WHO GLOBAL MALARIA PROGRAMME

EXECUTIVE SUMMARY

GLOBAL PLAN FOR INSECTICIDE RESISTANCE MANAGEMENT

IN MALARIA VECTORS

ROLL BACK MALARIA

World Health Organization

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FOREWORD

The past decade has seen unprecedented progress in malaria control, resulting in major declines in malaria mortality rates globally. This progress is attributed to a significant scale-up of vector control interventions, as well as better diagnostic testing and a wider availability of effective medicines to treat malaria. But 99 countries still have ongoing malaria transmission, and the disease killed an estimated 655 000 people in 2010, mostly children under five years of age. International funding committed to malaria, while now substantial, has fallen short of the amounts needed to meet global targets. In recent years, resistance to artemisinins and other antimalarial medicines in the Mekong sub-region of Asia has become a major concern.

The next few years will be critical in the fight against malaria. Vector control, primarily through the use of indoor residual spraying and long-lasting insecticidal nets, will remain a central pillar in our efforts. The good news is that tools for controlling malaria vectors remain highly effective in almost all settings. Unfortunately, this good news is under threat: mosquitoes are developing resistance to insecticides. Insecticide resistance among *Anopheles* malaria vectors has been identified in 64 countries with ongoing malaria transmission, affecting all WHO Regions. Countries in sub-Saharan Africa and India are of greatest concern. These countries are characterized by high levels of malaria transmission and widespread reports of resistance. In some areas, resistance to all four classes of insecticides used for public health vector control has been detected.

The global malaria community takes this threat seriously. The Global Plan for Insecticide Resistance Management in malaria vectors (GPIRM) is evidence of a broad commitment to act before insecticide resistance compromises current vector control strategies. The main factor driving resistance has been the heavy reliance by vector control programmes on a single class of insecticides, the pyrethroids. In some endemic areas, the use of insecticides in agriculture also appears to have contributed to the rise of resistant mosquitoes. Urgent action is required to prevent resistance from emerging at new sites, and to maintain the effectiveness of vector control interventions in the short, medium and long term.

This GPIRM was developed in response to requests from both the World Health Assembly and the Board of the Roll Back Malaria Partnership. The WHO Global Malaria Programme gathered, analysed and synthesized input from over 130 stakeholders representing all the constituencies of the malaria control community. These include national malaria control programmes, vector control specialists, major donor organizations and multilateral and implementing agencies, as well as representatives of academic institutions, product development partnerships and industry. We trust that the GPIRM will trigger coordinated action from all stakeholders and will lay the foundations for integrated practices for managing insecticide resistance in all malaria-endemic countries.

The GPIRM puts forward a comprehensive strategy for global and country levels, including a short-term action plan with clear responsibilities, and sets out research and development priorities for academia and industry. We urge affected countries and stakeholders to take immediate action to preserve the effectiveness of current vector control methods, and to ensure that a new generation of public health insecticides is made available as soon as possible. Close collaboration between malaria control programmes and the agricultural sector will also be crucial. In addition, targeted communication and educational activities will be needed to make communities aware of the problem.

Similar to the efforts to contain emerging drug resistance, implementing the GPIRM will have cost implications in the near term, for which many malaria endemic countries will need support. We are convinced, however, that such investment now will result in significant savings in the long run, improving the sustainability and public health impact of malaria interventions, especially on maternal and child health. We have the tools at hand to end deaths from malaria. But only through concerted action will we manage to maintain the effectiveness of our existing package of interventions. If our efforts succeed, we can overcome resistance to insecticides, and save millions of lives.

Dr Margaret Chan
Director-General
World Health Organization

EXECUTIVE SUMMARY

PART 1 THE THREAT OF INSECTICIDE RESISTANCE

1.1 MALARIA VECTOR CONTROL TODAY

The control of malaria currently relies on a handful of insecticide classes and on pyrethroids in particular.

Vector control is a central, critical component of all malaria control strategies. It relies primarily on two interventions: long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS). Use of both has increased significantly during the past 10 years as part of a drive towards universal coverage of all populations at risk, saving hundreds of thousands of lives.

The active ingredients of all WHO-recommended products for IRS come from only four classes of insecticide: pyrethroids, organochlorines (dichlorodiphenyltrichloroethane, DDT), organophosphates and carbamates. All currently recommended LLINs are treated with pyrethroids. From the points of view of both safety and effectiveness, pyrethroids are the best insecticides ever developed for public health use. They accounted for the majority of IRS coverage worldwide in 2009 and were used in all LLINs (*1*). The reliance of modern malaria control on pyrethroids and the increasing resistance of malaria vectors to these products put current global efforts at risk.

For these reasons, a group of experts was convened by WHO in 2010 to identify technical strategies for preserving the effectiveness of the insecticides used for malaria control (*2*). The Global Plan for Insecticide Resistance Management in malaria vectors is a further stage in preparing a global strategy, setting out the rationale and an action plan for insecticide resistance management (IRM) by a broad-based stakeholder community.

1.2 STATUS OF INSECTICIDE RESISTANCE

Insecticide resistance is widespread: it is now reported in nearly two thirds of countries with ongoing malaria transmission. It affects all major vector species and all classes of insecticides.

The significant increase in insecticide-based malaria vector control in the past decade has resulted in increasing resistance among malaria vectors because of the selection pressure placed on resistance genes. Data are still limited and difficult to consolidate as many countries have not yet carried out adequate routine susceptibility testing. But at the time of this report's publication, resistance to at least one insecticide had been identified in 64 countries with ongoing malaria transmission. Resistance to pyrethroids seems to be the most widespread.

For the time being, existing vector control tools remain highly effective in most settings but their effectiveness can only be maintained through urgent and concerted action by the global malaria community. Countries in sub-Saharan Africa and India are of greatest concern because of the combination of widespread reports of resistance—in some areas to all classes of insecticides—and high levels of malaria transmission.

