The evaluation process for vector control products

JUNE 2017

INFORMATION NOTE

The WHO process for the evaluation of vector control products has been revised to better meet the needs of countries endemic for, or at risk of, vector-borne diseases. The revised process came into effect on 1 January 2017 and is designed to accelerate product evaluation to support the continued scale up of core malaria vector control interventions, to strengthen vector control for neglected tropical diseases, and to address key challenges, such as emerging vector resistance to insecticides.

The key objectives of the revised process are to:

1. Enable access to safe, effective and high-quality vector control products;

2. Enhance evidence-based guidance to promote best use and management of vector control tools, technologies and approaches;

3. Promote product quality throughout the product's life cycle.

Under the revised process, the evaluation pathway to be followed is determined by whether or not a product is part of a class with an existing WHO policy recommendation. A policy recommendation is a position statement or recommendation issued by WHO, the most recent of which takes precedence over any previously issued recommendation.

Products covered by a policy recommendation will follow the *Prequalification Pathway*, while all others will follow the *New Intervention Pathway* to validate whether the product has public health value. In the latter case, WHO will issue a policy recommendation once the product's public health value has been validated. Both pathways involve the assessment of supporting data and inspections, and are designed to ultimately result in the prequalification of a product. This prequalification is communicated through the product's 'listing'.

World Health Organization

WHO/HTM/GMP/2017.13

The purpose of this information note is to describe the revised evaluation process following the transition from the WHO Pesticide Evaluation Scheme (WHOPES) to the WHO Prequalification Team (PQT), including a description of the role of the Vector Control Advisory Group (VCAG) as part of this process. It outlines the two pathways and their associated components, and is meant to guide interactions between product developers/manufacturers and WHO.

THE EVALUATION PROCESS

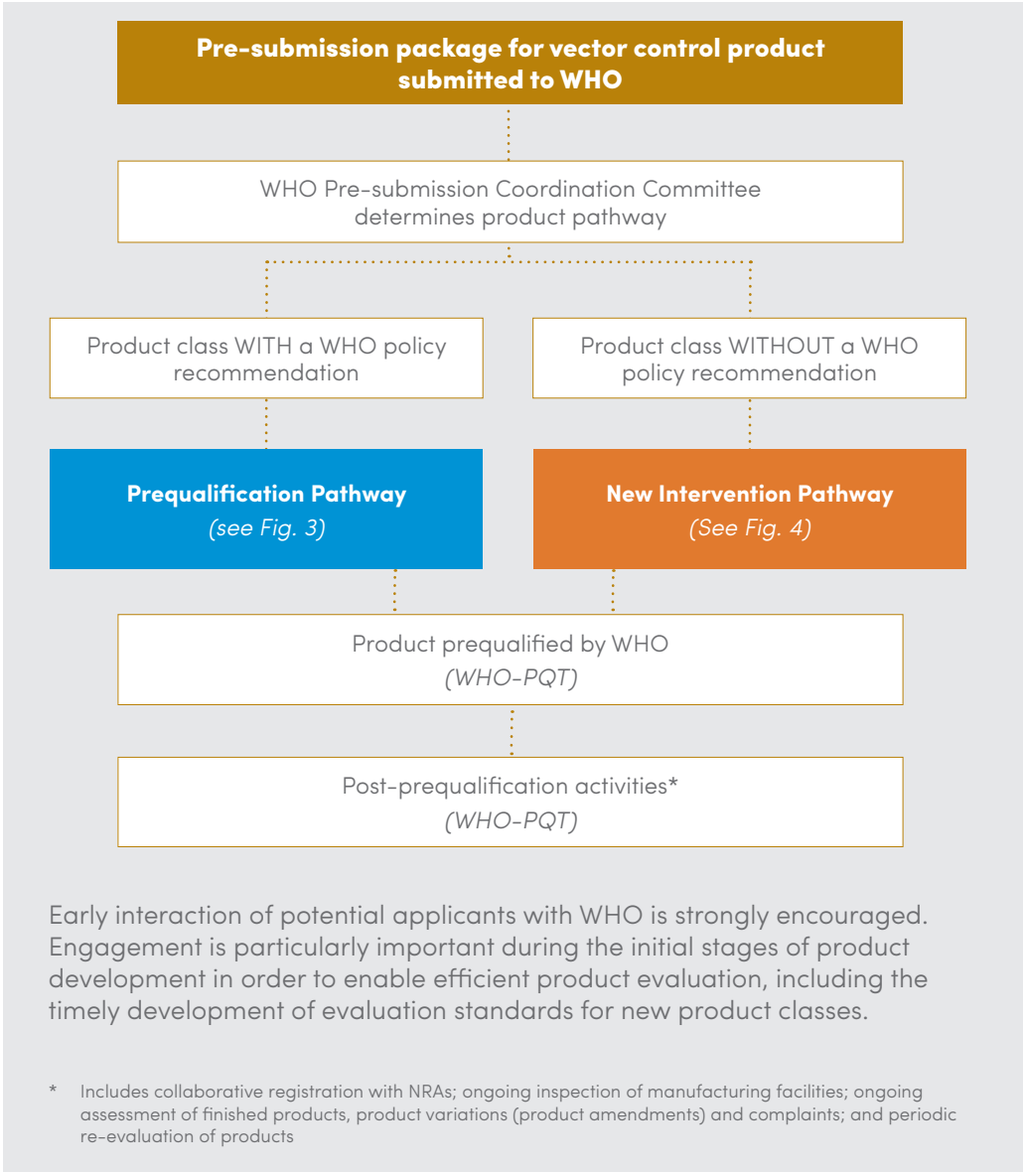
Under the revised WHO process, the evaluation of vector control products (Fig. 1) commences when a product developer/manufacturer submits a pre-submission package for a vector control product via the single entry portal managed by PQT (pqvectorcontrol@who.int). The pre-submission package must include a draft product label that specifies the intended product claim(s).

