# VERV programme – questions for the EPA

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Spraying to prevent malaria. Vanuatu 2009. Photo: AusAID

This is the second article in a two-part series regarding the intertwined problems of growing insecticide resistance and the lack of investment in novel public health use insecticides (Part I can be found in the November/December 2023 issue of IPC). A new US incentive programme aims to mitigate these problems. Reading the US Environmental Protection Agency (EPA) announcement of the new programme raises questions which EPA will need to clarify. Our questions and others will be discussed by stakeholders and EPA on February 28, 2024 in Washington, DC. Readers can register to attend the meeting using the link at the bottom of this article.

On December 18, 2023, EPA released Pesticide Registration (PR) Notice 2023-2, to announce the establishment of the Vector Expedited Review Voucher (VERV) Programme, which was mandated in the Pesticide Registration Improvement Act of 2022 (PRIA 5). VERV is a new incentive to stimulate the development of novel mosquito control products to help prevent the spread of mosquito-borne diseases such as malaria, dengue fever, and Zika.

VERV is modelled after the US Food and Drug Administration's (FDA) Priority Review Voucher (PRV) programme legislated in 2007 (Sec. 524 FDA Amendments Act), which offers a priority review of a second product as a reward for new treatments targeting selected diseases. While VERV and PRV are built upon the same value-creating model, there is a key difference between the two agencies: EPA does not have pre-existing, separate processes to accelerate the review of a product. FDA's four expediting programmes, accelerated approval, breakthrough, fast track, and priority review, are dedicated processes which are differentiated from standard reviews.

Under the law, EPA receives up to $500,000 annually for fiscal years 2022-2027 from the EPA Expedited Review and Reregistration Fund ("maintenance fee fund") for VERV programme administration. (FIFRA).

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The availability of resources raises the first of several potential questions regarding the new VERV programme.

**Q: How will EPA use the available funding to create a process to expedite the review when an awarded voucher is exercised on a second product?**

**Q: Does EPA's recent experience of expediting the review of products effective against the SARS-CoV-2 virus that causes Covid-19, provide a benchmark for a differentiated expediting process? (EPA COVID-related Expedited Product Reviews)**

VERV rewards the registrant of a new public health use insecticide, the "vector product", with a voucher. The registrant submits the vector product for the applicable PRIA category and pays the relevant registration fee. The review of the vector product follows the standard decision review timing for its PRIA category – it is not expedited. If the product is eligible and approved, the registrant is awarded a voucher. The eligibility criteria for VERV are described at EPA's VERV website. (EPA VERV Website)

The italicized text below is from the EPA VERV website.

1. *To qualify for a voucher under the VERV Program, application for a new vector control active ingredient must:*
2. *Demonstrates a proven efficacy (performance) against pyrethroid or other insecticide-resistant mosquitoes. Efficacy studies along with resistant ratio determinations of the resistant mosquito strain must be submitted to fulfil product performance requirements. On a case-by-case basis, EPA may accept a rationale for efficacy based on the active ingredient's novel mode of action to demonstrate control of insecticide-resistant mosquitoes. EPA will evaluate these studies and ensure efficacy data meet the same requirements required for other products intended for mosquito control.*

USAID supports internal residual spraying to prevent malaria in the high-risk region of Oromia. Photo: USAID

3. *Prevents, kills, mitigates, or repels pyrethroid- or other insecticide-resistant mosquitoes, with a novel or unique mechanism different from other insecticides already registered by the Agency for mosquito control. Requirement may be waived if the Agency determines there is a significant public health benefit. Waiver requests must be submitted with the application and decisions will be made on a case-by-case basis.*
4. *Targets mosquitoes capable of spreading such diseases as malaria, dengue, Zika, chikungunya, St. Louis encephalitis, eastern equine encephalitis, western equine encephalitis, West Nile encephalitis, Cache Valley encephalitis, La Crosse encephalitis, and yellow fever.*
5. *Is made accessible for use in the United States, including territories or possessions of the United States, and countries where mosquito-borne diseases, such as malaria, are prevalent.*
6. *Broadens the adoption of integrated pest management strategies, such as insecticide resistance management, or makes those strategies more effective.*
7. *Is not contained in any pesticide product registered by the Agency as of the date of the enactment of the Pesticide Registration Improvement Act of 2022 or does not contain an active ingredient approved in the 2-year period preceding the date of registration by any global stringent regulatory authority for the same uses, vectors, and applications. Requirement may be waived if the Agency determines there is a significant public health benefit. Waiver requests must be submitted with the application and decisions will be made on a case-by-case basis.*

EPA further elaborates the eligibility criteria for novel chemistries.

*EPA will determine whether or not an application has a unique or novel mode of action on a case-by-case basis. In making this determination, the agency will look for factors such as whether:*

1. *The mechanism targets new or different receptors.*
2. *The pesticide is in a new or different chemical class (including classification by the Insecticide Resistance Action Committee).*
3. *The mechanism uses special approach such as interrupting behaviour, targeting different life stages, or prohibiting reproduction.*
4. *Live release control techniques should target a specific species not controlled by another live-release product.*

Eligibility criteria suggested several questions.