Managing insecticide resistance is complex, in part because resistance takes a variety of forms. Therefore, local strategies must be tailored to the type of resistance present. The two main mechanisms—metabolic resistance[1] and target-site resistance[2]—include multiple forms[3], which are of varying importance for different classes of insecticide. A further complication is 'cross-resistance' between insecticides that have the same mode of action for killing mosquitoes. For example, vectors that are resistant to pyrethroids and have *kdr* target-site resistance will probably also be resistant to DDT. Cross-resistance restricts the choice of alternative insecticide available for resistance management.

Most experts consider that insecticide resistance will likely have significant operational impact if no pre-emptive action is taken.

There has been one broadly accepted case of control failure due to metabolic resistance to pyrethroids used in an IRS programme in South Africa in 2000. Data from experimental hut trials also suggest that resistance could contribute to a lower-than-expected level of control. Some experts are concerned there may be other such examples that have gone undetected because of the difficulty in linking increases in malaria cases to evidence of resistance. While further evidence is clearly needed to understand more about the operational impact of insecticide resistance on the effectiveness of vector control interventions, this should not prevent the malaria community from taking action now.

The evolution of insecticide resistance is of great concern; we must act early, before resistance becomes stable in the vector populations.

Immediate action is particularly important given the evolution of resistance. Resistance genes have spread rapidly in malaria vector populations over large areas. Data also suggest that resistance can evolve swiftly, occurring at low frequency for many years without being detected and then increasing rapidly to very high levels, to a stage at which it becomes less likely or even impossible to reverse the trend. Resistance can probably be reversed only if the vector incurs a 'fitness cost' for being resistant (if the resistance gene confers some disadvantage on these vectors in comparison with susceptible populations). Once the insecticide is changed, these resistant mosquitoes will no longer have an advantage, and will die out.

Some IRM strategies (e.g. rotations) are based on this concept — that removing selection pressure will reverse resistance, and that it may therefore be possible at some point to reintroduce the original insecticide into vector control programmes. Insecticide resistance management strategies must, however, be implemented before the resistance gene becomes common and stable in the population; otherwise, the resistant gene will not recede even if use of the insecticide causing selection pressure is discontinued.[4]

Current monitoring of insecticide resistance is inadequate and inconsistent in most settings in which vector control interventions are used. Often, monitoring is performed reactively or ad hoc, depending on local research projects being conducted. In addition, the limited availability of reliable routine monitoring data from epidemiologically representative sites makes decision-making on managing insecticide resistance difficult.

1 Metabolic resistance is mediated by a change in the enzyme systems that normally detoxify foreign materials in the insect; resistance can occur when increased levels or modified activities of an enzyme system cause it to detoxify the insecticide much more rapidly than usual, thus preventing it from reaching its intended site of action.

2 Target-site resistance occurs when the molecule that the insecticide normally attacks (typically within the nervous system) is modified, such that the insecticide no longer binds effectively to it, and the resistant insect is therefore unaffected, or less affected, by the insecticide.

3 At the target site, resistance mutations can affect either acetycholinesterase or voltage-gated sodium channels. The gene for this type of resistance is known as *knock-down resistance (kdr)*. For metabolic resistance, three enzyme systems are important: esterases; mono-oxygenases and glutathione *S*-transferases.

4 As demonstrated by a study of blowflies by McKenzie and Whitten in 1982 (*3*), fitness cost is not an intrinsic property of the gene. Therefore, if that gene is allowed sufficient time to become common in a population, the rest of the genome will adapt to incorporate it without a significant fitness cost. At this point, even if the selection pressure is removed, the resistance gene will remain in the population.

1.3 POTENTIAL EFFECT OF RESISTANCE ON THE BURDEN OF MALARIA

If nothing is done and insecticide resistance eventually leads to widespread failure of pyrethroids, the public health consequences would be devastating: much of the progress achieved in reducing the burden of malaria would be lost.[1]

For example, current coverage with LLINs and IRS in the WHO African Region is estimated to avert approximately 220 000 deaths among children under 5 years of age[2] every year. If pyrethroids were to lose most of their efficacy, more than 55% of the benefits of vector control would be lost, leading to approximately 120 000 deaths not averted.[3] If universal vector control coverage were achieved, insecticide resistance at this level would be even more detrimental if pyrethroids failed, with approximately 260 000 deaths of children under 5 years of age not averted every year.

The community currently has a window of opportunity to act, to ensure that malaria vector control interventions continue to be a pivotal component of malaria control, as endemic countries attain universal coverage with sustained malaria control and elimination.

1.4 AVAILABLE STRATEGIES FOR MANAGING RESISTANCE

Strategies to preserve the efficacy of insecticides have already been used in public health and agriculture; there is no magic wand to break resistance, but several strategies of proven use could delay the spread of resistance, at least until new classes of insecticides and new tools become available.

With the potential impact on the malaria burden in mind, action can and should be taken now. IRM, with the objective of preserving or prolonging the susceptibility of malaria vectors to insecticides in order to maintain the effectiveness of vector control interventions, is not a novel concept; it was used effectively in agriculture during the past century as well as in public health (e.g. in the Onchocerciasis Control Programme in the 1980s). As continued exposure to a given insecticide eventually results in resistance to that insecticide, IRM strategies and judicious use of insecticides are required in any programme in which insecticides are used.

Several strategies exist for IRM for vector control, which are based on use of IRS and LLINs. They include: rotations of insecticides, use of interventions in combination and mosaic spraying. Potential future strategies include use of mixtures. In some settings, resistance management strategies may be implemented in the broad context of integrated vector management. These strategies can have several effects on populations of resistant vectors: they can delay the emergence of resistance by removing selection pressure (e.g. rotations) or kill resistant vectors by exposing them to multiple insecticides (e.g. mixtures, when they become available).

