A New Incentive in the Battle Against Mosquito-Borne Diseases

Vector Expedited Review Voucher (VERV)

Congressional action to reduce a significant domestic and global health security risk

Malaria, Dengue fever, Zika virus, West Nile and Chikungunya are deadly and debilitating diseases. VERV incentivizes a steady pipeline of new insecticides which are necessary to avoid a health security problem in their absence.

Mosquito-borne global diseases pose a significant biosecurity and health security risk to the United States (U.S.) and the world. Malaria, Dengue fever, Zika virus, West Nile and Chikungunya affect people in poor and rich countries. Travel, immigration, tourism, and military operations overseas are increasing the health effects of malaria on Americans.

Malaria kills more than 400,000 people a year in sub-Saharan Africa; mostly children under the age of 5. Major vector-borne diseases account for about 17% of the global burden of communicable diseases. Eighty percent of the world's populations are at risk of one or more vector-borne diseases (mosquitoes, ticks, fleas and other insects are the "vectors" of certain infectious diseases) with over 700,000 deaths annually.

Medicines play a critical role in fighting these diseases, but a more efficacious and cost-effective approach is disease prevention using insecticides. Insecticides play a critical role in limiting deaths and disability by controlling disease-carrying mosquitoes. Between 2000 and 2015, approximately 500 million clinical cases of Malaria were averted due to vector control interventions like Long-Lasting Insecticidal Nets (LLINs) and Indoor Residual Spraying (IRS). However, the development of resistance to insecticides is a constant threat to their effectiveness. Our response must be to innovate novel insecticides faster than resistance to existing insecticides develops.

There are significant economic disincentives to developing new insecticides. So, today resistance is occurring faster than innovation which increases the biosecurity risk to Americans and to the world. The development costs for a new, novel chemistry insecticide can range from $100 to $250 million. They can also require as long as twelve years to enter the market. Upon market entry there is a poor prospect of recouping the invested time and money.

While resistance has increased over the past decade, particularly pyrethroid-resistant mosquitoes, no new classes of insecticides have been developed specifically for public health during that period.

The Vector Expedited Review Voucher (VERV), a virtually no cost new incentive, can mitigate the economic barriers to innovation. The VERV encourages leading R&D focused agriculture companies to invest in novel insecticide development. Smaller companies and universities can also receive the incentive. VERV rewards the registrant of a new public use insecticide with a voucher to receive an expedited review of a second, more profitable product. So, there are two chemicals for each voucher: the chemical needed to control disease-carrying vectors, and the more lucrative chemical that is accelerated by the regulator. Getting to market faster is valuable and gives an innovator registrant an opportunity to generate a financial return to mitigate the development cost losses on a public health use insecticide. The awarded voucher can also be sold.

Two Publications Make the Case for VERV

- Ridley, Moe, and Hamon "A Voucher System to Speed Review Could Promote a New Generation of Insecticides to Fight Vector-Borne Diseases." Health Affairs. 2017. Describes the economic value of the voucher.
- Moe, Ayers & Hamon "VERV Policy Brief" IVCC 2020. Describes the eligibility criteria and proposed mechanisms for EPA to administer the new incentive.

