Malaria Policy Advisory Committee Meeting

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Innovation to Impact – WHO change plan for strengthening innovation, quality and use of vector-control tools

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1 Introduction

Vector control can play an important role in reducing the transmission of malaria and major vector-borne neglected tropical diseases (NTDs) such as dengue, chikungunya, Chagas disease, lymphatic filariasis, visceral leishmaniasis, human African trypanosomiasis and schistosomiasis. Effective vector-control strategies have been pivotal in reducing worldwide mortality and morbidity from vector-borne disease. Over the past decade, the main vector-control tools that contributed to a reduction in malaria morbidity and mortality were pesticides and pesticide products. However, the later part of the 20th century has seen an expansion of areas with insecticide resistance in malaria vectors, coupled with low investment in development of public health pesticides; hence, there is currently a dearth of effective vector-control products.

WHO has recognized the need to change current systems to support the development, evaluation and appropriate use of new tools for vector control, and to manage pesticides throughout their life-cycle, to maximize their impact on disease and reduce risks to humans and the environment. Catalytic funding support is required to drive the change to strengthen innovation, assure quality and promote low-risk and judicious use of vector-control products. WHO has therefore recently submitted a funding proposal to the Bill & Melinda Gates Foundation to seek support for such a project.

The project proposes ambitious changes to improve the systems for vector-control product evaluation and quality, strengthen normative and technical guidance, and facilitate synergies and collaboration among the WHO Member States and other partners. The system developed will help to expedite the availability of effective, safe, high-quality and innovative vector-control tools, as well as guidance for their appropriate operational use and regulation. The project will also help to create conditions for greater investment in the development of new public health pesticides and their judicious use within an overall context of integrated vector management. Considering that vector control will constitute 50–60% of all investments required to eliminate and control malaria and NTDs from now until 2030, the project will help to catalyse the reforms required to meet future technical needs. Accelerated availability of innovative high-quality vector-control products, along with improved guidance on appropriate use, will greatly reduce the transmission of vector-borne diseases.

1.1 Background

Since 1960, the WHO Pesticide Evaluation Scheme (WHOPES) has been the primary global mechanism for assessing the efficacy and safety of pesticides for use in public health and in setting quality standards. WHOPES was established by the World Health Assembly with the

WHO/HTM/GMP/MPAC/2015.14

purpose of facilitating evaluation of pesticides and pesticide products for vector control, and providing guidance and setting policies for their sound use in public health. Today, WHOPES recommendations are relied on by Member States and by international procurers of pesticides and pesticide-related products.

WHOPES provides the following range of functions and activities:

- testing and evaluation of pesticides and pesticide products for public health, with the aim of facilitating their acceptance, national registration and use by Member States;
- normative functions such as setting norms and standards for the evaluation and use of pesticides and pesticide-related products, and promoting and monitoring their judicious use in various settings;
- technical support for vector-control policies and strategies, operational guidance, monitoring global insecticide use, building institutional capacity, and disseminating valuable knowledge; and
- policy for pesticide and pesticide-related products used in a public health context.

WHOPES facilitates testing of pesticides within established product categories – long-lasting insecticide-treated nets, indoor residual spraying, larvicides, space sprays and so on – whose public health impact is already accepted.

In 2013, WHO established a Vector Control Advisory Committee (VCAG) to assess the public health value of new paradigms (i.e. innovative concepts) of vector control, and shepherd the development of tools that represent these new paradigms. VCAG and its process for new paradigms are designed to provide WHO with broad recommendations on whether certain forms of vector control can affect disease transmission. The group is structured to guide prospective innovators of new paradigms to generate required data in the best, most scientifically robust and cost-effective way possible. VCAG is a normative activity jointly managed by the WHO Global Malaria Programme (GMP) and the WHO Department of Control of NTDs.

In recent years, the stakeholder community has expressed interest in collaborating further with WHO to accelerate the availability of vector-control tools to meet contemporary and future needs.

1.2 The need for reform

Increasing insecticide resistance, rapidly expanding arboviral diseases and the impact of climate change on vector distribution threaten to thwart the global gains in control of vector-borne diseases. New tools and strategies are needed to respond to these challenges; in particular, innovative products that can safely and effectively target key transmission settings (e.g. outdoor transmission, areas of high resistance and high-risk populations) and effective use strategies. WHO recognizes the need for reforms in evaluation of innovative tools; system quality; evaluation of vector control; and timely development of normative guidance to strengthen innovation, availability, quality and best use of vector-control tools for public health.