1 All assumptions for the estimates provided here can be found in the main document.
2 Current coverage with LLINs and IRS interventions as reported in the WHO *World Malaria Report 2010* and assuming an estimated efficacy of IRS and LLINs of ~55% on malaria-related child mortality.
3 Assuming 25% efficacy for LLINs, 10% for pyrethroid-based IRS, 55% for non-pyrethroid-based IRS; sensitivity analysis included in the main document.

PART 2 COLLECTIVE STRATEGY AGAINST INSECTICIDE RESISTANCE

2.1 OVERALL MALARIA COMMUNITY STRATEGY

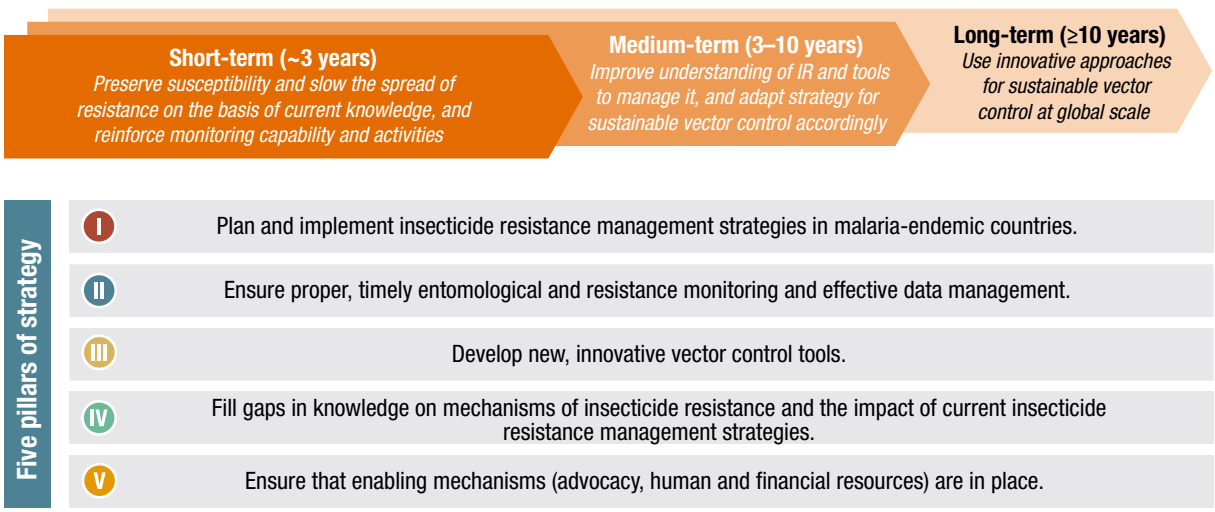
The global strategy consists of five activities (described as five 'pillars') spanning the short, medium and long term. Although some will be led by countries and others at global level, implementing all five pillars is the shared responsibility of all members of the malaria community.

The long-term goal of the malaria community is to maintain the effectiveness of vector control. It is our collective obligation to act in a coordinated manner against insecticide resistance immediately, in order to ensure the continued effectiveness of current and future malaria vector control tools to prevent malaria transmission, morbidity and mortality.

In the near term, prudent action should be taken to preserve the susceptibility of major malaria vectors to pyrethroids and other classes of insecticides, while making investments to ensure that new options for large-scale vector control become available as rapidly as possible.

The five pillars of the GPIRM are illustrated in Figure 1. Some of the activities (particularly pillars I and II) must be country driven but will require strong support from international partners. Although all countries are important to the success of the global strategy to manage insecticide resistance, in a resource-constrained environment, action is especially urgent in some high-priority areas,[1] particularly in sub-Saharan Africa.

Figure 1: Five pillars of the Global Plan for Insecticide Resistance Management in malaria vectors



IR, insecticide resistance

1 Including areas in which there is evidence of control failure, areas with significant resistance to pyrethroids, areas with a high malaria burden and intensive use of pyrethroid-based vector control interventions (so that control failure would have devastating consequences) or areas with unknown status of resistance.

2.2 COUNTRY ACTIVITIES

Pillar I. Plan and implement insecticide resistance management strategies in malaria endemic countries.

Countries should determine how their current vector control programmes should be modified to take account of insecticide resistance. The starting point is to establish the baseline of insecticide resistance and conduct a comprehensive situation analysis. This will require collecting available background data and, if necessary, conducting additional tests on vector susceptibility and on resistance mechanisms. The preparation and implementation of an IRM strategy should not, however, be delayed in order to complete a fully comprehensive situation analysis. Interpretation of the data must take into account the resistance situation in neighbouring countries as well as previous experience elsewhere with the same type of resistance mechanisms.

A national IRM strategy should be based on this analysis, with input from national, regional and global expertise as required. The strategy will determine the modifications necessary for current vector control practices. The national strategy for malaria vector control should be designed on the basis of the WHO policy framework for IRM as outlined in *The technical basis for coordinated action against insecticide resistance* (*2*) and further elaborated in the GPIRM (See Part 3, Technical recommendations for countries). WHO will regularly convene relevant experts to update the recommendations in the light of new evidence and vector control tools. In the long term, IRM should be an integral part of any vector control programme and not a 'stand alone' strategy. Part 3 gives an overview of technical recommendations for IRM at country level, depending on the type of intervention in place and the state of resistance.

Pillar II. Ensure proper, timely entomological and resistance monitoring and effective data management.

Sound IRM strategies must be based on robust, routine, and reliable data. Countries should design a monitoring plan that includes data on vector distribution and relevant vector attributes for transmission and control (biting and resting preferences), on susceptibility (and thus resistance) to currently used insecticides, and on the quality of vector control interventions. Other information, such as epidemiological data, will be necessary for decision-making. At the same time, country capacity and expertise should be built for designing monitoring plans and collecting and interpreting data. An aggregated global database should be created to provide global direction on IRM.

2.3 RESEARCH AGENDA

Pillar III. Develop new, innovative vector control tools.

