The Efficacy of ACTELLIC 50 EC, Pirimiphos Methyl, for Indoor Residual Spraying in Ahafo, Ghana: Area of High Vector Resistance to Pyrethroids and Organochlorines

GODWIN FUSEINI,1,2 PETER EBSWORTH,1 STEPHANIE JONES,1 AND DAVE KNIGHT3


ABSTRACT Insecticide resistance in the main malaria vectors in Africa is a major concern for malaria vector control program managers. The most common insecticides used for indoor residual spraying (IRS) and treating bed nets are becoming increasingly ineffective. The quest for safer and more effective insecticides for malaria vector control is urgent. This study sought to evaluate the efficacy of ACTELLIC 50 EC (pirimiphos methyl), an organophosphate, for IRS in Ghana, where there is high vector resistance to pyrethroids and organochlorines. Before the commencement of the study, standard World Health Organization (WHO) vector susceptibility tests against a common malaria vector, *Anopheles gambiae s.l.*, were conducted using preparations of pyrethroids, organochlorines, carbamates, and organophosphates. The vector was found to be resistant to the pyrethroids, the organochlorines, and the carbamates, but susceptible to the organophosphates. The emulsifiable organophosphate concentrate formulation, ACTELLIC 50 EC, was then evaluated to determine the efficacy and the length of its residual effect. The wall bioassay test, using recommended cones from WHO, was conducted on sprayed surfaces with ACTELLIC 50 EC from 27 July 2009 to 16 October 2009. After 15 wk of trials on painted cement surface, it was found out that the main malaria vector, *An. gambiae s.l.*, was susceptible to the insecticide even though the WHO Pesticide Evaluation recommends 2- to 3-mo duration of effective action. Therefore, it is recommended for use in IRS programs in this part of Ghana, where there is high vector resistance to most of the insecticides.

KEY WORDS insecticide resistance, ACTELLIC 50 EC, indoor residual spraying, malaria control, Ahafo Ghana

Malaria control in most African countries is given high priority at both national and international levels. The disease is not only a major public health problem, but an issue that severely restrains the economic growth of Sub-Sahara Africa (The Abuja Declaration on Roll Back Malaria in Africa 2000). Vector control, good case management, education, and communication are the main tools used to fight the disease. Vector control programs rely mostly on the use of insecticides that are applied as indoor residual deposits or used to treat mosquito nets or curtains. However, vector resistance to many of the insecticides is a growing problem. Vector resistance to pyrethroids and DDT has been reported across the continent (Chandre et al. 1999, Hargreaves et al. 2000, Mohloai 2006). In Ghana, it has been reported that the main malaria vectors, *Anoph eles gambiae s.l* and *Anopheles funestus*, are resistant to DDT, pyrethroids, and carbamates (Coetzee et al. 2005). Thus, the search for alternative effective insecticides becomes increasingly urgent.

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### Materials and Methods

#### Study Area.
The study was conducted in Kenyasi in the Asutifi district of the Brong Ahafo region, Ghana. The district has a population of 97,977 and land surface area of 1,500 square kilometers. Farming is the major economic activity. Cash crops, such as cocoa, oil palm, coffee, plantain, cassava, and maize, are produced. The use of pesticides on these high-value crops has been reported to be on the increase across the country (Gerken et al. 2001). Malaria is the commonest disease reported at health facilities, representing between 30 and 40% of outpatient attendance (Ghana Health Service 2006). NGGL has a gold mining site in the district and runs an integrated malaria control program in its operational area.

#### Vector Susceptibility Test.
Standard World Health Organization (WHO) susceptibility tests were conducted (WHO 1998). The insecticide-impregnated papers were obtained from University Sains Malaysia (Penang, Malaysia). The procedures and conditions for procuring the items were followed according to the specifications. All the treated papers were checked for efficacy by exposing known susceptible colonies to them at the National Institute for Communicable Diseases, South Africa. The survey was conducted during the rainy season in June 2008. Blood-fed *An. gambiae s.l* (Gillies and de Meillon 1968) were collected from rooms using torches and aspirators. Samples of the wild females were exposed to 0.05% deltamethrin, 5% malathion, 4% DDT, 0.1% bendiocarb, and 4% dieldrin in the field, whereas subsamples were taken to the National Institute for Communicable Diseases, South Africa, and exposed to 0.05% lambda-cyhalothrin, 0.75% permethrin, and 1% fenitrothion.