A Pre-Submission Coordination Committee (PCC) consisting of staff from PQT, the Global Malaria Programme (GMP) and the Department of Control of Neglected Tropical Diseases (NTD) will review the pre-submission package to determine whether: a) the product has potential for use in disease control programmes; and b) the product falls within an established product class (Fig. 2). For further information on product classes and associated policy recommendations for malaria vector control products please refer to the GMP information note *(1)*; policy recommendations for neglected tropical diseases will be made available on the VEM-NTD website at www.who.int/neglected_diseases/vector_ecology/en/.

Based on this review, the PCC will decide whether the product is eligible for WHO evaluation and, if so, which of the two evaluation pathways should be followed. The PCC will provide feedback through PQT to the "applicant" (a product developer/manufacturer who has submitted a pre-submission package to WHO), describing the applicable process and rationale for the determination. For each pathway, a point of contact will be identified in the respective WHO Department to guide the applicant through the process. The applicant should then submit a full application to PQT or to the WHO secretariat of VCAG, as directed.

FIG. 1:

Overview of the WHO process for the evaluation of vector control products

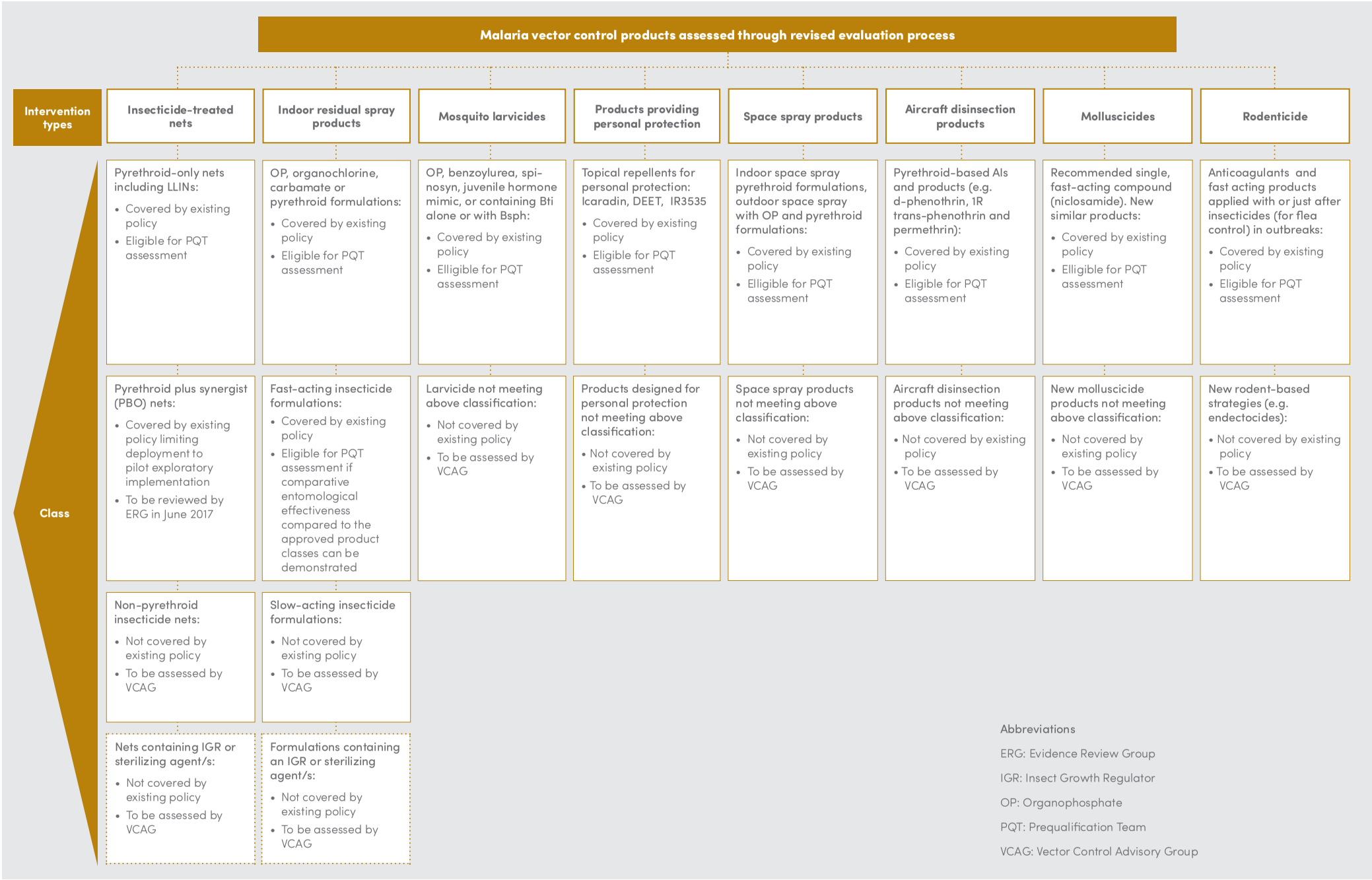


Early interaction of potential applicants with WHO is strongly encouraged. Engagement is particularly important during the initial stages of product development in order to enable efficient product evaluation, including the timely development of evaluation standards for new product classes.

* Includes collaborative registration with NRAs; ongoing inspection of manufacturing facilities; ongoing assessment of finished products, product variations (product amendments) and complaints; and periodic re-evaluation of products

FIG. 2:

Overview of vector control intervention types and product classes for vector control products, including a) the applicability of WHO policy recommendations and b) related assessment pathways under the revised WHO evaluation process. Note that some products have a specific product claim that distinguishes them from other products of the same class.



