Development Support for Public Health and other Minor Use Pesticides – Lessons from the IR-4 Project

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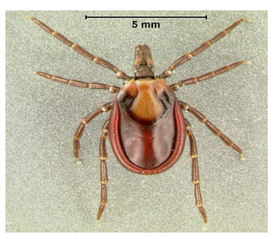


The Problem: Too many disease vectors, but not enough vector control tools.
The Solution: Public funding for the development and registration of public health and other minor use pesticides.

Thesis: The significant challenges facing developers of new or repurposed public health pesticides are not unique, but commonly confront those that develop or register minor use agricultural chemicals.

Thus, while the development process for vaccines and therapeutic pharmaceuticals can provide public health pesticide advocates with important lessons (e.g. regarding finance or protection of intellectual property), in other realms, such as environmental risk assessment and regulatory data collection, the most relevant examples may come from innovation in minor use agricultural pesticides.

The IR-4 Project has supported development and registration of improved minor use agri-chemicals with public funds for almost 50 years in the U.S. and globally, and has recently begun to support the development and registration of public health pesticides. We expect that lessons learned on other minor use pesticides can help accelerate the introduction of new tools for vector control.

The Global Challenge of Public Health Pests.

Mosquitoes, sand flies, ticks, and other vectors of pathogenic infectious disease are examples of public health pests – insects, other arthropods, or other animals that can make people sick – and they pose challenges in all parts of the world.

Malaria is the big killer globally, but many other vector-borne pathogenic diseases can be regionally or locally significant causes of morbidity and mortality (e.g. dengue, West Nile virus, Lyme disease), and global trade and travel means that outbreaks are possible in many areas that have not had active transmission in years.

In addition to illness due to pathogenic microorganisms transmission, public health pests cause disease through allergic reactions or secondary infections after scratching breaks the skin. Even when pathogens are not transmitted, the nuisance of bites from public health pests can significantly impact the quality of life.

The disease burden from public health pests is immense, with billions of humans at risk and millions sickened each year by vector-borne diseases. In addition, the zoonotic disease burden is huge, with extensive mortality and morbidity in both domestic and wild animals. Unfortunately, vaccines and medicines have been insufficient against vector borne diseases, and vector control remains a critical public health intervention.

Public Health Pesticides (PHP's).

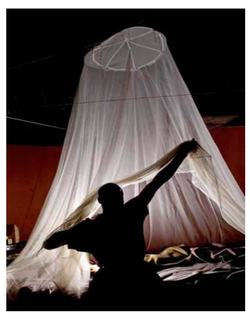
Public Health Pesticides are some of the primary tools used to control public health pests, together with screens and other exclusion devices, habitat management practices to reduce their abundance, and bio-control through support for predators or parasites of the pest species.

There are several possible definitions of PHP's, but a useful approach places all chemicals, both natural and synthetic, that help control or manage public health pests, under this term. With this definition, PHP's including toxicants (active vs. both juveniles and adults), insect growth regulators, repellents or attraction inhibitors or biting inhibitors which reduce disease transmission without reducing pest populations, attractants which can entice pests into traps, and other semiochemicals that influence pest behavior, such as insect sex pheromones.

The Global Challenge of Public Health Pesticides.

For virtually all vector-borne diseases, the toolbox of public health pesticides is insufficient, and in many cases the shortage of tools is critical. Effective, affordable, and environmentally benign PHP's are essential, but are increasingly rare as resistance spreads and the demands for protection of the environment become more stringent.

All commercial bed nets use a single class of PHP's – pyrethroids – to which resistance is common and spreading. IRS relies on only four classes of chemicals, all of which face resistance issues. Sand fly vectors of leishmaniasis and tick vectors of Lyme Disease have few demonstrably effective control measures. Even public health pests like bed bugs which are not known to transmit pathogenic disease have become a major problem in the U.S. and elsewhere, largely because effective interventions are lacking.