#### IRS Application.
Nineteen liters of ACTELLIC 50 EC were sent to Ahafo (ACTELLIC 50 EC, Syngenta) for the trial. The recommended dilution rate for residual application for the control of mosquitoes is 1–2 g of active ingredient per meter square of spray surface. Thus, 50–100 ml of ACTELIC 50 EC is needed in 1 liter of spray. The 15-liter-capacity H. D. Hudson Manufacturing Company (Chicago, IL) 67422 AD, Hudson X-pert spray pumps, recommended by the WHO for use in IRS, was used. One liter (1000 ml) of ACTELLIC 50 EC was mixed in 10 liters of clean water in the spray can and pressurized to 55 Psi (Syngenta 2005). The application rate was 1 m in 2.2 or 4.5 s for 2 m height of wall (WHO 2007). The spray operators were trained at the AngloGold Ashanti Malaria Training Centre at Obuasi, and all are certified operators.

#### Bioassay Test.
The residual activity of ACTELLIC 50 EC on the sprayed surface was monitored for a period of 15 wk using the cone bioassay (WHO 2006a). Adult *An. gambiae s.l* were collected from villages close to the mine site at intervals of 2 wk. Three replicates of the WHO cones were adhered to the top, middle, and bottom of the surface sprayed with ACTELLIC 50 EC. A control cone was adhered to a sheet of un-sprayed cardboard and placed close to the experimental site. Fifteen to 20 blood-fed mosquitoes were aspirated, placed in each cone, and observed 60 min. After the 60 min, the anophelines, dead or alive, were aspirated and put back in the paper cups with 10% sugar solution, to observe for 24-h delayed mortality. The percentage mortality was calculated, and the mosquitoes were identified morphologically to species level (Gillies and de Meillon 1968).

#### Consent.
Verbal consent was sought from the residents before entry into their rooms for the collection of the mosquitoes. In rooms without a bed net, one long lasting insecticide treated net (PermaNet 2.0, Vestergaard Frandsen, Geneva, Switzerland) was given to the occupant of the room.

### Results

#### Vector Susceptibility Test.
The vector susceptibility tests conducted in 2008 found that the main malaria vector in the region is highly resistant to pyrethroids, organochlorines, and carbamates. The organophosphate class of insecticides remains effective against the vector, although there is the possibility of resistance to fenitrothion that needs to be monitored. All the insecticides belonging to the pyrethroids recorded <50% mortality, and the organochlorines <20% mortality, whereas those in the organophosphate class recorded >95% mortality. There was 100% survival to DDT and 100% mortality to malathion. Table 1 summarizes the exposure time mortality of *An. gambiae s.l* with impregnated WHO test kits.

#### Bioassay Test.
ACTELLIC 50 EC was tested on painted concrete-rendered surfaces. A total of 754 wild caught female *An. gambiae s.l* was exposed on the painted surface during the 4-mo period. The bioassay test was conducted every 2 wk for 15 wk from 27 June 2009 to 16 October 2009. From weeks 1 to 13, the percentage mortalities after 24 h of observation were

### Table 1. Standard WHO susceptibility test with Anopheles gambiae s.l on treated papers

<table>
<thead>
<tr>
<th>Insecticide (concentration)</th>
<th>Class</th>
<th>Mortality (%) at 24 h post exposure</th>
<th>Sensitivity status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deltamethrin (0.05%)</td>
<td>Pyrethroids</td>
<td>41</td>
<td>Resistant</td>
</tr>
<tr>
<td>Lambda-cyhalothrin (0.05%)</td>
<td>Pyrethroid</td>
<td>19</td>
<td>Resistant</td>
</tr>
<tr>
<td>Permethrin (0.75%)</td>
<td>Pyrethroid</td>
<td>15</td>
<td>Resistant</td>
</tr>
<tr>
<td>Bendiocarb (0.1%)</td>
<td>Carbamate</td>
<td>75</td>
<td>Resistant</td>
</tr>
<tr>
<td>Dieldrin (4%)</td>
<td>Organochlorine</td>
<td>12</td>
<td>Resistant</td>
</tr>
<tr>
<td>DDT (4%)</td>
<td>Organochlorine</td>
<td>0</td>
<td>Highly resistant</td>
</tr>
<tr>
<td>Fenitrothion (1%)</td>
<td>Organophosphate</td>
<td>96</td>
<td>Possible resistant</td>
</tr>
<tr>
<td>Malathion (5%)</td>
<td>Organophosphate</td>
<td>100</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

**Postexposure Sensitivity status**

- 95% mortality
- 0% mortality
- 100% survival
- 100% mortality
- <50% mortality
- <20% mortality
- >95% mortality

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Fig. 1. Exposure time mortality bioassay of An. gambiae s.l with ACTELLIC 50 EC.

