A New Classification System for the Actions of IRS Chemicals Traditionally Used For Malaria Control

John P. Grieco[1]*, Nicole L. Achee[1], Theeraphap Chareonviriyaphap[2], Wannapa Suwonkerd[3], Kamal Chauhan[4], Michael R. Sardelis[1], Donald R. Roberts[1]

1 Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, Bethesda, Maryland, United States of America, 2 Department of Entomology, Kasetsart University, Bangkok, Thailand, 3 Office of Disease Prevention and Control, Ministry of Public Health, Chiang Mai, Thailand, 4 Chemicals Affecting Insect Behavior Laboratory, United States Department of Agriculture, Beltsville, Maryland, United States of America

Knowledge of how mosquitoes respond to insecticides is of paramount importance in understanding how an insecticide functions to prevent disease transmission. A suite of laboratory assays was used to quantitatively characterize mosquito responses to toxic, contact irritant, and non-contact spatial repellent actions of standard insecticides. Highly replicated tests of these compounds over a range of concentrations proved that all were toxic, some were contact irritants, and even fewer were non-contact repellents. Of many chemicals tested, three were selected for testing in experimental huts to confirm that chemical actions documented in laboratory tests are also expressed in the field. The laboratory tests showed the primary action of DDT is repellent, alphacypermethrin is irritant, and dieldrin is only toxic. These tests were followed with hut studies in Thailand against marked-released populations. DDT exhibited a highly protective level of repellency that kept mosquitoes outside of huts. Alphacypermethrin did not keep mosquitoes out, but its strong irritant action caused them to prematurely exit the treated house. Dieldrin was highly toxic but showed no irritant or repellent action. Based on the combination of laboratory and confirmatory field data, we propose a new paradigm for classifying chemicals used for vector control according to how the chemicals actually function to prevent disease transmission inside houses. The new classification scheme will characterize chemicals on the basis of spatial repellent, contact irritant and toxic actions.

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INTRODUCTION

Science and society label almost any chemical used against insects as an "insecticide." By definition, an insecticide (insect-icide or insect-icidal) is a chemical that kills insects. This single term is not adequate for meaningful discourse about chemicals, chemical actions, insect responses to chemicals, and the different ways in which chemicals are used. However, this single response is the foundation for the old paradigm that classifies chemicals sprayed on house walls for malaria control based solely on their killing action. A new paradigm is needed to take into account the behavioral actions of these chemicals in disrupting man-vector contact and thereby breaking disease transmission. The fact that repellent and irritant actions were first documented more than 60 years ago [1] but given no importance, illustrates how lack of appropriate labels and a conceptual framework of multiple chemical actions can work against knowledge and understanding. Today, any discussions about insecticides for malaria control operate under a de facto assumption that the chemical is toxic and it's only important function is to kill mosquitoes. As will be shown by research presented here, this assumption is wrong.

Over 45 years ago Dethier [2] showed that chemicals elicit multiple actions and that insects respond to those actions through a variety of behaviors. He noted that if we were to take a closer look at modes of action, we could find a much more diverse set of terms for oriented movements of insects toward or away from a chemical source. As early as 1953, Muirhead-Thomson [3] concluded chemicals could disrupt contact between humans and malaria-transmitting mosquitoes and stop disease transmission without killing the mosquitoes. Subsequent authors speculated that space repellents applied to house walls could have advantages over topical repellents on skin. In contrast to topical repellents, repellents designed for application on walls could be formulated for longer persistence and might even have a lower cost of production. Regardless, the search for alternative compounds has focused almost entirely on toxicity. Evidence that this search has not emphasized DDT's true mode of action is revealed by the fact that even now there are no labeled compounds for IRS use that elicit a spatial repellent response. Insecticides recommended for indoor residual spraying (IRS) continue to be evaluated almost entirely on mosquito mortality [4] and laboratory evaluations continue to use toxicity as the primary measure of success [5–7].

The overall aim of this research was to quantify and accurately describe chemical actions and mosquito responses to those actions using *Aedes aegypti* mosquitoes as a model system. Although *Ae. aegypti* does not transmit malaria, it is responsible for transmitting dengue and yellow fever viruses in urban environments. This species was selected as our model system because of its medical importance and because eggs can be stored dry and used when needed for producing test populations. Additionally, new colonies are easily established by bringing wild caught material from the field.

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*** To whom correspondence should be addressed.** E-mail: jgrieco@usuhs.mil