by PTLS, malaria incidence particularly in young children provides a clearer measure of effectiveness than malaria prevalence, an observation which is relevant for the design of future studies. One reviewed study in a stable transmission setting found a 14% reduction of malaria incidence in children between 1 and 5 years of age[25]. In unstable transmission environments, 2 studies found between a 31% and 79% reduction in malaria incidence among all ages.

37. In their review of ITN, IRS, and larviciding effectiveness, Shaukat, Breman, et al.—hereafter SBM—select the entomological inoculation rate (EIR) as their measure of effectiveness. The EIR is the product of the human biting rate and the fraction of vectors which are infectious (a.k.a the sporozoite rate). They analyze the results of 8 vector control intervention studies: Four evaluated ITNs, 3 evaluated IRS, and 1 evaluated larviciding. One of the IRS studies—the Garki project study by Molineaux and Gramiccia[26]—is also addressed by PTLS. Of the IRS studies, one analyzed the impact of DDT-based IRS in a stable transmission setting, finding a 56% reduction in the EIR. This can be compared to the other 2 IRS studies, which find a 93% and 71.4% reduction in EIR for ICON®-based and propoxur-based IRS, respectively. However, coverage levels among the target population are not reported for any of the 3 IRS studies reviewed, and the spray frequency for the DDT study is not reported, precluding the possibility of any scientific comparison of insecticide effectiveness in IRS based on these studies. Of the 4 ITN studies reviewed by SBM, the relative reduction in EIR rangedfrom 75% to 97% in the second year of the trial. The single larviciding study found a 47% reduction in EIR using the biopesticide*Bti*.

38. Pfau, Kim et al.—hereafter PKK—build on the review by PTLS by expanding the study inclusion criteria, in order to obtain sufficient data points for a statistical meta-analysis of IRS effectiveness. The expanded inclusion criteria yielded 45 data points reporting findings from IRS evaluations in 9 countries. The meta-regression results suggest that DDT is most effective in IRS malaria control, followed by pyrethroids, carbamates, and lastly by organophosphates.[27]PKK also find that the pre-intervention prevalence of malaria increased the estimated effectiveness of IRS, whereas larger population sizes decreased IRS effectiveness. Moreover, study design attributes—e.g. whether a cross-sectional or cohort design was used—significantly affected estimated effectiveness: RCT designs estimated significantly higher levels of IRS effectiveness.

39. The model-based evaluations by Chitness, Shapira et al. and Griffin, Hollingsworth, et al.—hereafter CSSS and GHOC—complement the findings of the field trials summarized above, by examining the predicted effectiveness of various interventions in a range of transmission settings. Model-based studies such as these take published data and estimated statistics from field experiments and combine these numbers using a set of mathematical formula. The resulting mathematical models

24 Out of 134 potentially relevant studies, 128 did not meet the criteria for inclusion in the review.

25 Curtis, C., S. Misra, and M. Rowland, Comparison of house spraying with insecticide treated bednets in Tanzania, India, Pakistan, Second Multilateral Initiative on Malaria Pan-African Conference on Malaria, Editor 1999, Bethesda (MD): Fogarty International Center: Durban, South Africa.

26 Molineaux, L. and G. Gramiccia, The Garki project: research on the epidemiology and control of malaria in the Sudan savanna of West Africa1980, Geneva: World Health Organization.

27 It is not clear how PK control for the differing spray frequencies for each of these insecticide classes: Some of the studies included in the analysis examined only a single round of IRS, whereas others analyzed multiple rounds.

can be used to predict health outcomes under a set of "counterfactual" intervention scenarios—i.e. combinations of interventions and transmission settings for which an experiment cannot be performed.

40. Using such a model, CSSS compared the predicted effectiveness of ITNs, IRS with DDT, and IRS with bendiocarb. The authors find that for a given level of coverage in a high-transmission setting where *A. gambiae* (an indoor resting mosquito)is the primary vector, IRS using bendiocarb is the most effective intervention, followed by ITNs and lastly by IRS using DDT. Importantly, the authors do not consider insecticide resistance or seasonal volatility in vector populations in their analysis.

41. GHOC conduct a similar model-based comparison of IRS using DDT and LLINs (with other interventions). The authors analyze predicted effectiveness in a range of malaria transmission settings, from epidemic to endemic, using a database of field studies from 6 countries in Africa. While the GHOC model is in principle capable of comparing the predicted effectiveness of different vector control interventions, the authors only report results for a comparison of LLIN scale-up, as compared to LLIN scale-up in combination with scale-up of IRS using DDT. Therefore, while the results of this study cannot directly aid policymakers in evaluating the effectiveness of different vector control interventions, the models and estimation done by both the GHOC and CSSS teams provide a way forward for obtaining a tool with which policymakers can evaluate the predicted effectiveness of different vector control interventions.

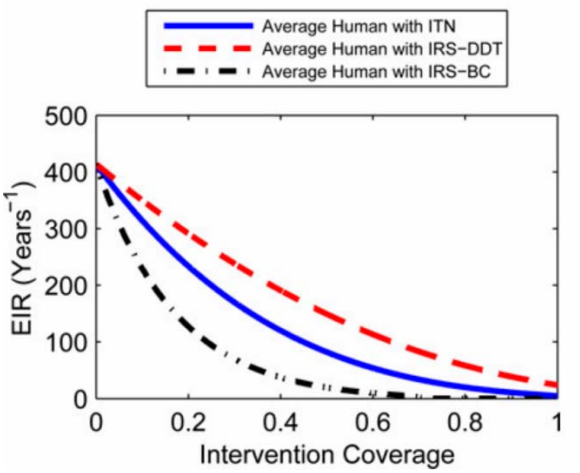

Figure 5: Predicted malaria exposure rates for three vector control interventions from Chitnes, N. et al.17. This figure shows results from a mathematical model fitted to data from Namawala, Tanzania. The entomological inoculation rate (EIR), a measure of malaria exposure, is plotted for a range of population coverage levels using IRS with DDT (IRS-DDT), ITNs, or IRS with bendiocarb (IRS-BC). Figure re-produced with permission from the American Journal of Tropical Medicine and Hygiene.

4.3. Reviewing the costs of DDT and alternatives

42. As summarized in Section 4.1.2, the full cost of using DDT and alternative insecticides in vector control includes the financial costs, the opportunity costs, and the external costs of the intervention. Financial costs of IRS, LLIN, and larviciding can be ascertained relatively easily by program managers and technical staff. See Sine and Doherty [4] for examples on estimating financial expenditures for 5 USAID-supported IRS programs. More difficult is assessing opportunity and external costs from vector control interventions. As mentioned above, external costs include environmental and health costs from insecticide usage. This section focuses on these costs.

43. Van den Berg [11] concludes from a review of the literature that, while negative human health effects from DDT exposure are possible, scientific tests of this hypothesis are ambiguous due to methodological limitations. These limitations and hence the ambiguity of the human health risks of DDT exposure remain at present, even while further epidemiological studies are published on the topic[e.g. Bomman, R., et al.[28]]. Moreover, the same methodological limitations also apply to the study of the health effects of alternative insecticides in malaria control. Table 3 summarizes environmental assessments of the 13 WHOPES-approved vector control insecticides, using information from Biscoe, Lewandowski et al.[29]. As can be seen, the known information about these

28 Bornman, R., et al., DDT and urogenital malformations in newborn boys in a malarial area. BJU International, 2009. 106(3): p. 405-411.