Prequalification Pathway

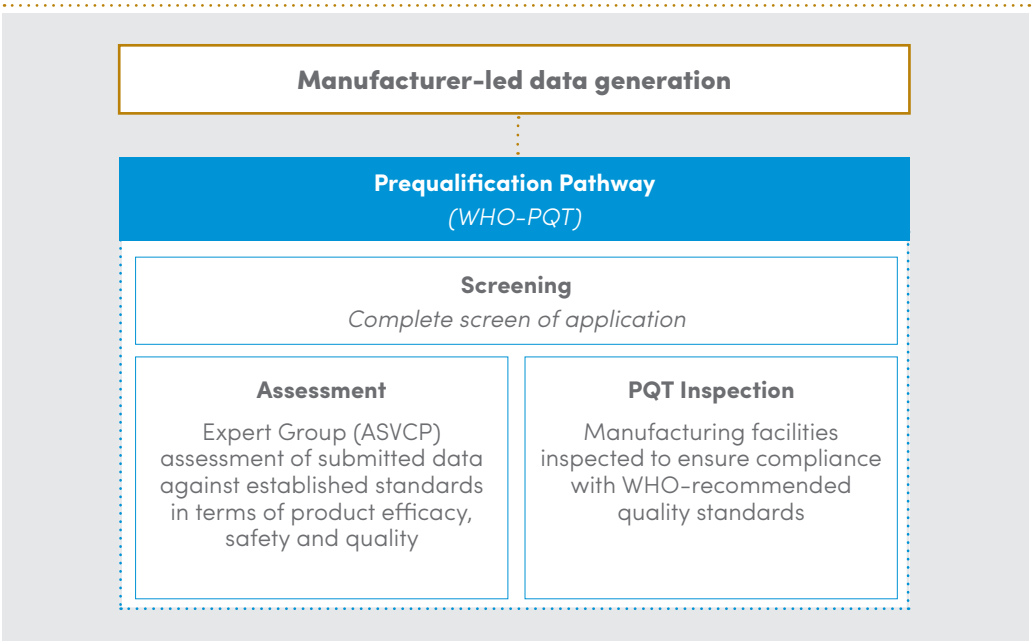
Products categorized by the PCC as belonging to a class for which a WHO policy recommendation has been issued will enter the *Prequalification Pathway* (Fig. 3). The *Prequalification Pathway* is managed by PQT under the WHO Department of Essential Medicines and Health Products (EMP).

The applicant will need to provide PQT with a full product dossier consisting of safety, efficacy and quality requirements as elaborated in the PQT-VC procedure currently under development. Once submitted, the application will be screened for completeness. If the application is deemed complete, two parallel activities will commence: 1) assessment of the application by experts at the Assessment Session for Vector Control Products (ASVCP); and 2) inspection of the manufacturing facilities to ensure compliance with WHO-recommended quality standards.

PQT's decision on whether to prequalify the product will be made based on the review of the submitted application and the outcome of the inspection procedure. Once the product is prequalified, the applicant will be informed and the product will be listed on the WHO PQT-VC website (http://www.who.int/pq-vector-control/en/).

PQT-VC will be responsible for the maintenance of the product throughout its life cycle. This includes product change management (formulation and labelling), post marketing surveillance, product testing, and periodic monitoring of manufacturing sites.

FIG. 3:
Key steps of the Prequalification Pathway



New Intervention Pathway

Products that do not fall within an established class will enter the *New Intervention Pathway* (Fig. 4). The *New Intervention Pathway* is jointly managed by GMP and NTD; it also requires the close involvement of PQT, and relies on assessments and advice from the VCAG on new vector control tools (http://www.who.int/neglected_diseases/vector_ecology/VCAG/en/).

FIG. 4:
Key steps of the New Intervention Pathway

MPAC: Malaria Policy Advisory Committee; STAG: WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases, VCTEG: Vector Control Technical Expert Group (of GMP); TWG: Technical Working Groups for diseases (of NTD)

The product concept will be reviewed to determine the data required to: a) validate its public health value; b) substantiate the new product class and associated claim(s); and c) support the formulation of a WHO policy recommendation. The applicant will be advised on the data requirements and test procedures to be used, including guidance on appropriate trial design(s). WHO will also guide the applicant to undertake hazard/risk assessments where applicable and to develop product specifications.