Given the current reliance on insecticide-based strategies for vector control and the inevitability of insecticide resistance arising if selection pressure is maintained, sustained investment is required to develop new active ingredients with different modes of action. Ultimately, these new compounds will be required to manage resistance. The purpose of the IRM strategies discussed above is to delay the spread of resistance and preserve susceptibility to insecticides, at least until these new classes or molecules are available.

This is essential for LLINs, for which pyrethroids are currently the only class of insecticides used: nets with new active ingredients are urgently needed. IRS and LLIN products containing a mixture of novel active ingredients could be effective in delaying the evolution of insecticide resistance. Two new products—a reformulation of an existing active ingredient and an active ingredient 'repurposed' from agricultural use—are expected to become available for IRS in the near future, which will facilitate the adoption of rotation strategies.

New, non-insecticide-based vector control tools may also be important in the long term to reduce the reliance on insecticides in controlling malaria transmission.

Pillar IV. Fill gaps in knowledge on mechanisms of insecticide resistance and the impact of current insecticide resistance management strategies.

Current understanding of insecticide resistance is sufficient to justify immediate action to preserve the susceptibility of malaria vectors to pyrethroids and other insecticide classes. Scientific theory and experience from agriculture provide enough encouraging information on currently available IRM strategies to allow the design of such strategies for malaria vectors.

Nevertheless, there are important gaps in current knowledge; while these gaps should not preclude immediate action, additional information and evidence will be needed to further refine IRM strategies. In particular, little is known about the link between resistance and control failure (including the impact of the different resistance mechanisms). Furthermore, methodologies need to be developed to measure the effectiveness of IRM strategies and to determine the conditions under which these strategies are likely to be cost-effective in the long run. The GPIRM sets out some priorities for research in the short, medium and long term.

2.4 ENABLING MECHANISMS

Pillar V. Ensure that key enabling mechanisms (advocacy, human and financial resources) are in place.

Several elements are required for successful implementation of the GPIRM. Firstly, advocacy: the importance of insecticide resistance and its threat should be communicated to major donors and national political leaders to ensure that human and financial resources are mobilized and allocated to IRM. Secondly, further modelling is needed of the health and financial impacts of insecticide resistance, building on the initial estimates in the main document. Thirdly, resource mobilization is essential both today and tomorrow. It should include:

- financial resources to monitor insecticide resistance and to prepare and implement IRM plans and conduct research;
- human capacity and technical expertise (particularly entomological) in countries to plan and implement monitoring and management of insecticide resistance; and
- capacity at global level and within partner organizations to fulfil their roles in IRM.

2.5 FINANCIAL COST

Monitoring and managing insecticide resistance will have a significant short-term cost. Most experts agree that, although pre-emptive IRM will increase costs in the short term, it should result in long-term savings by preserving the effectiveness of insecticides and sustaining their usability. The GPIRM is based on this expectation.

Managing insecticide resistance often implies modifying current vector control practices by adding an insecticide with a different mode of action. Results from models[1] indicate that changing from IRS with only pyrethroids to a rotation that includes organophosphates and carbamates could increase the cost by approximately 20% and 45% in areas with short and long malaria transmission seasons, respectively. Where LLINs are used, combining non-pyrethroid IRS with LLINs while waiting for bednets with new active ingredients or mixtures would have high associated costs but could be targeted to areas with very high, confirmed levels of resistance.

It is assumed that such pre-emptive IRM strategies will delay the evolution of resistance, lengthen the usefulness of current insecticides and even reverse resistance in some settings. Experience suggests that, if nothing is done, resistance will stabilize in the vector population and reversal will be difficult or even impossible, so that some of the most effective insecticides will no longer be usable. Hence, the GPIRM includes not only estimates of the cost of pre-emptive action but a comparison with the cost of acting after control failure has already occurred. For instance, the above-mentioned 20% and 45% increases in the cost of IRS rotations would increase to ~30% and ~70% if action were delayed until pyrethroids were no longer usable.

The overall cost of implementing the five pillars of the GPIRM is expected to be about US$ 200 million per year. This calculation takes into account: implementation of IRM strategies (which would provide at least the same vector control coverage as today); capacity-building for monitoring at country level (assuming that these activities will be performed in all countries); costs of operational research into insecticide resistance; increased investment in research and development for new vector control products; and increased coordination and capacity at global level to support implementation of the GPIRM. This overall estimate is for a 'fully loaded' annual cost at its peak: if all countries were able to implement all GPIRM recommendations on IRM, insecticide resistance monitoring, capacity building and global activities.

There are obvious parallels between mosquito resistance to insecticides and parasite resistance to drugs. Combating antimalarial drug resistance involved the transition to artemisinin-based combination therapies. This required rapid development and adoption of new combination products and of new treatment policies at global and country levels, despite fears of a massive increase in unit costs, with consequent concerns of adequate supply and coverage. Ultimately, the price increase and the supply shortages were not nearly as large as had been predicted, and artemisinin-based combination therapies quickly became accepted as both the standard of care and an essential step in preserving the susceptibility of *Plasmodium falciparum* to our most valuable treatments. Now, the malaria community must tackle the threat of insecticide resistance, giving the highest public health priority to coordinated, pre-emptive action to preserve vector susceptibility to insecticides.

1 All assumptions for the estimates provided here can be found in Part 2.5 of the main document.

PART 3 TECHNICAL RECOMMENDATIONS FOR COUNTRIES

Defining the appropriate IRM strategy for a given situation is highly complex, as it depends on multiple entomological, ecological, epidemiological and operational considerations. The technical recommendations proposed in the GPIRM are built on the recommendations initiated in the WHO document, *The technical basis for coordinated action against insecticide resistance: preserving the effectiveness of modern malaria vector control* (2). The GPIRM recommendations are valid as of May 2012. They are initial working proposals for IRM strategies and will be revised as more evidence and research results become available. Updated versions of these recommendations will be available at http://www.who.int/malaria.