29 Biscoe, M., et al., Integrated Vector Management Programs for Malaria Control: Programmatic Environmental Assessment, United States Agency for International Development, Editor 2007: Washington, DC.

insecticides lacks standardized, quantifiable measures of human health and environmental impact. This lack of quantifiable measures for health and environmental impacts of insecticide exposure currently precludes an economic valuation of the risks of insecticide exposure based on toxicological or epidemiological studies. Although such an approach—essentially multiplying the risk increase for a particular endpoint (e.g. cancer) by the economic cost of that endpoint—is theoretically appealing, the scientific data are currently insufficient to permit this kind of valuation.

44. An alternative approach to evaluating health and environmental costs of insecticide is to evaluate stakeholders' preferences for avoiding insecticide exposure or preventing diffusion into the environment. Such evaluations can employ a number of social science methodologies, including direct econometric estimation of stakeholders' willingness to pay (WTP) to avoid a risk using contingent valuation (CV) or discrete choice experiments (DCE). CV is a survey methodology in which respondents are asked to report their willingness-to-pay for certain good; the methodology is designed to control a range of respondent biases that can occur in this so-called "stated-preference" format[30]. DCEs consist of presenting a set of alternatives to respondents, each with different attributes (e.g. amounts of monetary compensation, levels of insecticide exposure, levels of malaria risk, etc.). By administering a range of choice tasks to a large sample within a given population, the mean WTP for a given risk reduction can be estimated [20]. All of these methods have distinct flaws, and it is recommended for CEA that a suite of methods are employed to estimate the costs of insecticide exposure and diffusion.

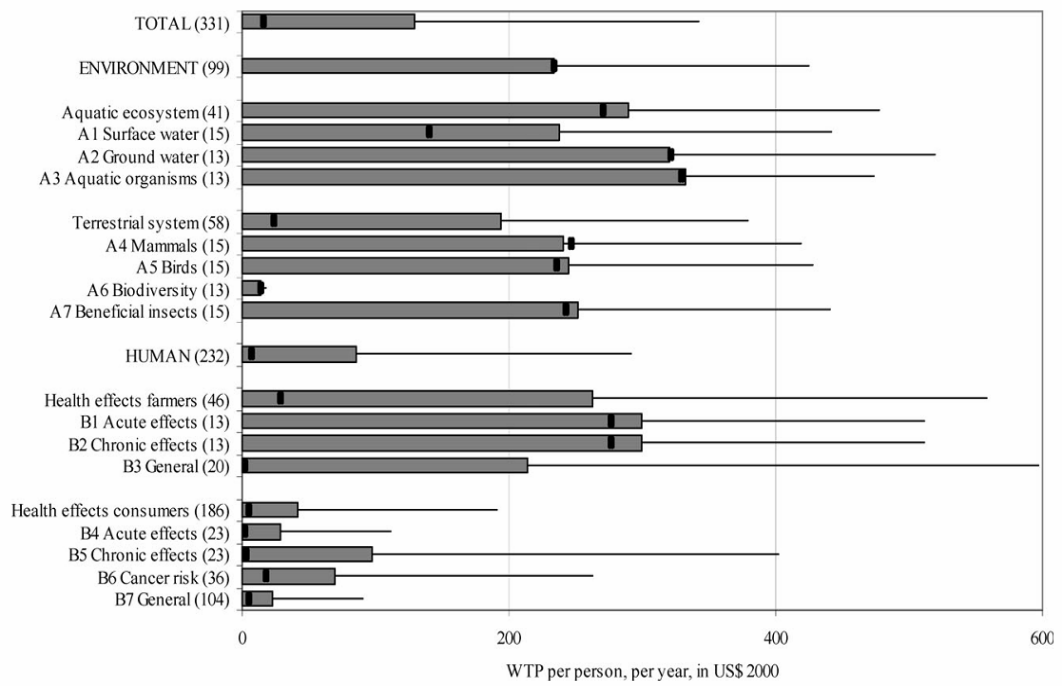

Figure 6: Willingness to pay for elimination of different pesticide risks, Reproduced from Florax, Travisi, and Nijkamp[31] with permission from the European Review of Agricultural Economics.

45. Florax, Travisi, and Nijkamp[31]conduct a meta-analysis of CV and DCE studies analyzing WTP to reduce different agricultural pesticide risks across a variety of studies. These authors find that the baseline level of risk and proposed change in risk dramatically affect WTP for risk reductions. However, these authors caution:

46. "Given the intrinsic heterogeneity in effects of pesticide usage across different target types (food safety, health effects on farmers, and aquatic and terrestrial ecosystems) as well as across geographical space, and given the non-negligible impact of research designs on the estimated WTP values, more primary research on pesticide risk valuation is called for."

47. Despite the preliminary stage of pesticide risk valuation research (at least from a CEA point of view), some interesting patterns were shown by Florax, Travisi, and Nijkamp (Figure 6). In particular, the costs of health risks among those with the highest levels of exposure (i.e. farmers) was roughly the same—at $200 to $300 per person per year—as the environmental risks. Furthermore, the meta-

30 Alberini, A. and J.R. Kahn, eds. Handbook on Contingent Valuation. Elgar Original Reference2009.

31 Florax, R.J.G.M., C.M. Travisi, and P. Nijkamp, A meta-analysis of the willingness to pay for reductions in pesticide risk exposure. European Review of Agricultural Economics, 2005. 32(4): p. 441-467.

analysis did not find any evidence that there was a positive income elasticity with respect to WTP to reduce pesticide risks. That is, the evidence suggests that higher income people are not willing to pay any more than lower income people to reduce the risks associated with insecticide usage. However, a broader knowledge base is needed in order to confirm this result.

48. Garming and Waibel[32] present results from a CV exercise among farmers in Nicaragua, among whom pesticide poisoning was a significant risk at the time of the study. The authors find that farmers would be willing to spend approximately 28% of their current pesticide expenditure in order to avoid the health risks associated with these chemicals.

Table 2: Requirements for studies evaluating willingness to pay to reduce insecticide exposure in vector control.

1. The studies need to be conducted in a range of countries where insecticides are being used for vector control.
2. The studies need to focus on insecticide usage in public health rather than agriculture, and they need to explicitly consider mode of exposure, e.g. LLINs versus IRS.
3. The studies need to estimate willingness-to-pay for a range of stakeholders, from individuals exposed to IRS, to sprayworkers, to policymakers.
4. The studies need to distinguish between different insecticides and, in the case of stated preference (SP) studies, need to supply information about the distinguishing characteristics of the 13 WHOPES insecticides prior to eliciting respondent preferences.
5. The studies should incorporate current design procedures for stated preference (SP) and revealed preference (RP) valuation exercises.[33]

49. In order to obtain reasonable estimates of environmental and health costs—and hence the full economic costs—of insecticide usage in vector control, it will be necessary to perform further studies of the type described above, with the following modifications summarized in Table 2. Ideally, WHO and in-country partners would adopt a standardized framework for assessing the in-country external costs of insecticide usage. Compiling a database of these standardized cost measures, with contextual information about each of the reporting countries, would prove useful in standardizing a CEA for vector control insecticides.