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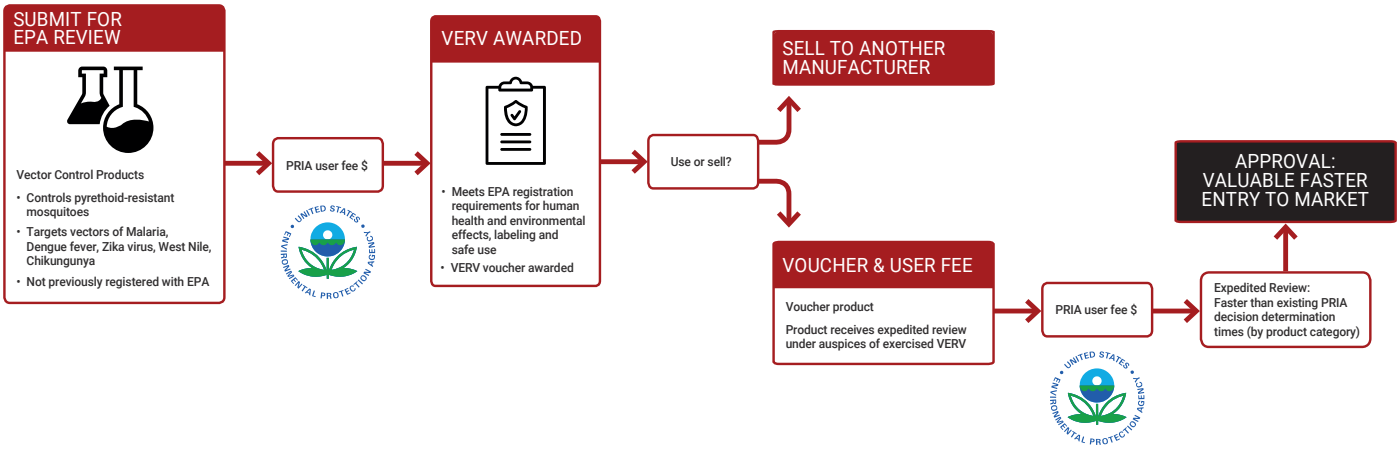
How Will the VERV Program Work?



Key Features of VERV Pilot Test Amendment

- Rewards registrants developing new insecticides effective against pyrethroid-resistant mosquitoes.
- Enacted as a pilot program over 5 years or until 3 VERVs are awarded.
- Proposes a $5.5 million one-time appropriation for the pilot to address the U.S. Environmental Protection Agency (EPA)'s limited resources for timely reviews and to establish theadministrative mechanisms.
- Pilot approach allows EPA, registrants, and all stakeholders experience with the program to evaluate and improve it before including the new incentive in PRIA 5 (2023).
- VERV is modeled after the Priority Review Voucher (PRV) program (Sec. 524 2007 FDA Amendments Act) which is a proven incentive for sponsors registering new treatments for neglected tropical diseases, rare pediatric disorders or medical counter-measures. The FDA has awarded 43 (January 2021) PRVs over the 13 years since the program was enacted. (Read the history of the PRV program at: *www.priorityreviewvoucher.org*).
- Congressional action is needed to fund a pilot version of the new incentive. Based on the pilot experience VERV can be enacted into the PRIA 5 (2023) re-authorization. Immediate action will save thousands of lives.

VERV Eligibility Criteria

- New insecticide active ingredient which controls pyrethroid-resistant mosquitoes.
  - *Mosquito strain shows <98% mortality at 5x the discriminating dose of pyrethroid; EPA will prescribe the appropriate test method and comparator.*
- Targets vectors of Malaria, Dengue fever, Zika virus, West Nile, Chikungunya and other mosquito-borne diseases.
  - *Appears on PR Notice 2002-1 "Lists of Pests of Significant Public Health Importance".*
- Not previously registered with the U.S. EPA.
  - *EPA may at its discretion:*
    a) grant an exception where a previously registered agricultural use insecticide has been re-purposed and submitted for a public health use;
    b) recognize data and evaluations made by a stringent regulatory authority regarding human health and environmental risk assessments, product labeling and safety including approvals granted through a joint review in which EPA was a participating member.
- Meets EPA registration requirements for human health and environmental effects, labeling and safe use.

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Established in 2006, brings knowledge from every corner of Duke University to bear on the most important global health issues of our time. DGHI was established as a University-wide institute to coordinate, support, and implement Duke's interdisciplinary research, education, and service activities related to global health. DGHI is committed to developing and employing new models of education and research that engage international partners and find innovative solutions to global health challenges.

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Duke University's Fuqua School of Business is dedicated to advancing the understanding of management through research and providing the highest quality education for business and not for-profit leaders worldwide.
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