Ultimately, new active ingredients are needed for both LLINs and IRS for the management of insecticide resistance in the medium to longer term. As soon as they become available, bednets with non-pyrethroid active ingredients should be used; if possible, these new active ingredients could be used in a mixture in order to delay the spread of resistance to the new insecticide. In the meantime, a pragmatic approach is proposed to prevent and manage insecticide resistance with the tools currently available. Specific IRM strategies for each geographical area should be based on current vector control interventions, the status of resistance and the epidemiological context.

For IRS, the recommendations focus on pre-emptive use of rotations. For LLINs, the options are more limited, and IRM strategies will require consideration on a case-by-case basis. As described in the GPIRM, the response should focus on areas where resistance is of greatest concern. Wherever possible, countries should introduce focal IRS with non-pyrethroids in addition to LLINs in resistance 'hot spots'.

PART 4 NEAR-TERM ACTION PLAN

4.1 ROLE OF EACH STAKEHOLDER GROUP

4.1.1 INSECTICIDE RESISTANCE MANAGEMENT IS A SHARED RESPONSIBILITY FOR ALL RELEVANT STAKEHOLDERS

Figure 2: Main roles and responsibilities of each stakeholder group

	Global norms and guidelines	Designing IRM strategies	Implementation	Evaluating IRM strategy	Monitoring	Coordination of action / info	IR research	R&D	Resource mobilization	Advocacy
NMCPs and other VBD programmes	✓	✓	✓	✓	✓	✓	✓		✓	✓
Senior government officials			✓			✓			✓	✓
Other health programmes and agricultural sector					✓	✓	✓			
Implementation agencies / NGOs		✓	✓	✓	✓	✓			✓	✓
WHO GMP	✓	✓	✓	✓	✓	✓	✓		✓	✓
WHO regional and country offices	✓	✓	✓	✓	✓	✓			✓	✓
Multilateral agencies		✓	✓						✓	✓
Funding agencies and bilateral donors					✓		✓	✓	✓	✓
WHOPES	✓			✓			✓	✓	✓	✓
Research Institutes and academia		✓		✓	✓		✓			✓
Manufacturers of VC products / PDPs				✓				✓	✓	✓

✓ Primary role ✓ Secondary role: support

NMCP, national malaria control programme; VBD, vector-borne disease; NGO, nongovernmental organization; GMP, Global Malaria Programme; WHOPES, WHO Pesticide Evaluation Scheme; VC, vector control; IRM, insecticide resistance management; IR, insecticide resistance; R&D, research and development; PDPs, Product Development Partnerships

Every stakeholder group in the community must fulfil its responsibilities in managing resistance of malaria vectors to insecticides, as outlined in the GPIRM. The roles listed in Figure 2 are described in more detail on the following pages and will be refined over time. The description may not be exhaustive, and some stakeholder groups might have additional roles.

While this section addresses the role of each stakeholder group, section 4.2 describes concrete, immediate steps to be taken in the community to support IRM.

Roles of national malaria control programmes.

- Design and implement appropriate IRM strategies, in line with policy and guidelines set by WHO (and seek support as necessary).
- Increase monitoring in order to understand the current situation, and implement routine monitoring of insecticide resistance.
- If required, seek help from research and academic institutions to conduct such monitoring activities.
- Assess the effect of IRM strategies on: slowing down or reducing the frequency of insecticide resistance; decreasing malaria transmission (if implemented as a result of control failure); and entomological and epidemiological effectiveness of vector control.
- Participate in coordination at regional level to ensure sharing of data and best practices.
- Coordinate IRM strategy with other relevant sectors, including agriculture, environment, and finance, as well as with municipalities and local governments.
- Work with local academic and research institutions to ensure that relevant research is conducted in-country (e.g. on links to control failure) and data are shared.
- Identify and mobilize human and financial resources for monitoring insecticide resistance and IRM plans.
- Consider whether current budgets could be reallocated to provide funds for monitoring insecticide resistance and management activities.
- Engage high level government support, particularly from ministries of health, finance and agriculture, by raising the profile of insecticide resistance.
- Provide feedback, where relevant, to help WHO to refine policies on vector control in general and monitoring and management of insecticide resistance in particular.

Role of senior government officials.

- Make funds available for monitoring insecticide resistance and IRM strategies.
- Encourage neighbouring governments and donors that are reluctant to take the threat of insecticide resistance seriously.

Role of the agriculture sector.

- Try to use classes of insecticides that are not available for public health use.
- Conduct research on insecticide resistance in agriculture, and share the results with the malaria control community.
- Share information on insecticide resistance with vector control advisors, national malaria control programmes and, when necessary, prepare an intersectoral IRM strategy.

Role of implementation partners and nongovernmental organizations.

- Where appropriate, support national malaria control programmes in the design and implementation of IRM strategies, in line with policy and guidelines set by WHO.
- Support national malaria control programmes in monitoring insecticide resistance, and ensure that monitoring is conducted as a routine component of every malaria vector control programme.
- With national malaria control programmes and local research institutions, assess the impact of IRM strategies, particularly: on slowing down or reducing the frequency of insecticide resistance; on decreasing malaria transmission; and on the entomological and epidemiological effectiveness of vector control.
- Coordinate with and provide technical assistance to national malaria control programmes, and make sure that information is shared with them.
- Identify and mobilize human and financial resources for monitoring insecticide resistance and for IRM strategies.
- Advocate for the inclusion of insecticide resistance as a priority in global malaria control and resource mobilization.

Role of the WHO Global Malaria Programme.

- Refine and update global policies and guidelines for monitoring and managing insecticide resistance on the basis of new evidence and information.
- Provide leadership, oversight and coordination of activities triggered by the GPIRM. This includes increasing awareness about the urgency of the threat, and advocating for increased funding for IRM strategies and research.
- Coordinate support for countries in the design and implementation of IRM strategies; in particular, convene international experts on insecticide resistance.
- Convene experts to review new science on insecticide resistance, including evidence on subregional and regional spread of resistance, on resistance mechanisms, on the impact of resistance on malaria control and on IRM methods. These evidence reviews will be the basis for policy refinement and revision.
- Coordinate support for countries in building capacity and training staff to collect data for monitoring insecticide resistance – including their analysis and interpretation for global policy and direction.
- Consult with countries, Regional Offices and partners to identify a reputable institution to host a global database, to be overseen by WHO on behalf of member states; ensure the flow of data on insecticide resistance from countries to the hosting institution.
- Advocate for sufficient capacity at global, regional and country levels of WHO to support countries in implementing the recommendations contained in the GPIRM.