Table 3: Human health and environmental effects of vector control insecticides. Source: [29].

Insecticide	Non-cancer health effects	Cancer-related health effects	Half-life (aquatic/terrest.)	Ecological Effects
DDT	*Acute:* Disrupts nervous system. *Chronic:* Disruptsendocrine system.	Probable human carcinogen, but more data required.	28-56 days / 2-15 years	Highly toxic to aquatic species and insects. Slightly toxic to birds.
Malathion	Disrupts nervous system.	"Suggestive evidence of carcinogenicity" (USEPA)	7-14 days / 6 days	Highly toxic to beneficial insects.
Fenitrothion	*Acute:* Muscle weakness, decrease in cholinesterase activity. *Chronic:* Reproductive and developmental toxicity.	"Evidence of noncarcinogenicity for humans." (USEPA)	0.82-7 days / 7 days	Moderate-high toxicity in birds and fish.

32 Garming, H. and H. Waibel, Pesticides and framer health in Nicaragua: a willingness-to-pay approach to evaluation. European Journal of Health Economics, 2009. 10: p. 125-133.

33 There has been dramatic progress in experimental design procedures for methods such as DCEs in recent years.

Insecticide	Non-cancer health effects	Cancer-related health effects	Half-life (aquatic/terrest.)	Ecological Effects
Pirimiphos-methyl	Muscle weakness, decrease in cholinesterase activity.	Insufficient evidence.	1 day in sunlight / 7.3-62 days	Moderate toxicity to birds.
Bendiocarb	Reversible decrease in cholinesterase activity.	Noncarcinogenic to humans .	45mins-48days/ 20-21 days	Highly toxic to fish, birds, and mammals.
Propoxur	Reversible decrease in cholinesterase activity.	Probable human carcinogen, but more data required.	14-50 days / 6-8 weeks	Toxic to birds. Groundwater penetration likely.
Alpha-cypermethrin	*Acute:* Skin irritation. *Chronic:* No evidence.	No evidence.	8 days- 125yrs / < 2 weeks	Low toxicity in birds. Medium toxicity in fish
Bifenthrin	*Acute:* Tremors, vomiting, diarrhea. *Chronic:* Possible endocrine effects	Possible human carcinogen (USEPA)	50 days - 3100 yrs / 7 days – 8 mos.	Highly toxic to fish and beneficial insects.
Cyfluthrin	*Acute:* Neurological effects. *Chronic:* Weight changes.	No evidence.	2-231 days / 48 hrs. – 63 days	Highly toxic to fish and beneficial insects.
Deltamethrin	*Acute:* Dermal irritation, tingling. *Chronic:* None with LLINs.	"Not classifiable as to its carcinogenicity in humans." (IARC)	70hrs-100yrs / 2 weeks-100 days	Highly toxic to fish and beneficial insects.
Etofenprox	Skin irritant, no other evidence.	"Possible human carcinogen" (USEPA)	>1 yr / 9-79 days	Highly toxic to aquatic organisms.
Lambda-cyhalothrin	*Acute:* Dermal irritation, tingling. Neurological effects. *Chronic:* NA.	"Not classifiable as to human carcinogenicity" (USEPA)	Not reported / 4-12 weeks	Highly toxic to fish and beneficial insects.
Permethrin	*Acute:* Dermal irritation, tingling. Neurological effects. *Chronic:* NA.	"Likely to be carcinogenic to humans" (USEPA)	48hrs-14days / 30-38 days	Highly toxic to fish.

4.4. Accounting for insecticide resistance in cost effectiveness analysis of vector control interventions

50. As summarized by van den Berg[11], the proven ability of vectors population to evolve resistance to the 13 WHOPES-approved insecticides presents a major challenge for maintaining reductions in vector-borne diseases, in particular malaria, over the long-run. This section first summarizes the scientific literature on vector resistance to public health insecticides, and then discusses ways to incorporate insecticide resistance considerations into a CEA.

51. At least two "knockdown resistance" (kdr) mutations, kdr-w (or L1014F) and kdr-e (or L1014S), are known to impart simultaneous vector resistance to DDT and all availablepyrethroids by blocking these insecticides' interference with voltage-gated sodium channels in synapses[34,35]. The *ace-1*-G119S (or *ace-1*^{R}) mutation in the vector *Anopheles gambiae*confers resistance to both

34 Djogbénou, L., V. Noel, and P. Agnew, Costs of insensitive acetylcholinesterase insecticide resistance for the malaria vector Anopheles gambiae homozygous for the G119S mutation. Malaria Journal, 2010. 9(12).

35 Reimer, L., et al., Relationship Between kdr Mutation and Resistance to Pyrethroid and DDT Insecticides in Natural Populations of Anopheles gambiae. Journal of Medical Entomology, 2008. 45(2): p. 260-266.

carbamates and organophosphates through a modification of acetylcholinesterase, which is the synapse-regulating enzyme targeted by these insecticides[36].

52. Recent studies have examined the "fitness costs" associated with these mutations. Such costs determine whether or not vector susceptibility will return following the suspension of an IRS or LLIN campaign, or the rotation from one insecticide to another in IRS. Thus, knowledge of fitness costs is critical in determining the sustainability of these interventions. For the kdr mutations, Okoye et al[37], in a laboratory study, found no statistical evidence that pyrethroid resistance in the southern African malaria vector *Anopheles funestus* was associated with developmental, reproductive, or survival related fitness costs. In other malaria vectors, researchers have found direct and indirect evidence consistent with the existence of substantial fitness costs[38,39,40,41]. Djogbénou et al. [34] found substantially lower pupal survival rates among *Anopheles gambiae*mosquitoes possessing the *ace-1*-G119S mutation. Sarita, Anita et al[42] found large reproductive differences between pyrethroid susceptible and resistant types of the dengue vector *Aedesaegypti*. In the West Nile vector *Culexpipiens*, thirty years of data on organophosphate resistance have shown substantial fitness costs in terms of survival and reproductivity associated with the G119S mutation[43]. In summary, there appears to be evidence that—for some vectors and resistance mutations—insecticide resistance will die out over time if the intervention that is causing the resistance is suspended.

53. Further knowledge is still needed on how quickly resistance accumulates in a vector population for a given intervention at a given level of coverage within the human population. Resistance to DDT has been reported to emerge on the order of decades[44]. In a particularly sobering study, Trape, Tall, et al.[45] find that increasing pyrethroid resistance of *A. gambiae* vectors in Senegal contributed to a rebound of malaria between 2007 and 2010, during which the prevalence of the kdr-w mutation increased 8% to 48%. But peer-reviewed studies on the speed of resistance accumulation remain isolated, and improved data are required before resistance can be incorporated into CEAs.

54. The way in which knowledge of insecticide resistance should be incorporated into a CEA depends on the timescale of an intervention, and the value policymakers place on maintaining the efficacy of an intervention beyond this timescale. If significant resistance is expected to occur within the timescale of the intervention, this should be factored into the expected effectiveness of the intervention. If resistance is only expected to occur on a longer timescale, outside of the planning horizon for the intervention, then it is the choice of the policymaker how much efficacy they would like to maintain for a given intervention at the end of the planning horizon. For the purposes of CEA, it could be useful to elicit from policymakers or other stakeholders the unit cost they place on rendering an intervention completely ineffective at the end of the planning horizon.Expert elicitation (EE) is well-suited method for this type of query [19].