Based on this guidance, the applicant will need to develop study protocols and SOPs for the entomological and epidemiological evaluation of the product, identify testing sites and undertake the studies. Regular interaction with the WHO secretariat of VCAG during protocol development and study implementation is encouraged in order to ensure that product data meet the required standards. This will ensure that VCAG can promptly assess the data when they become available. The efficacy, safety and quality standards for the new product class will be established as part of the process. Once all of the requested entomological and epidemiological data have been reviewed, VCAG will provide a recommendation to WHO on the public health value of the product class. In parallel, the PQT-VC inspection process will be initiated, timed so that its completion coincides with the publication of the WHO policy recommendation.

VCAG's final evaluation of the data will also include the development of a target product profile (TPP). WHO will develop evaluation standards for the product class, including guidelines and performance criteria, to facilitate the evaluation of other products within this class once they become available.

If VCAG provides a positive recommendation on a product's public health value to the relevant policy advisory committee – STAG for neglected tropical diseases and MPAC for malaria – and it is endorsed by either, WHO will issue a policy recommendation and operational guidance. The product will then be deemed "first in class" for a new product class or product claim. Development of a WHO policy recommendation and operational guidance for use of the new product will draw on the normative functions performed by NTD or GMP; these will be developed in parallel so as to ensure both types of guidance are made available at the same time. Once a policy recommendation has been issued, a decision to prequalify the product will be made based on the assessment and inspection.

Information and data generated for VCAG's assessment will be reviewed with PQT throughout the process, and, once complete, the contents of the full application will be transferred to PQT for the management of post-prequalification activities. Entomological data generated as part of the evaluation process are consistent across both pathways, thereby avoiding the duplication of reviews or additional data requirements.

CONVERSION OF WHOPES RECOMMENDATIONS TO PQT LISTING

To facilitate the migration of products to the revised evaluation system, products with a full WHOPES recommendation will be provided with a PQT listing over the course of 2017. LLINs with a WHOPES interim recommendation will be given time-limited WHO prequalification and will be listed accordingly. The manufacturers of these products will need to submit additional product-specific data on the duration of bioefficacy and, chemical/physical durability in order to prove that they meet LLIN requirements and thus maintain their listing. If data requirements are not met within the specified timeframe, the product will be delisted.

To provide clarity on each product's status during transition, each listing will specify the product's suitability with respect to the eligibility criteria, the claims for which it has been assessed, whether additional data are required for further product evaluation, and the timeframe for the product developer to provide these data. All products transferred from WHOPES will be subject to manufacturing site inspections to ensure that WHO quality standards are met.

APPENDIX. GLOSSARY OF KEY TERMS

Biochemical mode of action

A biochemical mode of action describes the manner in which pesticides interfere with the biochemistry of animals and plants.

Entomological effect

Entomological effect refers to a product's effect on a disease vector in terms of killing, deterring, and reducing fertility or susceptibility to infection. Products with different biochemical modes of action may have similar entomological effects on target insects; for example, indoor residual spraying (IRS) formulations with pyrethroids and carbamates differ in their biochemical modes of action, yet are considered to have a similar impact on the target insect in areas of insecticide susceptibility.

First in class

First in class refers to the first product with a novel entomological effect (e.g., reducing human–vector contact, or decreasing vector survivorship, or susceptibility to infection or transmission), the public health value of which is ascertained by VCAG based on the demonstration of its entomological and epidemiological efficacy against vectors and human infections and/or disease, respectively. Once the public health value of a 'first in class' product is ascertained, a new product class is established.

Intervention type

Intervention type is a broad category referring to the entomological effect and use pattern of an intervention. Vector control interventions include tools, technologies and approaches. Note that some intervention types do not necessarily have associated pesticide products, e.g., biological control with fish.