PHP Discovery Efforts.

The last decade has seen a renewed interest in PHP's and their availability, largely because of the continuing high morbidity and mortality associated with malaria. A renewed commitment to combating malaria and the insects that transmit it has been reflected in the global Millennium Development Goals, the U.S. President's Malaria Initiative, the formation of numerous aid and advocacy groups, and the funding priorities of the Gates Foundation and other philanthropists. While most of these efforts have focused on distribution of insecticide-treated nets and other interventions, important PHP research and development has also occurred, much of it sponsored by the Gates Foundation through the IVCC (Innovative Vector Control Consortium) in Liverpool, or the U.S. National Institutes of Health, and some of it addresses diseases beyond malaria.

The Challenge of Developing PHP's and other Minor Use Pesticides.

Over the last few decades, the PHP market has faced similar challenges facing other minor-use pesticide markets —high costs relative to small markets often means there is insufficient financial incentive for private industry to invest heavily in research, development, and regulatory approvals.

In particular, regulatory requirements and the associated costs are high, increasing, and increasingly inconsistent between jurisdictions. In addition, concerns about liability and litigation can dissuade commercial product development.

Only large, for-profit entities typically have the resources to discover, develop, and register new pesticide types. If the margin between cost and potential market is slim, private developers of small market pesticides may strongly emphasize products for larger markets, the protection of intellectual property (i.e. shelving promising but unprofitable materials), and/or the promotion of new materials with exclusive sales rights.

Minor Use Pesticide Regulatory Approvals.

Once a new pesticide compound or product has been discovered and its efficacy demonstrated, the next steps in converting this into a usable product include formulation and other development steps, and pesticide registration with government regulators. Pesticide registration is always important, but for PHP's it is especially critical as these products are generally used in public areas or homes and are frequently paid for with public funds. Demonstrating the human and environmental safety of PHP's is as important as proving that they work.

However, while ensuring pesticide safety and public confidence is essential, high regulatory costs can stifle innovation or drive products from the market even when there is little or no evidence that they pose significant risks. Finding the right strategy to encourage availability of affordable products, innovation, and protection of health and the environment has been challenging in all small pesticide markets.

Public Support for Development of Minor Use Pesticides: The IR-4 Project and the IR-4 Public Health Pesticide Program.

Since 1963, the IR-4 Project, a partnership between the U.S. Department of Agriculture and the state Land Grant universities, has been the primary resource in the United States for using public funding to facilitate registration of conventional pesticides and biopesticides on specialty food crops and non-food ornamental horticulture crops, where the market is insufficient to rely on private R&D.

Initiated in 2008, the IR-4 Public Health Pesticide Program expands the mission of IR-4 to include the facilitation of the development and registration of new public health pesticides to protect the public from insects and other arthropods that transmit human diseases. Major partners include the USDA Agricultural Research Service and the U.S. Department of Defense's Deployed War-fighter Protection Program.

Lessons Learned from Minor Use Pesticides:

The product development pipeline can be expanded through partnerships; and effective pesticide development partnerships include consumers/users, regulators, universities, chemical developers, and, frequently, other public entities to help coordinate the process.

Public funding is critical when markets are insufficient to support research, development, and registration of minor-use pesticides. In particular, public funding is often needed for regulatory data collection, especially for data that cannot be amortized on large market agricultural crops.

Intellectual property and return on investment matter, but tools exist to provide incentives to commercial developers of minor-use pesticides.

Environmental stewardship and sustainability, not only efficacy, must be key goals.

Data can and should be collected to maximize regulatory approvals (e.g. index pests, regionalized efficacy evaluations).

Good lab practices are critical for building trust in privately generated data.

Transparency and predictability in regulatory processes can be more important that strict consistency.

Global regulatory harmonization works.

Global minor use summits work.

Good product stewardship can reduce resistance development (i.e. development of pesticides specifically for public health may not be necessary).