36 Nauen, R., Insecticide resistance in disease vectors of public health importance. Pest Management Science, 2007. 63: p. 628-633.

37 Okoye, P.N., et al., Relative developmental and reproductive fitness associated with pyrethroid resistance in the major southern African malaria vector, Anopheles funestus. Bulletin of Entomological Research, 2007. 97: p. 599-605.

38 Rowland, M., Behaviour and fitness of Gamma-HCH Dieldrin resistant and susceptible female Anopheles gambiae and Anopheles stephensi. Med Vet Entomol, 1991. 5: p. 193-206.

39 Rowland, M., Activity and mating competitiveness of Gamma-HCH Dieldren resistant and susceptible male and virgin female Anopheles gambiae and Anopheles stephensi mosquitoes, with an assessment of an insecticide-rotation strategy. Med Vet Entomol, 1991. 5: p. 207-222.

40 Agnew, P., et al., Parasitism increases and decreases the costs of insecticide resistance in mosquitoes. Evolution, 2004. 58(3): p. 579-586.

41 Stump, A.D., et al., Dynamics of the pyrethroid knockdown resistance allele in western Kenyan populations of Anopheles gambiae in response to insecticide-treated bed net trials. American Journal of Tropical Medicine and Hygiene, 2004.

42 Sarita, K., et al., Diminished reproductive fitness associated with the deltamethrin resistance in an Indian strain of dengue vector, Aedes aegypti L. Top Biomed, 2009. 26(2): p. 155-64.

43 Raymond, M., et al., Insecticide resistance in the mosquito Culex pipens: what have we learned about adaptation? Genetica, 2001. 112-113: p. 287-296.

44 Penilla, P.R., et al., Resistance management strategies in malaria vector mosquito control. Baseline data for a large-scale field trial against Anopheles albimanus in Mexico. Medical and Veterinary Entomology, 1998. 12(3): p. 217-233.

45 Trape, J.-F., et al., Malaria morbidity and pyrethroid resistance after the introduction of insecticide-treated bednets and artemisinin-based combination therapies: a longitudinal study. The Lancet Infectious Diseases, 2011.

5. Decision support tools for national vector control programmes

55. Decision support systems (DSS) are ways of organizing and presenting information, normally computerized, to aid managers in decision making. CEA, as described in Section 2, is an example of a DSS which combines information on costs and effectiveness in particular ways. A DSS may not always constitute a CEA, but often the information contained in a DSS can be used to conduct a CEA [e.g. Kim, A. et al [46]]. Although the technical term "decision support" is not often used in the malaria control community, there has been a proliferation of tools for monitoring impacts and informing decisions in malaria interventions. This has paralleled the general trend of increasing funding for malaria control (Figure 7).

56. To understand how these tools may substitute or complement each another, it is helpful first to understand the major global funding sources for national malaria control programmes, since it is often the case that some tools (e.g. guidelines for performance assessments) are associated with monitoring and reporting requirements tied to various funding sources.

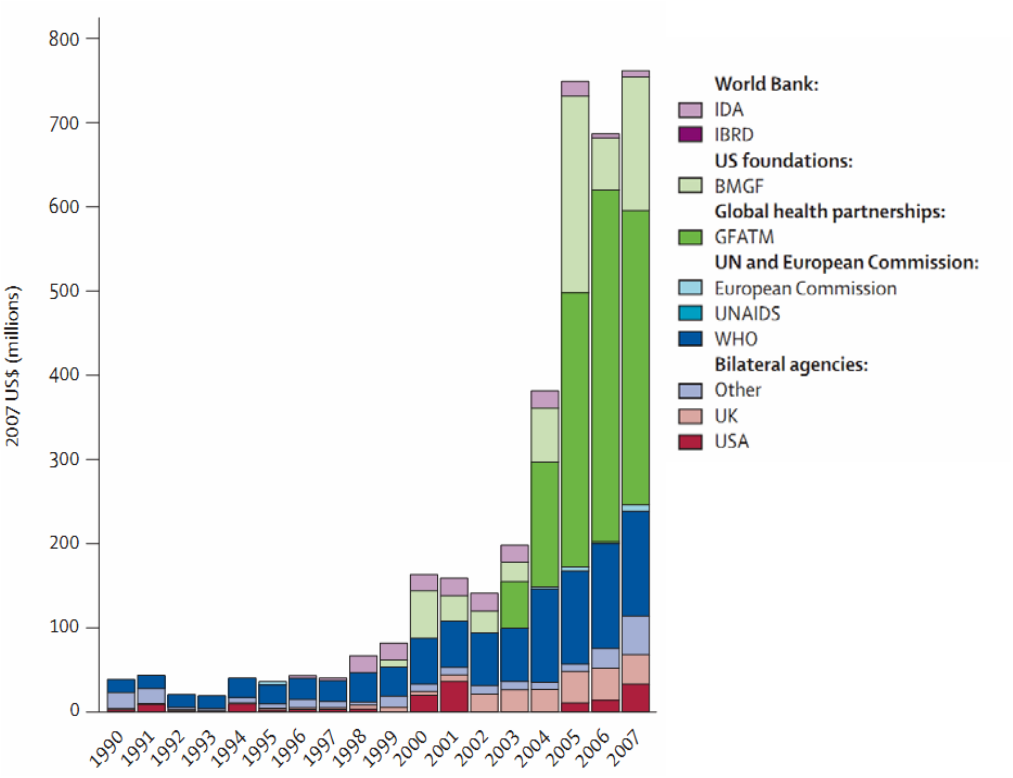

Figure 7: Development assistance for malaria prevention and control. Reproduced with permission from the publisher[47]. For acronyms not listed elsewhere in this report: IDA = International Development Association, IBRD = International Bank for Reconstruction and Development, UNAIDS = Joint United Nations Programme on HIV/AIDS.

57. Since 2004, the primary contributors to malaria control programmes have been the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM), the WHO, and the Bill and Melinda Gates Foundation (BMGF), and the WHO. Other significant sources of malaria control funding include the US through the President's Malaria Initiative (PMI) in that country, the UK, and the World Bank. All of these donors coordinate their activities through the Roll Back Malaria (RBM) partnership, which also includes a number of other members. Currently, the RBM Secretariat is hosted by the WHO in Geneva.