Pesticide

Any substance, mixture of substances, or microorganism (including viruses) intended for repelling, destroying or controlling a pest. Targets include vectors of human or animal disease, nuisance pests, and unwanted species of plants or animals that are causing harm or otherwise interfering with the production, processing, storage, transport or marketing of food, agricultural commodities, wood and wood products or animal feeding stuffs. Pesticides may be administered to animals for the control of insects, arachnids or other pests in or on their bodies. The term also includes substances intended for use as insect or plant growth regulators; defoliants; desiccants; agents for setting, thinning or preventing the premature fall of fruit; and substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport. Pesticide synergists and safeners, where they are integral to the satisfactory performance of the pesticide, also come under this term.

Pesticide product

A pesticide product is the active ingredient(s) and other components of the pesticide in the form in which it is packaged and sold.

Prequalification

Prequalification for pesticides is WHO's standardized assessment procedure for evaluating the acceptability, in principle, of vector control products for purchase by United Nations agencies. Agencies using the information resulting from the prequalification procedure should perform additional assessment prior to purchasing,

such as verifying the supplier's financial stability, standing and ability to supply the required quantities; ensuring the security of the supply chain; and evaluating pre-shipment quality control and other related aspects.

Product

A vector control product is any tool designed to reduce infection and/or disease caused by a vector-borne disease through control of the disease vector.

Product amendment

A product amendment is a change in the specification of an active ingredient and/or a formulation (including source of materials), labelling, production process or manufacturing site of a prequalified product; any amendment must be submitted to WHO for review.

Product claim

A product claim is information contained in the product's label and advertisement materials. For vector control products, this includes the product's chemical content; target arthropod vector; entomological effect in controlling target vectors or protecting against infection and/or disease; duration of effect; and role in mitigating insecticide resistance.

Product class

A product class in vector control is a group of products that share a common entomological effect by which it reduces pathogen transmission and thus reduces infection and/or disease in humans. For products in a class not currently recommended by WHO, efficacy trials with a 'first in class' product must generate epidemiological evidence of protective efficacy against infection and/or disease. The evidence is then reviewed by VCAG to validate the public health value of the product class. This validation forms the basis of a WHO policy recommendation for the new product class. A product class may contain one or more target product profiles (TPPs) depending on the intended effect of the product(s) and claim(s).

Product label

The written, printed or graphic matter on or attached to the pesticide or its immediate container, as well as the outside container or wrapper of its retail package.

Product life cycle

This refers to the time period over which a proposed product is presented to WHO, evaluated, prequalified, and maintained as an active product. The management of the product life cycle refers to the applicant's continual updating of product information (formulation, labelling, production sites and manufacturing processes) to WHO. A product that has been withdrawn or delisted has effectively ended its life cycle, and there will be no further maintenance of the product's prequalification.

Public health value

A product has public health value if it has proven protective efficacy to reduce or prevent infection and/or disease in humans.

Target product profile

A target product profile (TPP) is a detailed technical description that defines the preferred characteristics of a product and guides the development process to demonstrate its performance. A product class may contain one or more TPPs depending on the intended effect of the product(s) and claim(s).

Endnotes

1. Includes collaborative registration with National Regulatory Authorities; ongoing inspection of manufacturing facilities; ongoing assessment of finished products, product variations (product amendments) and complaints; and periodic re-evaluation of products

REFERENCES

1. Malaria vector control policy recommendations and their applicability to product evaluation. Geneva: World Health Organization; 2017 (http://www.who.int/malaria/publications/atoz/vector-control-recommendations/en/)

This information note was prepared jointly by:

- the WHO **Global Malaria Programme**
  http://www.who.int/malaria/en/
- the WHO department of **Control of neglected tropical diseases**
  http://who.int/neglected_diseases/en/
- the **vector control group of the WHO Prequalification Team (PQT-VC)**
  http://who.int/pq-vector-control/en/