Role of WHO regional and country offices.

- Provide regular opportunities for sharing information on insecticide resistance and best practices at regional level, between countries and across public health and other relevant sectors (e.g. agriculture).
- Advocate for inclusion of insecticide resistance priorities in malaria control and research agendas at country level.
- Support national malaria control programmes in increasing awareness, and obtain support at national and regional levels; advocate for increased funding for IRM strategies and research.
- Promote intersectoral interaction and coordination for the implementation of IRM at country level.
- Coordinate and support countries in the design and implementation of monitoring plans for IRM.
- Coordinate support for countries in building capacity and training staff to collect data (susceptibility tests and advanced testing methods).
- Advocate for sufficient capacity at WHO regional and country offices to support countries in their IRM efforts.

Role of other multilateral organizations (depending on their focus).

- Advocate for inclusion of insecticide resistance priorities in global malaria control and research agendas.
- Support national malaria control programmes in increasing awareness, and obtain support at national and regional levels.
- Advocate for increased funding for IRM strategies and research.
- Commit funding for IRM and encourage other multilateral organizations and funding agencies to do the same, if appropriate.
- Coordinate with WHO to offer technical support to countries for the design and implementation of IRM strategies.

Role of funding agencies and bilateral donors.

- Encourage the establishment of insecticide resistance monitoring for all vector control programme grants, in coordination with WHO.
- Support countries in meeting the conditions of grants.
- Make resources available for the academic research (operational and laboratory research) required to improve understanding of insecticide resistance and effective IRM strategies.
- Invest in the development of new products and vector control tools.
- Commit funding to support the financial costs of IRM strategies and capacity-building for monitoring, in coordination with WHO.

Role of WHOPES.

- Prepare guidelines for safety and efficacy assessment of new public health pesticides.
- Conduct independent assessment of new vector control pesticides, through its networks of collaborating centres.
- Develop specifications for quality control and international trade of public health pesticides.
- Support Member States in life-cycle management of public health pesticides.
- Monitor and publish information on use of pesticides for vector-borne disease control.
- Increase WHOPES capacity at global level and in collaborating centres to enable timely response to the growing number of new vector control products in the development pipeline.

Role of research and academic institutions.

- When needed, support national malaria control programmes in interpreting data and making decisions on an IRM strategy.
- With the national malaria control programmes, conduct trials and research to assess the effectiveness of IRM strategies for both maintaining effective vector control and reducing insecticide resistance.
- When needed, support national malaria control programmes in collecting data on and testing for insecticide resistance (particularly biochemical and molecular testing).
- Seek funding to conduct research on identified priorities and undertake this research together with national malaria control programmes.

Role of manufacturers of vector control products.

- Invest in development and in bringing to market new products and vector control tools to support IRM.
- Work with partners to find ways to reduce the cost of insecticides and other vector control products to make IRM strategies more affordable.

Given that most of these constituencies are part of the RBM Partnership, RBM has a critical role in implementing the GPIRM, especially with regard to advocacy, resource mobilization, and harmonization of partner efforts.

4.2 ACTION PLAN

A near-term action plan has been prepared to clarify priorities, particularly for the next 12 months. These activities are important prerequisites for proper implementation of the recommendations of the GPIRM. The activities are aligned with the five pillars of the strategy (see section 2.1). The timelines for each activity will serve as indicators to monitor progress in implementation of the recommendations.

In Figure 3 and in the rest of this section, three colours are used: activities in green should be implemented in malaria-endemic countries, usually by the national malaria control programme; activities in blue represent regional or global activities to support countries; and activities in brown are to be implemented at all levels: country, region and global.

4.2.1 PILLAR I: INSECTICIDE RESISTANCE MANAGEMENT STRATEGIES

Within 6–12 months.

Modification of vector control practices

- **National malaria control programmes** should consolidate recent data on insecticide resistance (less than 12 months old), conduct additional susceptibility tests and, where insecticide resistance has been detected, identify the mechanisms (see section 2.2).
- **National malaria control programmes** should compile existing information on other factors in order to put resistance data in a broader context (see section 2.2).
- **National malaria control programmes** should then analyse the data and prepare appropriate IRM strategies, with the support of partners as detailed below.
- **National malaria control programmes** may have to seek external technical expertise and should contact WHO country offices to coordinate support from regional and global level.

Decision support materials

- **WHO will work with partners** to develop decision support materials for interpreting data on insecticide resistance.