46 Kim, A. and B. Benton, Cost-benefit analysis of the onchocerciasis control program (OCP), 1995, World Bank.

47 Ravishankar, N., et al., Financing of global health: tracking evelopment assistance for health from 1990 to 2007. The Lancet, 2009. 373: p. 2113-2124

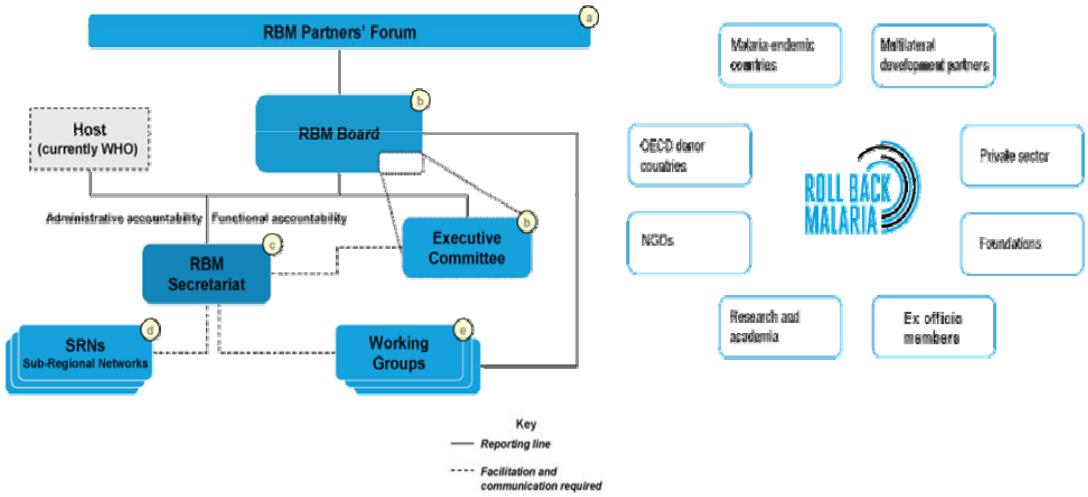

Figure 8: A. Organizational Structure of the Roll Back Malaria Partnership. B. Constituencies represented on the RBM Board. Source: http://www.rbm.who.int.

58. The individual partners and the RBM Secretariat provide resources for improving decision making in national malaria control programmes. These tools are discussed below, organized by source.

5.1. WHO-UNEP decision support activities

59. Cost-effectiveness has figured prominently into WHO documents providing guidance and support to national vector control programmes. Probably the most famous example of a decision support tool's use in controlling a vector-borne disease can be found through a study of the WHO's successful OnchocerciasisControl Program (OCP), which spanned the years 1974 to 2001[48]. One key to the OCP's success was the use of a DSS known as ONCHOSIM [46,49], which allowed users to project the disease reduction impacts of different intervention strategies.

60. As discussed above, in 1993 the WHO solicited a manual for conducting CEAs of alternative vector control interventions[2]. This manual appears to fallen out of use, despite the continued relevancy of its content. More recently, WHO has published guidelines for "generalized" CEA for all health interventions under the title WHO-CHOICE[50]. However, the primary measure of effectiveness under these guidelines is the disability-adjusted life year (DALY). DALYs "averted" due to an intervention are calculated by subtracting the years of healthy life lost **with** the intervention from the years of healthy life lost **without** the intervention. When the objective is to conduct a CEA only among alternative vector control interventions, using the DALY as a measure of effectiveness is suboptimal for reasons discussed in Section 4.1.1.

61. Returning to vector control, the WHO document on "Decision-making for the judicious use of insecticides"[51] has this to say to program mangers about cost-effectiveness criteria for choosing the "what, how, when, and where" of an insecticide-based vector control programme:

62. "Cost, in terms of economics, is the value of resources used in a particular situation to achieve an objective. Costing is defined as the process by which estimates are made of the costs of an action. Cost-effectiveness is a measure of cost to achieve a level of effectiveness for a predetermined target.

63. To reduce the cost without affecting the outcome, consider rational use of the limited resources available for a given programme. For example, three cycles of indoor residual spraying with a particular insecticide may be necessary to control malaria in situations where transmission is perennial. If there are seasonal variations in the transmission and the majority of cases are reported as occurring during the monsoon and post-monsoon seasons, spraying can be restricted to the peak transmission seasons thereby reducing the cost. This will be more cost-effective than spray coverage throughout the year."

48 WHO. Onchocerciasis Control Programme. 2011 [cited 2011 August 29]; Available from: http://www.who.int/blindness/partnerships/onchocerciasis_OCP/en/.

49 Plaisier, A.P., et al., ONCHOSIM: a model and computer simulation program for the transmission and control of onchocerciasis. Computer Methods and Programs in Biomedicine, 1990. 31(1): p. 43-56.

50 WHO. WHO-CHOICE. 2011 [cited 2011 August 30]; Available from: http://www.who.int/choice/en/.

51 WHO, Decision-making for the judicious use of insecticides: a facilitator's guide, WHO Pesticide Evaluation Scheme, Editor 2004: Geneva.

64. However, it is somewhat striking that this document makes no reference to Phillips, Mills [2]. Potential reasons for this disconnect are speculated in Section 3.

Region: _____ Country: _____

Year	Compound	Class	Formulation	Concentration	Type of application	For control of	Amount of formulaion used	Amount of active ingredient

Completed by: _____ Name: _____

Postal address: _____

_____

_____

Tel: _____ Fax: _____ Email: _____

Figure 9: Standard reporting form used by WHO to collect national insecticide usage data. Source: [10].

65. In addition to providing guidance documents, WHO also maintains an international database of annual, national-level insecticide usage in vector control programmes. The standard reporting form used to collect these data is shown in Figure 9. Over 87% of 143 targeted countries (97% of the targeted population) provided at least one completed reporting form between 2000 and 2009, 40 countries provided completed forms for 5-9 of those 10 years, and 43 countries provided completed forms for the entire decade. Lastly, the WHO has initiated some regional projects for monitoring and evaluating the status of insecticide resistance in malaria vector populations, as evidenced by the African Network on Vector Resistance [52].

66. As the host organization for the Stockholm Convention, UNEP—in partnership with WHO—is perhaps the most visible in developing decision support systems and databases for vector control. As the host of the Stockholm Convention, UNEP maintains a database of global DDT use.[53] Parties to the Stockholm Convention who are registered DDT users are requested to complete a questionnaire regarding DDT stocks, procurement, and disposal every 3 years. At 5 pages, the POP-DDT questionnaire is more detailed than the annual reporting forms collected by WHO. For example, for DDT-importing countries, it collects information on the source countries and corporations for DDT imports. It also collects information on vector control programmes' use of alternative vector control strategies and the source of imported materials (e.g. LLINs) used in these alternative strategies. However, response rates have been low, in contrast to the WHO reporting form.

67. UNEP has also initiated projects to enhance the capacity of national, regional, and global institutions to evaluate the continued need for DDT in vector control programmes. The primary funding vehicle for these projects has been the Global Environment Facility (GEF). The GEF projects addressing DDT use in vector control fall under the heading of "Demonstrating and Scaling-up Sustainable Alternatives to DDT in vector control" or DSSA[54]. The 2008 description of the Global DSSA project [55]declared the objective of reducing global yearly DDT use by 4,000 tonnes by 2014, and summarized a number of subprojects for meeting this objective. These subprojects include regional DSSA efforts aimed at demonstrating sustainable alternatives in a variety of contexts, as well as 2 decision support (DS) subprojects.

52 ANVR, Atlas of insecticide resistance in malaria vectors of the WHO African region, Regional Office for Africa, Editor 2005, WHO: Harare.

53 Recall that registration is required under the Convention as a condition for using DDT.

54 GEF. Global Environment Facility Project Database. 2011; Available from: http://www.gefonline.org/.

55 UNEP. Global - DSSA Demonstrating and Scaling-up of Sustainable Alternatives to DDT in Vector Management (PROGRAM). 2008 [cited 2011 August 30]; Available from:http://www.gefonline.org/projectDetailsSQL.cfm?projID=3648.