Several key areas have been identified for improvement:

- shorten timelines to bring products to market;
- increase transparency and improve communication with stakeholders;
- streamline product-evaluation processes to comply with ongoing practice in medicines, vaccines and diagnostics (under the WHO Prequalification programme);
- include pre- and post-marketing quality assurance (QA); and

- facilitate registration, quality control (QC) and sound management of pesticides by working with national authorities.

2 The process of change and internal coordination

Over the past 6 months, WHO has been detailing its plans to improve current systems and procedures for pesticide evaluation, and to strengthen vector-control normative functions. These activities are part of a larger *Innovation to Impact Initiative* (I2I), which is supported by the Bill & Melinda Gates Foundation. The main aim of I2I is to encourage the development of innovative, effective and high-quality products for vector control. I2I is part of a larger goal to eliminate and eradicate malaria and NTDs by engaging many stakeholders in vector control, including industry, procurement agencies, regulatory bodies and WHO.

Within WHO, the senior leadership has been highly supportive of the restructuring of vector-control evaluation processes and the strengthening of normative vector control. Changes to WHOPES will be part of a broader package of collaboration between NTD, the WHO Vector Ecology and Management (VEM) unit, the GMP, the Entomology and Vector Control (EVC) unit, and the Regulation of Medicines and other Health Technologies (RHT)/Prequalification Team (PQT).[1]

2.1 Approach

Over a transition period that will end in December 2018, WHO will implement a series of reforms leading to key outcomes for which the three departments (NTD, VEM and GMP, EVC) have agreed on division of functions. The key outcomes, discussed below, are:

- driving innovation in public health vector control;
- accelerating the availability of vector-control products;
- improving the quality of vector-control products;
- increasing the appropriate use of vector-control products; and
- developing a sustainability plan.

2.1.1 Driving innovation in public health vector control

To address the great need for innovative vector-control products, WHO will work to foster a product development environment that supports innovation by:

- developing a network of test sites that are accredited for good laboratory practice/good experimental practice, and that can be used to generate quality-assured data for WHO to evaluate – this will shift data generation to manufacturers;
- reviewing the existing technical criteria for equivalency for evaluation of generic products; and
- optimizing processes for assessing new vector-control paradigms (via VCAG).

WHO oversight will involve a variety of factors, including:

- pre-submission guidance;
- prior agreement on trial site selection, to ensure that field trials are representative of product claims and geographical diversity factors (related to diverse vectors, seasonality and other entomological requirements);

1. The prequalification programme is abbreviated as PQ or RHT/PQ within text

- protocol review and agreement before trial initiation, to align with WHO guidelines and harmonize across sites;
- monitoring of agreed timelines;
- trial site inspections, where technically necessary; and
- further site capacity development to meet new or revised needs.

2.1.2 Accelerating the availability of vector-control products

The goal defined by WHO within this grant proposal is to align and integrate pesticide evaluation in RHT/PQ by the end of 2016, while maintaining strong links with other important functions such as setting norms and standards, and life-cycle pesticide management. During the transition period, product-evaluation functions will continue to be managed by WHOPES, but PQ will build internal capacity to fully take over these functions. Therefore, the current structure of WHOPES will be maintained in the interim period between the current and end states. However, reforms will be made to current evaluation processes, to improve efficiency and transparency and to accelerate the availability of vector-control products on the market, aligned with best practices within RHT/PQ. Key reforms proposed include:

- formalizing procedures for product testing and evaluation during the transition period;
- formalizing pre-submission guidance for manufacturers to align on data and testing requirements;
- implementing a "clock-stops" mechanism[2] and real-time tracking of progress on product evaluation; and
- recruiting an expanded pool of independent experts to review efficacy, safety and quality data for public health pesticide products, and to make recommendations as needed.

2.1.3 Improving the quality of vector-control products

To ensure that WHO-recommended pesticides are of high quality, the PQ will develop a pre-marketing QA system analogous to that used for medicines and similar products. This will involve factory inspections to improve the manufacturing processes and development of QA systems. NTD/GMP will initiate measures to improve post-marketing quality management through situational analyses of post-marketing QC regulatory practices in 10 priority countries (1–2 per region, including major procurers of public health pesticides and countries with poor-quality management systems). Additionally, in collaboration with PQ, an assessment of best practices in quality management for other product streams will be undertaken, looking at stringent regulatory authorities (Australia, Canada, Europe, Japan and the United States). Measures taken to strengthen post-marketing quality management will include:

- developing guidelines and training documents for regulators on post-marketing quality management; and
- conducting regional policy workshops for capacity-building in this area.