Coordination among endemic countries and between partners

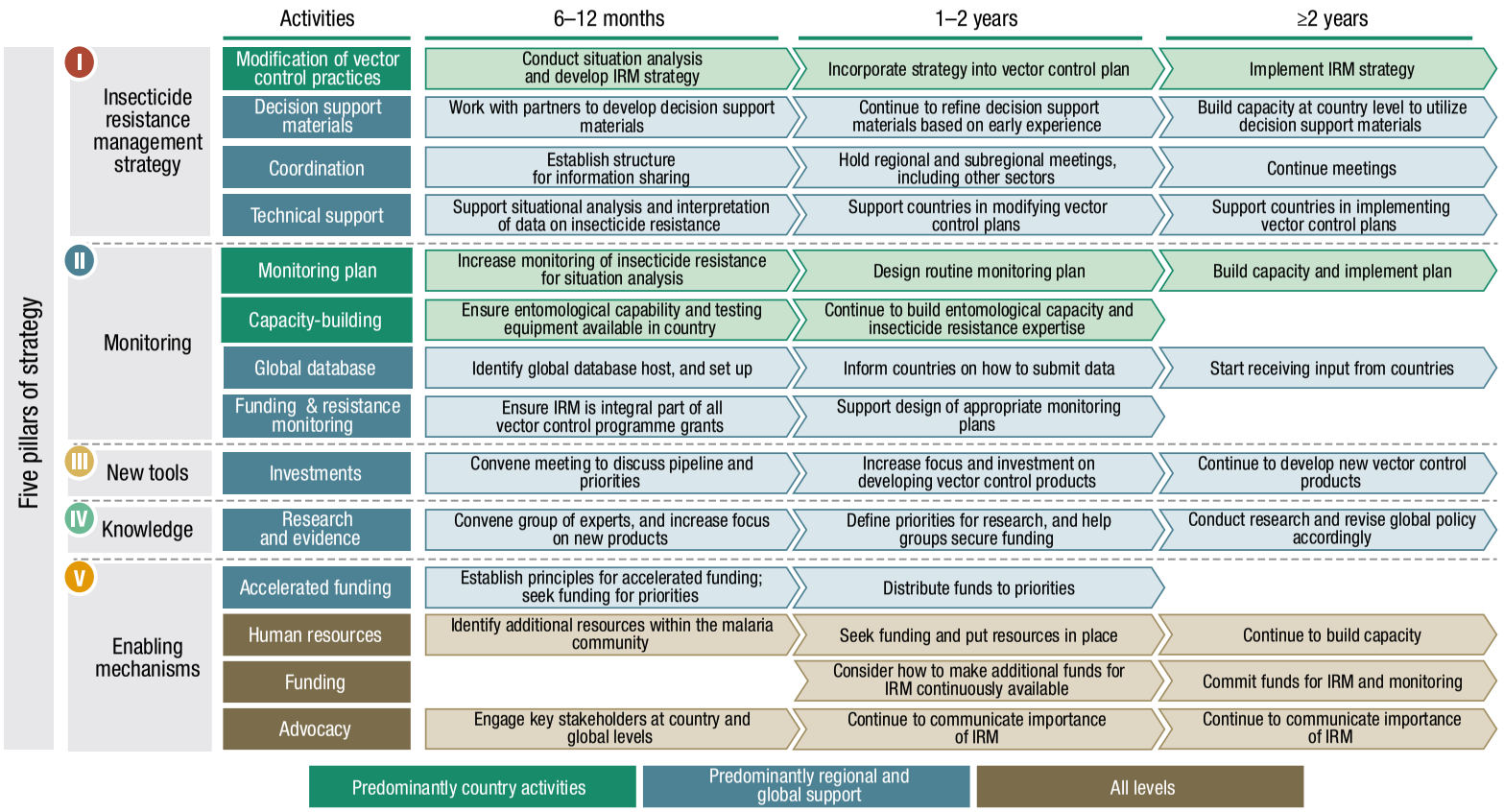
- **Networks for regional coordination (national malaria control programmes, multilateral organizations, implementing agencies, local nongovernmental organizations)** should devise a formal process for sharing information and coordinating strategies for national malaria control programmes, other implementing agencies (including nongovernmental organizations), the public health and agriculture sectors (e.g. in quarterly meetings).

Technical support to countries

- **Experts in insecticide resistance** should support countries in interpreting data on insecticide resistance. WHO, at country, regional, and global levels can provide this technical support and coordinate additional support from relevant malaria control partners.

FFigure 3: What should we do during the next 12 months and beyond?

Overview of the key activities required to implement GPIRM in the near future



IRM, insecticide resistance management

Within 1–2 years.

Modification of vector control practices

- **National malaria control programmes** should review and, when relevant, modify all components of their vector control plan to incorporate an IRM strategy, with the support of external technical experts, if needed.
- **National malaria control programmes** should pursue procurement options for different insecticides and other vector control tools, in line with WHO guidelines and recommendations.

Decision support materials

- **Continue to refine the decision support materials** based on early experience.

Coordination among endemic countries and between partners

- **Regional and country partners** (in both public health and agriculture sectors) should be convened to share information on the insecticide resistance situation and IRM strategies.

Technical support to countries

- **Partners with experience in vector control planning** should support overall revision of the IRM plan and the subsequent budget.
- **Representatives of ministries** should support national malaria control programmes with regulatory procedures allowing implementation of IRM strategies.

2 years and beyond.

Modification of vector control practices

- **National malaria control programmes** should implement their revised or reoriented vector control plans, taking into account insecticide resistance. This will require additional training and capacity building.

Decision support materials

- **WHO and partners** should build capacity at country level to utilize decision support materials.

Coordination among endemic countries and between partners

- **Regional coordination** should continue between neighbouring countries, including other sectors such as agriculture.

Technical support to countries

- **WHO regional and country offices, together with nongovernmental organizations and implementing agencies** should support national malaria control programmes in implementing reoriented vector control plans, for example by offering advice, expertise and resources, as needed.

4.2.2 PILLAR II. MONITORING ACTIVITIES

Within 6–12 months.

Monitoring plan

- **National malaria control programmes** should consolidate all existing data on insecticide resistance, and conduct additional testing if the data are more than 12 months old, to form the basis for a situation analysis of insecticide resistance in the country (see Pillar I).

Capacity-building

- **National malaria control programmes** should identify the human and infrastructural capacity required for monitoring and investigate ways to build the capacity.
- **Regional initiatives** should continue to develop monitoring capacity.
- **Implementing agencies and donors** should continue to implement and fund capacity-building for monitoring.

Global database

- **The WHO Global Malaria Programme** should consult with countries, Regional Offices and partners to identify a reputable institution to host the database, to be overseen by WHO on behalf of Member States.
- **The WHO Global Malaria Programme** should ensure the flow of data on insecticide resistance from countries to the institution hosting the global database.
- **The host organization** should set up the database and work with WHO to design an input template for countries. WHO would manage data requests from partners in consultation with countries.