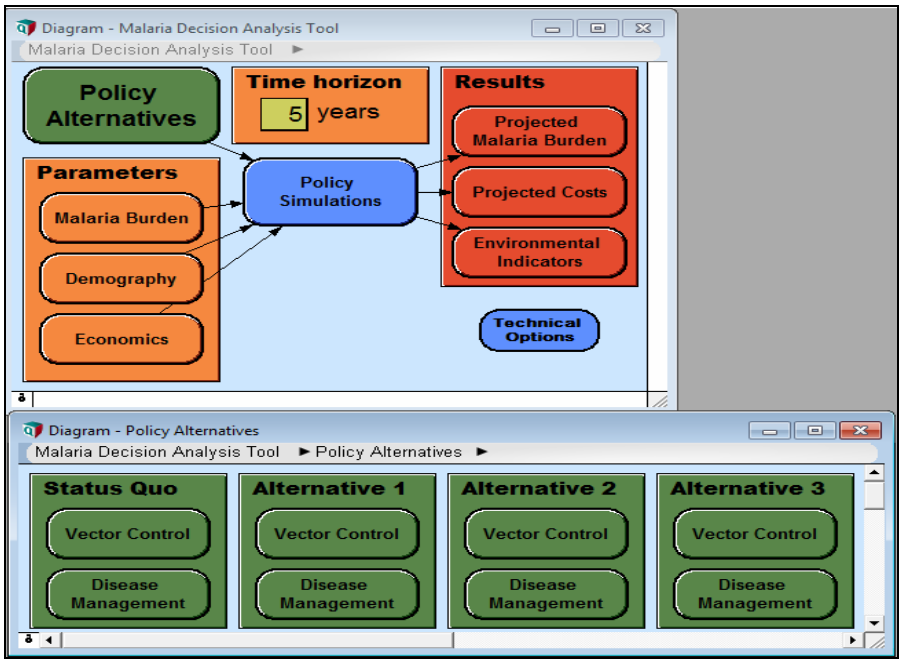

Figure 10: The user interface for the Malaria Decision Analysis Tool.

68. The first of these subprojects is the development of a Malaria Decision Analysis Support Tool (MDAST). This tool, depicted in Figure 10, combines scientific knowledge about malaria transmission with economic and decision analysis principles in order to project the health, environmental, and economic impacts of a given malaria intervention package[56]. The MDAST is being developed and implemented along with partners in the Ministries of Health in Tanzania, Kenya, and Uganda. Currently, the MDAST project is half-way through its 3 year funding cycle. Rollout of a completed version of MDAST will be in March 2012, at which point the project will commence training and collecting feedback with MOH officials and technicians.

69. The second DSSA subproject focusing on DS is aimed specifically at improving the capacity of Convention Parties to fulfil their DDT reporting requirements. As stated in the project description [7], the primary activities for this work will be to build standardized reporting routines into national institutions responsible for vector control. These routines are intended to be implemented all the way down to the level of IRS spray teams, i.e. those who actually apply DDT will be trained in recordkeeping for that project. As with the MDAST, this project will address potential institutional barriers to adopting a unified DDT data collection framework through ongoing stakeholder involvement. This three-year project was scheduled to commence in January 2010.

70. Lastly, a recent decision of the 4th Conference of Parties to the Stockholm Convention has led to the launch in 2010 of a Global Alliance for Alternatives to DDT, of which WHO and UNEP are both members. **The mission of the alliance is organized around 3 goals: (I) Strengthen the knowledge base for informing policies on DDT and alternatives in vector control, (II) overcome the complexity and cost of deploying alternatives to DDT, and (III) make available alternative vector control chemicals[57].** The work of the Global Alliance is just beginning, but proposals are being considered for work on CEA of DDT and alternatives[58].

5.2. Global Fund decision support activities

71. The GFATM provides an array of tools for monitoring and evaluation (M&E). These activities are foundational principles in the architecture of the GFATM, and the Fund is quite public in the competitive nature by which grants are awarded to national programmes. Tools provided by the GFATM include manuals, guidelines, online learning modules, and templates for project workplans and budgets. Access is at http://www.theglobalfund.org/en/me/documents. Compulsory M&E for

56 Kramer, R.A., et al., Using decision analysis to improve malaria control policymaking. Health Policy, 2009. 92(2): p. 133-140.

57 The Stockholm Convention. Global Alliance to Alternatives to DDT. 2011; Available from: http://chm.pops.int/Implementation/DDT/GlobalAlliance/tabid/621/mctl/ViewDetails/EventModID/1421/EventID/136/xmid/6821/Default.aspx

58 The Stockholm Convention. Thematic Groups of the Global Alliance. 2011; Available from: http://chm.pops.int/Implementation/DDT/GlobalAlliance/ThematicGroups/tabid/623/Default.aspx.

GFATM grantees consists of comparing the performance of a health improvement project to pre-agreed targets. Setting these targets is a condition for receiving funds. Although no online databases or guidance documents for CEA at the national level were found on the GFATM website during the drafting of this report, the GFATM has recently endorsed and outlined a 'Value-for-money' component in its M&E activities (Figure 11).

72. For the purposes of establishing a framework for evaluating the cost-effectiveness of DDT in vector control relative to alternative insecticides, the highest level of the pyramid in Figure 11—cost per unit of health impact—corresponds most closely to a CEA of alternative interventions. At the time this report was drafted. The GFATM M&E has focused on lower levels of the pyramid, which correspond to measures of "operational efficiency," i.e. the cost per unit of service procured and/or delivered. For GFATM-supported malaria programmes, a stated key for implementing this framework is the use of questionnaires administered to National Malaria Control Programmes (NMCPs) by the RBM Partnership.

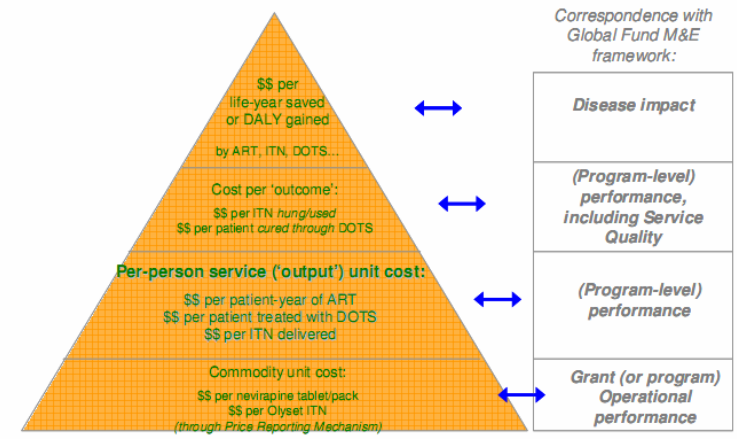

Figure 11: Schematic of the Value-for-Money framework adopted by the Global Fund. Source: Korenromp[59] .