Also, as a joint activity of NTD/PQ and GMP, meetings will be held with global and national procurement agencies to encourage the development of coordinated quality tracking systems, which can then feed into PQ quality management systems once developed, which in turn may be linked with product evaluation and listing, as defined by PQ.

2. This refers to calculating exact time taken by the industry and WHO for assessment of a product, including time taken to respond to a request for particular information.

2.1.4 Increasing appropriate use of vector-control products

The following normative, technical and strategic functions will be enhanced:

- supporting insecticide resistance monitoring and management for vectors of NTDs and malaria through capacity building of control programmes and operational guidance;
- normative guidance supporting pesticide product evaluation (efficacy, safety and quality);
- normative and technical guidance support for judicious and appropriate use of product through implementation of integrated vector management and through situational targeting; and
- building national regulatory capacity for the sound management of public health pesticides, including registration, and regulatory practices, according to the *International Code of Conduct on Pesticide Management*.[3]

2.1.5 Developing a sustainability plan

A final outcome of the project will be the development of sustainable systems supporting activities from NTD/GMP (normative, technical and strategic) and RHT/PQ (evaluation) related to vector control, with reduced need for donor funding. Strong governance will ensure that the proposed activities are implemented effectively. A joint project management committee of NTD, GMP and PQ will ensure close collaboration across departments for the project, which will be especially important for developing new systems for pesticide product evaluation within WHO.

2.2 Overall impact

Through these changes, WHO aims to support the development, evaluation, QC, adoption and sound management of pesticides and their products for the control and elimination of vector-borne diseases.

Vector-control product manufacturers will benefit from faster, clearer and more transparent vector-control product-evaluation systems, including a new and independent evaluation review process, control over data generation and priority given to innovative products with stronger pre-submission guidance support to manufacturers. The aim would be rapid evaluation of completed dossiers and subsequent normative guidance on use of new paradigm products. Evaluation functions will move to RHT/PQ to be aligned with evaluation of other product streams in WHO by the end of 2016.

National regulatory authorities will benefit from a more transparent global evaluation system in support of countries and regional systems, and stronger support for national registration through more transparent global evaluation. Additionally, increased support and guidance on registration, capacity strengthening and QC will be provided.

Procurement sectors will benefit from a larger array of products and strengthened development of normative guidance for deployment of innovative tools. This is expected to include more efficient evaluation, to enable innovative tools to be available faster for procurers, as well as timely and strengthened development of normative guidance for innovative tools and new product categories.

WHO Member States will benefit from decreased incidence of vector-borne disease because of the availability of high-quality and effective products in the field, and strong normative support to monitor and manage insecticide resistance and manage pesticides over their life cycle.

3. Available at: http://who.int/whopes/resources/en/

3 Conclusions

Effective vector-control strategies have been pivotal in reducing worldwide mortality and morbidity from vector-borne diseases. Despite these gains, such diseases continue to be a leading cause of mortality and morbidity across sub-Saharan Africa, Asia and other regions. Also, the NTDs such as dengue are continuing to cause outbreaks, and have emerged as the most prevalent vector-borne diseases in several countries of South-east Asia and Latin America. New innovative tools and methodologies are needed to confront challenges such as increasing insecticide resistance across vectors; outdoor transmission; impact of global climate change; and the rising incidence of dengue, chikungunya and other arboviral diseases. WHO has initiated ambitious reforms in response to the needs of the vector-control community and within the broader context of the I2I initiative. This proposal details WHO change plans to foster a greater drive for development of innovative high-quality products, and efficient evaluation and QC systems supported by normative guidance and technical guidance, with the aim of moving towards effective evidence-based use, regulation and life-cycle management of products in the field. This investment will help to:

- develop global capacity to evaluate and efficiently manage vector-control tools; and
- strengthen health systems in:
    - monitoring the impact of interventions and environmental changes; and
    - developing guidance for entomological surveillance during the post-elimination phase of all vector-borne diseases.