100%. However, at week 15, the percentage mortality was 95%. The summary results of the exposure time mortality bioassay with ACTELLIC 50 EC are shown in Fig. 1.

Discussion

The susceptibility test results reveal the main malaria vector in the Brong Ahafo region, Anopheles gambiae s.l, is highly resistant to pyrethroid and organochlorine classes of insecticide. Widespread resistance in Anopheles gambiae to pyrethroids and DDT associated with the kdr mechanism have been reported across the African continent (Chandre et al. 1999, Hargreaves et al. 2000, Coetzee et al. 2005, Mohloai 2006, WHO 2006b). Unfortunately, the only group of insecticides recommended by the WHOPES for treating nets is pyrethroids, with deltamethrin and permethrin being the most widely used in this regard. This has the potential to hinder the impact of insecticide-treated nets for malaria control, which has become the main method of malaria prevention in most endemic countries in Africa (WHO 2002). The need for pyrethroid alternatives for long lasting insecticide treated nets (LLITN) programs is required. Vestergaard Frandsen has introduced a new generation LLITN, PermaNet 3.0. This is a combination of two chemicals, deltamethrin and a synergist, for improved bioefficacy. Large-scale field evaluation of the product is necessary to inform policy change.

With the support of the WHO Global Fund to fight AIDS, Tuberculosis, and Malaria and with the United States President Initiative on Malaria, African countries are embracing the use of IRS to complement LLITN in vector control programs. The key factors in the choice of an insecticide for IRS are the susceptibility of the main malaria vectors to the insecticide and the safety of the chemical. Overreliance on one class of insecticides, the organochlorines, used in the 1950s malaria eradication era, contributed significantly to the development of vector resistance (Farley 1994). Insecticides belonging to the carbamate and organophosphate classes are sought for IRS programs in Africa. These groups of insecticides are also heavily used with minimal regulation, in the agricultural sector (Gerken et al. 2001, Obeng-Ofori et al. 2002), thereby increasing the potential for resistance among malaria vectors. This may constitute a major threat to the use of insecticidal controls for malaria vectors and probably the cause of the resistance profile seen locally.

In the Brong Ahafo region of Ghana, the principal malaria vector remains susceptible to the organophosphate class of insecticides. For IRS in this class, WHOPES (2009) recommends malathion (wettable powder), fenithrothion (wettable powder), and pirimiphos methyl (wettable powder and emulsifiable concentrate). In the susceptibility test, the percentage mortality for fenithrothion was 96%, suggesting possible resistance. Further testing is needed to confirm the sensitivity of the malaria vector to fenithrothion. Wettable powder formulations of malathion for IRS are not readily available, and the odor generated by this formulation is widely disliked. Currently, malathion is not registered with the Environmental Protection Agency of Ghana, and its importation is restricted. It was therefore appropriate to conduct the wall bioassay trial with pirimiphos methyl, which is registered for use in Ghana, and which has both wettable powder and emulsifiable concentrate formulations. ACTELLIC 50 EC used for this evaluation showed high levels of vector susceptibility for period of ~4 mo, exceeding the effective minimum duration action of 2–3 mo recommended by WHOPES. A similar trial conducted in Mozambique (Casimiro and Goncalves, unpublished data) demonstrated the effectiveness of ACTELLIC 50 EC for the control of Anopheles arabiensis for at least 5 mo on a variety of surfaces. It is therefore recommended for use in IRS in Ghana and may be rotated with carbamate as a strategy for managing vector resistance. It is also recommended that malaria vector control initiatives in the country should assess the resistance status of the malaria vector mosquitoes before deciding on the control strategy. Other interventions, such as the use of Bacillus thuringiensis variety israelensis, environmental management, and house screening, have been successfully and effectively integrated into the NGGL control program in addition to the use of IRS and LLITNs, along with case management. This range of interventions should also be considered in addition to IRS and LLITN programs.

Limitations of Study. There was a lack of insectary to raise known age vectors for exposure; thus, only blood-fed anophelines were used. There was limited diversity of surfaces used for the trial. Large numbers of An. funestus, second most abundant vector in this region, could not be obtained for exposures. An. gambiae s.l was therefore the only species used.

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