5.3. USAID/PMI decision support activities

73. The President's Malaria Initiative (PMI), an initiative of USAID, supports the conduct of regular programmatic environmental assessments (PEAs) of its Integrated Vector Management (IVM) activities, which include IRS with a variety of insecticides and the distribution of LLINs. For example, in their PEA for its Africa-wide IVM activities, PMI reports results from a formal risk assessment of the WHOPES-approved IRS insecticides as well as for ITN re-treatment [29] Supplementary environmental assessments (SEAs) are also performed for proposed projects that are deemed to be environmentally sensitive. For example, an SEA of the introduction of DDT-based IRS activities in 2 districts of Uganda was performed in 2007, prior to implementation in 2008. **As part of that SEA, provisions were included to monitor the environmental fate and transport of the DDT used in IRS[60,61]. This included before/after sampling of environmental media for concentrations of DDT and metabolites. These evaluations have been completed, though they are not currently available on the PMI website.**

74. In addition, PMI supports monitoring for vector resistance in a number of areas, and feeds this information back into the NMCPs it has partnered with. For example, results from such monitoring indicating high levels of DDT and pyrethroid resistance in portions of Uganda were used to justify the introduction of carbamates and organophosphates into Ugandan IRS operations [62,63].

59 Korenromp, E. Value-for-Money in Global Fund-supported HIV, TB, and malaria programmes. 2008; Available from: http://www.theglobalfund.org/documents/performance/Performance_ValueForMoney_Framework_en/.

60 RTI International, Spray performance report for Apac and Oyam Districts, Uganda, President's Malaria Initiative, Editor 2008, United States Agency for Internationl Development: Washington, DC.

61 RTI International, Supplementary Environmental Assessment: Pyrethroid-Based Indoor Residual Spraying and Piloting of DDT-Based IRS for Malaria Control in Uganda, P.s.M. Initiative, Editor 2007, United States Agency for Internationl Development: Washington, DC.

62 Okia, M. and N. Protopopoff, Malaria vector susceptibility to public health insecticides in Uganda: September to October 2009, P.s.M. Initiative, Editor 2010, United States Agency for International Development: Kampala, Uganda.

63 Okia, M., Personal communication, 2011: Kampala, Uganda.

5.4. RBM decision support activities

75. As an umbrella organization tasked with coordinating global malaria control activities, the RBM Secretariat gathers together a wide array of tools for malaria control from its constituencies, including the research sector. It organizes these tools by function and provides them (or URL links) for download from the RBM website. The screenshot in Figure 12 shows the tools disseminated by RBM for assessing and planning NMCPs.

76. The malaria costing tool (developed by WHO), in particular, would serve as a useful building block for an algorithmic CEA framework for vector control programs, if such a framework were developed. The Malaria Costing Tool permits the evaluation of past and future financial expenditures for a number of malaria interventions, including IRS and LLIN distribution.

77. In addition, the Global Fund documents on Value-for-Money [59] make reference to RBM-sponsored questionnaires administered to NMCPs. However, the author of this report was not able to find further information about such questionnaires.

Key Area	Tool Name
Program Assessments	Needs Assessment - RBM Partnership
Program Assessments	Guidelines for Assessing the Management and Organizational Capacity of National Mlaria Programs - USAID
Country Planning	Malaria Costing Tool - RBM Partnership
Country Planning	Planning and Budgeting for National Malaria Control - RBM Partnership
Country Planning	Final Reports of Technical Review of Costing Tools - PATH

Figure 12: Tools provided by the RBM Partnership for country planning and program assessment. Screenshot of the RBM website from: http://www.rollbackmalaria.org/toolbox/toolbox_AssessingAndPlanning.html

6. Implementation barriers

78. The utility of a CEA goes only as far as the interest that policymakers have in such analyses and the incentives they have to use their results. Consequently, any successful decision support framework for the purposes of DSSA (including CEA as a special case) will involve stakeholder participation and feedback through the entirety of implementation. In particular, the unique knowledge of national program managers of barriers to and opportunities for collaboration between different national institutions needs to inform the development of a decision support system for vector control. For example, the relationship between Ministries of Health and Ministries of Environment, or the relationship between an NMCP and the National Institute of Medical Research could determine where a successful implementation of decision support framework for vector control should begin.

79. Very little published research exists on “institutional barriers” to implementing decision support (including CEA) systems in malaria control programs. Most research in the area of implementation barriers for malaria control programs comes in the form of case studies. Barat [64]focuses on four countries that successfully reduced malaria and identifies some common factors in these cases, including active leadership at all levels of government.Njau, de Savigny[65]examine the implementation of the national ITN voucher scheme currently in place in Tanzania, focusing on the reasons for the delay in that program’s implementation. While insightful, it is difficult to draw specific, technical recommendations from these studies for the national-level implementation of a vector control CEA framework, especially with regard to valuing the environmental and health effects of insecticide usage.

64 Barat, L.M., Four malaria success stories: How malaria was succesfully reduced in Brazil, Eritrea, India, and Vietnam. The American Journal of Tropical Medicine and Hygiene, 2006. 74(1): p. 12-16.

65 Njau, R., et al., Implementation of an insecticide-treated net subsidy scheme under a public-private partnership for malaria control in Tanzania - challenges in implementation. Malaria Journal, 2009. 8(1): p. 201.

80. Given that the published research in this area remains sparse, it is important to recognize the methods available for analyzing any institutional barriers that may arise in implementing a decision support or CEA system for evaluating DDT against alternative vector control methods. Some of these methods such as EE, have been described above (Section 4.1.2), and are useful for taking stock of stakeholders' preferences (values over given outcomes) and beliefs (perceptions as to the likelihood of different outcomes). A complementary method that has been utilized for understanding and solving institutional barriers to policy implementation is *stakeholder analysis*[66,67,68].

81. Some efforts have already made at eliciting stakeholders' knowledge and beliefs about institutional capacities for implementing CEA and decision support tools, as part of the activities discussed in 5. All of the GEF-funded DSSA projects include language about stakeholder involvement throughout implementation. For example, the MDAST project administers written questionnaires at the end of all seminars or presentations to the potential users—the NMCP managers and technicians in Kenya, Tanzania, and Uganda. The most recent MDAST consultations included a special anonymous questionnaire on policymakers' perceptions about the environmental impacts of vector control. While this questionnaire was only administered to 8 NMCP staff members (most of them responsible for chemical-based vector control), the results from the questionnaire indicated that the respondents thought LLIN/ITN disposal to constitute one the most serious environmental impacts that should be considered in MDAST, followed by IRS with DDT, and subsequently by IRS with pyrethroids. As the other DSSA projects under the GEF are rolled out around the globe, it will be important to conduct similar (and more systematic assessments) of the perceptions of NMCP staffers.

Strategic Management Function or Activity:	**Stakeholders to Approach by Which Means:**				
	Inform	**Consult**	**Involve**	**Collaborate**	**Empower**
	Promise: We will keep you informed	**Promise: We will keep you informed, listen to you, and provide feedback on how your input influenced the decision.**	**Promise: We will work with you to ensure your concerns are considered and reflected in the alternatives considered, and provide feedback on how your input influenced the decision.**	**Promise: We will incorporate your advice and recommendations to the maximum extent possible.**	**Promise: We will implement what you decide.**
Organizing Participation					
Creating Ideas for Strategic Interventions (including Problem Formulation and Search for Solutions)					
Building a Winning Coalition Around Proposal Development Review and Adoption					
Implementing, Monitoring and Evaluating Strategic Interventions					

Figure 13: Example participation planning matrix. Source: Bryson 66.

66 Bryson, J.M., What to do when Stakeholders matter. Public Management Review, 2004. 6(1): p. 21-53.

67 Varvasovszky, Z. and R. Brugha, How to do (or not to do)... A stakeholder analysis. Health Policy and Planning, 2000. 15(3): p. 338-345.