**Q: For a chemistry that does not have an existing IRAC classification, what evidence is required to prove a new mode of action?**

**Q: Is the judgment of the Insecticide Resistance Action Committee (IRAC) a recommendation or a final decision?**

**Q: To what level of detail does the registrant address "integrated pest management strategies, including insecticide resistance, or makes those strategies more effective" in its submission?**

**Q: Which non-US registration bodies are "stringent regulatory authorities" (SRA); is the World Health Organization's Pre-Qualification (which is not a stringent regulatory authority) considered an SRA for this requirement?**

**Q: What is the process to seek a VERV award for products that were submitted between Dec 29th 2022 – Dec 2023 and not yet received a final registration decision? [Our reading of the VERV PR Notice is chemistries previously registered for agricultural, but not mosquito control, are eligible to amend their submission to seek the VERV award].**

In addition to meeting the eligibility requirements, the applicant must submit a Global Access Plan (GAP).

*The application must also include a global access plan that will be made publicly available for the active ingredient and that addresses: a) manufacturing locations, including any licensed third-party manufacturers; b) distribution and procurement processes for malaria vector control programmes in selected countries (when the product targets Anopheles mosquitoes); and c) the prices for common quantities of the product.*

The access and GAP requirements raise additional questions.

**Q: Are all product "accessibility" requirements covered in the Global Access Plan or, for example, does product access in the US and territories require a separate verification or attestation in the submission?**

**Q: When the criteria specify "be made available in countries where mosquito-borne diseases, such as malaria, are prevalent", does that mean one, multiple, or all countries where the disease is found; how is "prevalent" defined?**

**Q: It is likely that manufacturing sites, product prices and other information may change after a product is submitted for review and before a VERV, if approved, is awarded.**

**Q: How is a Global Access Plan (GAP) amended after submission?**

**Q: Does an amended GAP need to be re-submitted to the EPA?**

As with other pesticide registration actions, registrants can apply for the registration of VERV submission through the agency's Pesticide Submission Portal (PSP) which is accessed through the EPA's Central Data Exchange (CDX) Network (https://cdx.epa.gov/). At the time of submission, registrants must indicate that the product is a VERV candidate on EPA Form 8570-1. Registrants must also submit supplemental information including the Global Access Plan.

EPA will issue the voucher to the registrant at the time that it approves the registration of the vector control product. The awarded voucher can be exercised on a second product, the "voucher product", to receive an expedited EPA registration review. The voucher product registration fee is set by the applicable PRIA category. Accelerating the registration review of the voucher product, faster market entry, provides the registrant a speed-to-market value which mitigates the developmental costs and possible losses on the vector product. An awarded voucher can be sold or transferred an unlimited number of times.

A redeemed VERV shortens the decision review time for any product submitted under the following PRIA codes (see table above).

| PRIA CATEGORY | DECISION REVIEW TIME REDUCTION TARGET |
|---|---|
| *New active ingredient; food use (R010)* | 6 months less |
| *New active ingredient; food use; reduced risk (R020)* | 6 months less |
| *New active ingredient; non-food use; outdoor use; reduced risk (R060)* | 6 months less |
| *New active ingredient; non-food use; indoor (R110)* | 6 months less |
| *New active ingredient; non-food use; outdoor; reduced risk (R070)* | 4 months less |
| *New active ingredient, non-food use; indoor; reduced risk (R120)* | 2 months less |

The Dec 29, 2022 VERV-enacting legislation was explicit in stating that VERV review decision date reductions are "targets; not guarantees". We hope when the first awarded vouchers are redeemed, after VERV(s) are awarded, EPA will achieve all or most of the decision review time reductions. The value of VERV rests on the review time reductions. We can be cautiously optimistic the reductions will be achieved when we note that EPA expedited many Covid-related product reviews at the apex (2020 – 2021) of the US pandemic. (EPA Covid-related Expedited Product Reviews)

Registrants must provide EPA with 90-days notice before redeeming a voucher. Any registrant who purchases a voucher must provide documentation about the sale or transfer at the time of redemption and also adhere to the 90-day notification requirement. EPA will provide selected information regarding awarded vouchers on the agency's VERV website. (EPA VERV Website)

Awarded VERVs suggests two questions.

**Q: How quickly will EPA update information when a VERV is awarded?**

**Q: Will EPA update the information on its website when an awarded VERV is sold or transferred?**

## Meeting registration

On February 28, 2024, Duke University and DC Legislative and Regulatory Services are hosting a ½-day meeting at 1200 Pennsylvania Avenue NW, Washington DC. A vector control stakeholder panel will discuss the new programme and raise questions along with the participants. Key staff from EPA will present the new VERV programme and take questions. Registration for the meeting is found at https://sites.duke.edu/vervdukeindc/. ■

### REFERENCES


EPA COVID-related Expedited Product Reviews https://www.epa.gov/coronavirus/disinfectant-use-and-coronavirus-covid-19

EPA Central Data Exchange (CDX) Network. (https://cdx.epa.gov/)

EPA Form 8570-1. https://www.epa.gov/pesticide-registration/pesticide-registration-manual-blank-forms

EPA VERV Website: https://www.epa.gov/mosquitocontrol/vector-expedited-review-voucher-verv-program

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) FIFRA §4(k)(7)(B)(ii)) https://www.epa.gov/laws-regulations/summary-federal-insecticide-fungicide-and-rodenticide-act

Insecticide Resistance Action Committee https://irac-online.org/mode-of-action/classification-online/

PR Notice: https://www.regulations.gov/document/EPA-HQ-OPP-2023-0476-0003