Funding and IR monitoring

- **Donor agencies** should ensure that insecticide resistance monitoring is an integral part of all vector control programme grants.

Within 1–2 years.

Monitoring plan

- **National malaria control programmes** should, after conducting an initial situation analysis, prepare a plan for routine monitoring of insecticide resistance (see section 2.2).
- **National malaria control programmes** should raise funds (by mobilizing national and external resources) as required to build monitoring capacity and procure the necessary equipment.

Capacity-building

- **National malaria control programmes** should continue to build expertise in entomology and insecticide resistance; partnerships should be formed with local and regional research institutes.

Global database

- **The WHO Global Malaria Programme,** through the WHO Regional Offices, should contact national malaria control programmes, implementing agencies and research institutions to explain the data that are needed and how they are intended to be used.

Funding and IR monitoring

- **Donor agencies and multilateral organizations** should support countries in preparing appropriate monitoring plans for the implementation of large vector control grants.

2 years and beyond.

Monitoring plan

- **National malaria control programmes** should implement routine monitoring plans.

Global database

- **Malaria-endemic countries** should submit data on insecticide resistance for inclusion in the database.
- **WHO, at global, regional, and country level** should conduct further discussions with countries and with research and academic institutions as required to encourage submission of data.

4.2.3 PILLAR III. NEW TOOLS

Within 6–12 months.

Investment

- **Partners in innovative vector control** should continue to meet to discuss the current pipeline and urgent needs, with a view to increasing the focus on products with IRM properties.

Within 1–2 years and 2 years and beyond.

Investment

- **Partners in innovative vector control** should increase their focus on new products for IRM.

4.2.4 PILLAR IV. KNOWLEDGE

Within 6–12 months.

Research and evidence

- **The WHO Global Malaria Programme** should convene a group of experts focusing on knowledge needs in insecticide resistance, after consultation with the Malaria Policy Advisory Committee.
- **Partners from research institutes and academia with national malaria control programmes** should continue current trials and studies on insecticide resistance.

Within 1–2 years.

Research and evidence

- **The experts** should finalize the research agenda and communicate the highest priorities to the malaria community.
- **Partners in research institutes and academia** should apply to donors, with support from experts, to secure funding for the research priorities.

2 years and beyond.

Research and evidence

- **Partners in research and academic institutions with national malaria control programmes** should initiate additional high-priority research.
- **The experts** should review new evidence (in coordination with the global database and national malaria control programmes) and prepare an annual report on insecticide resistance.
- **The experts** should consider whether global policies should be revised in the light of new evidence.

4.2.5 PILLAR V. MECHANISMS

Within 6–12 months.

Accelerated funding

- **A group of donors, multilateral organizations and other relevant partners** (e.g. from the private sector) should convene to investigate the possibility of accelerating funding to allow urgent action in countries in which the situation of insecticide resistance is critical. For instance, the creation of a 'catalytic fund' has been proposed to initiate monitoring or implementation of IRM strategies in defined high-priority geographical areas.
- **This group** should define the principles and mechanisms for such 'accelerated funding', identify priorities and seek funding commitments.

Human resources

- **Malaria-endemic countries, implementing agencies and other partners** should identify the human resources needed to implement the recommendations of the GPIRM.
- **WHO at global, regional and country levels** should identify the technical capacity needed for the design and implementation of plans for monitoring and managing insecticide resistance.
- **WHOPES** should identify additional capacity at global level and collaborating centres to respond to the growing number of IRM products in the pipeline.

Advocacy

- **WHO** should provide leadership, oversight and coordination of the GPIRM, including advocacy to increase awareness of the urgency of the threat of insecticide resistance and funding for implementation of IRM strategies. The World Health Assembly and WHO regional committee meetings should be used to solicit support from Member States and partners.
- **National malaria control programmes** should seek government support, particularly from ministries of health and agriculture, by raising the profile of insecticide resistance.
- **Government officials** should encourage other governments and donors that appear reluctant to react seriously to the threat of insecticide resistance.
- **Stakeholders in the Roll Back Malaria Partnership and specialists in advocacy and communication** should take opportunities to communicate the importance of insecticide resistance, advocate for IRM and raise appropriate funds.

Within 1–2 years.

Accelerated funding

- **Accelerated funding, when identified,** should be allocated to areas with high insecticide resistance.

Human resources

- **Endemic countries, implementing agencies, other partners, the WHO Global Malaria Programme, WHOPES and WHO regional offices** should seek funding where necessary for building additional entomological capacity and ensure that resources are allocated as soon as possible after they have been received.
- **WHO** should continue to identify and build capacity.

Funding

- **National malaria control programmes** should review options for funding IRM strategies and monitoring, including grant proposals, requests to national governments and reallocation of their current vector control budgets when appropriate.
- **Donor agencies** should discuss internally and with the malaria community how to commit sufficient funds to malaria vector control to meet the increased costs associated with insecticide resistance.
- **Fund-raising entities** should add IRM to their list of priorities.

Advocacy

- **All stakeholders** should continue to communicate the importance of insecticide resistance and use the GPIRM to advocate for political commitment and for resource mobilization.
- **WHO** should make sure that insecticide resistance is an integral part of reports on malaria.

2 years and beyond.

Human resources

- **Endemic countries, implementing agencies, other partners, the WHO Global Malaria Programme, WHOPES and WHO regional offices** should continue to build capacity.

Funding

- **Donor agencies and governments** should commit funding to allow additional countries to implement IRM strategies and monitoring plans.

Advocacy

- **All stakeholders in the Roll Back Malaria Partnership** should continue to communicate the importance of insecticide resistance.
- **WHO** should coordinate with other partners to ensure that insecticide resistance is an integral part of reports on malaria control.

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For more information, please contact:

Vector Control Unit
Global Malaria Programme
World Health Organization
20 avenue Appia
1211 Geneva 27
Switzerland
gmpvectorcontrol@who.int
http://www.who.int/malaria.