68 Brugha, R. and Z. Varvasovszky, Stakeholder analysis: a review. Health Policy and Planning, 2000. 15(3): p. 239-246.

Annex III

Comments submitted by the World Health Organization on the document "Developing a framework for the assessment of alternatives to DDT"

1. Comments from WHO/GMP, J Lines, September 2011

1. The document focuses mainly on cost-effectiveness, and it makes suggestions that could improve the quality and quantity of cost-effectiveness comparisons between alternative vector control interventions.

2. Most vector control experts would agree that cost-effectiveness measures deserve more attention, and that more formal and more careful methods should be encouraged. For example, the Global Fund has been emphasizing the importance of "value of money" as a criterion for the assessment of interventions.

3. However, in presenting the issue of cost-effectiveness, the document focuses mainly on the economic issues and the estimation of costs, and it underestimates both the overall biological and environmental complexity of the issue. In particular, it fails to acknowledge the significance of insecticide resistance, which WHO recommends should now be the dominant consideration in selecting vector control interventions.

4. Environmental factors have a major influence on the relative effectiveness of different vector control interventions. For example, the length of the malaria transmission season is a critical limiting factor in the selection of an insecticide for IRS (Indoor residual spraying). Some insecticides have an effective life of more than 6 months, while others are effective just 3 months; in places with a long transmission season, a single annual round of spraying may be adequate with an insecticide of long residual activity, while a short-lived compound may have to be sprayed two or even three times per year in order to maintain effectiveness. Since some places have more than one rainy season per year, the potential for complex interactions is obvious.

5. A further dimension of variation arises from differences between the biology of different species of *Anopheles*. Consider, for example the three species *An. funestus*, *An dirus* and *An. culicifacies*, which are major vectors of malaria in Africa, the Mekong subregion, and India respectively. *An. funestus* and *An. dirus* (in most locations) bite late at night and prefer human blood, so we would expect them both to be strongly affected by the use of treated nets. However, they differ in that *funestus* almost always rests indoors after feeding, while *dirus* feeds indoors but then immediately leaves and rests outdoors; as a result, *funestus* is highly vulnerable to IRS and sometimes completely disappears after spraying, whilst *dirus* is much less effected by spraying. *An. culcifacies* is different again: it prefers to feed very early in the evening on cattle outdoors, and then to go inside houses to rest in the walls. For this reason, this species is known to be especially vulnerable to house-spraying, and might be expected to be less vulnerable to the use of treated nets. This is complicates the task of generalization: we can measure the relative cost-effectiveness of IRS and treated nets in one location, but we cannot assume that it will be same in other locations where other mosquito species are important as vectors.

6. However, the most important weakness of the document is its under-estimation of the dominance and complexity of the issue of insecticide resistance. Over the last two decades, pyrethroids have come to be the most commonly-used class of insecticides in public health: they are cheap, safe for people, and do not persist either in animal tissue or the environment, and they are also very effective, with a relatively long duration of residual activity. Hence they are the only class of insecticide used on WHO-recommended insecticide-treated-nets, and in most countries they are by far the most common class of insecticide used for IRS.

7. The problem is that in Africa, where more than 80% of malaria deaths occur, a variety of genes for insecticide resistance have been spreading over the last ten years, and are now widespread. Pyrethroid resistance is also reported from several locations in India. The possibility that our main malaria control tools could lose a large part of their effectiveness is now one of the most urgent and most dangerous threats facing malaria control at the global level.

8. As a result, WHO now recommends that decisions about vector control interventions should no longer be made on the basis of cost-effectiveness alone, but should be driven primarily by considerations of insecticide resistance and the need to conserve insect susceptibility to insecticides, especially pyrethroids. This includes all decisions about whether to use IRS and/or treated nets, and insecticide choice for IRS.

9. This, and a series of other basic technical recommendations, were published in a report of a meeting convened in May 2010 (WHO 2011: *The technical basis for coordinated action against insecticide resistance* http://whqlibdoc.who.int/publications/2011/9789241501095_eng.pdf). These recommendations should be seen as additional to those published in earlier guidance documents, such as that on "Decision-making for judicious use of insecticides". The new recommendations have been incorporated into WHO's technical briefing for countries preparing Global Fund proposals in Round 10 and Round 11 (http://www.who.int/malaria/publications/atoz/malaria_gf_proposal_dev_who_policy_brief_201106.pdf).

10. These recommendations embrace a wide range of measures, including the specific recommendation that, as the minimum acceptable resistance management strategy, programmes should not spray a single insecticide year after year, but should adopt a system of rotation, spraying different insecticide classes in successive years. Unfortunately, the number of available classes is extremely limited, and there are already some malaria control programmes that are running out of options of alternative compounds. In some of these places, DDT is not an option because the local vectors already have genes conferring specific resistance to DDT, or cross-resistance between pyrethroids and DDT. In other places, however, the local vectors remain fully susceptible only to DDT and to one other class of insecticides. Thus, as resistance spreads, the availability of other insecticides – especially alternatives that are environmentally-friendly and not much expensive – is becoming more and more restricted.

11. In some cases, resistance mechanisms selected by pyrethroids confer unexpected forms of cross-resistance. For example some forms of metabolic resistance to pyrethroids in *An funestus* confer a degree of cross-resistance to carbamate insecticides, which means that the choice of alternative insecticides, to which the local vector remain susceptible, is greatly restricted. There is a real possibility that some countries will soon face the choice of control failure or switching to DDT. Indeed, control failure of this kind has already been seen in South Africa.

12. Because of this dangerous and rapidly changing situation, there are now persuasive arguments for retaining sanction for use of DDT for disease control under the Stockholm Convention (a) as one component of a rotation system, and/or (b) as an insecticide of last resort, in case of failure of all the alternatives.

13. WHO is now developing a comprehensive implementation plan for these recommendations; a first draft of the WHO Global Plan for Insecticide Resistance Management in malaria vectors (GPIRM) is scheduled for limited release at the next meeting of the Board of the Roll Back Malaria Partnership in Nov 2011.

14. Finally, it should also be noted that the document does not refer to another relevant WHO reference document : WHO (2006) *Malaria vector control and personal protection: report of a W HO study group. (W HO technical report series;* http://whqlibdoc.who.int/trs/WHO_TRS_936_eng.pdf).

2. Other comments

15. WHO appreciates the Stockholm Convention Secretariat's request that the consultant include reference to the WHOPES risk assessment models and we look forward to seeing this reflected in the final version.

16. The document also needs to state that WHO risk assessments are also available, the most recent of which is Environmental Health Criteria Document 241, DDT in Indoor Residual Spraying: Human Health Aspects (2011). http://www.who.int/entity/ipcs/publications/ehc/ehc241.pdf

17. Table 3: Human health and environmental effects of vector control insecticides, needs to be deleted because it is out of date, the material cited in it is almost entirely unreferenced, and the selection of data presented appears to be biased (for example, in the case of Deltamethrin the IARC classification is presented, but for DDT an unattributed statement "probable human carcinogen" is provided when in fact the IARC classification is "possible human carcinogen". Deletion of this table will present no difficulties for the document as a whole, because the document sets aside the information and does not rely on it.