SUMITOMO CHEMICAL

SumiShield™ 50WG

A Breakthrough for Resistance Management

SumiShield® 50WG is an Indoor Residual Spray (IRS) containing a new mode of action active ingredient. SumiShield 50WG provides excellent control of malaria transmitting mosquitoes and is especially valuable when used in insecticide resistance management strategies.

Contents
Clothianidin 50.0% w/w
Water Dispersible
Granule (WG)

Table of Contents

Breakthrough: There has been no new mode of action IRS product in over 30 years.

Introduction and Background

There is a long history of using Indoor Residual Spraying (IRS) for malaria control and it has proved very effective in many countries; however the usefulness of IRS is under threat due to increasing resistance to all 4 classes of insecticides and the many products containing them. There has long been a need for a new mode of action (MoA) product and nothing has been introduced for more than 30 years resulting in the continued use of old active ingredients like DDT which presents many risks to the environment. Insecticide resistance is increasing in many parts of the world so there is a great need for an insecticide with a new MoA and one that can be used in resistance management and rotational programmes.

Sumitomo Chemical researched its portfolio of active ingredients and identified the neonicotinoid clothianidin as an insecticide with good potential for use in IRS against malaria vectors. Laboratory and field trials have shown great promise resulting in Sumitomo submitting SumiShield 50WG to the Pre-Qualification system (previously WHOPES*) for evaluation and recommendation.

* World Health Pesticide Evaluation Scheme

Because of increased resistance to existing insecticides there is a great need for an insecticide with a new mode of action. SumiShield 50WG addresses this need.

Product Concept

Sumitomo Chemical has developed a new mode of action Indoor Residual Spraying (IRS) that is effective against many mosquitoes that have already developed resistance to one or all of the major classes of insecticides currently available for IRS.

Key Features & Benefits

- New mode of action chemistry for Indoor Residual Spraying (IRS).
- A breakthrough for resistance management programmes.
- Contains single mode of action chemistry allowing flexibility to use in IRS rotational strategies, or in combination with pyrethroid nets.
- Up to 8 months activity under field conditions.
- Non-repellant formulation compared with pyrethroid and DDT based IRS products.
- Pre-qualified by the World Health Organization (previously WHOPES).
- Additional kill effect over time.
- Low mammalian toxicity.
- Low odour.
- Readily dilutes in water.
- Easy to handle sachets.
- Easy to transport — one sachet per tank, 60 sachets per carton.

SumiShield 50WG is odourless, has low toxicity, readily dilutes in water, and is easy to transport. New mode of action makes it a breakthrough for resistance management programmes.

Insecticide resistance in malaria vectors is one of the major issues concerning stakeholders today.

SumiShield 50WG meets the changing needs of today's IRS programs.

Directions for Use

SumiShield 50WG has been developed for Indoor Residual Spraying (IRS) and can be sprayed on the inside of houses and residences on walls and other surfaces that serve as resting places for mosquitoes.

Mixing instructions

- Fill sprayer with half the required volume of clean or filtered water. The amount of water will depend on whether the sprayer is fitted with a pressure regulating device set at 1.5 bar (red CFV).
- Tear or cut open end of sachet and put entire contents directly into spray tank.
- Top up sprayer with the required volume of clean or filtered water.
- Close sprayer, pressurize and mix by inverting spray tank several times before spraying.

Application rates and method

The target dose of SumiShield 50WG is 300 mg ai/m². The product must be applied with a sprayer that meets WHO specifications and should be fitted with a No. 8002E nozzle. It is recommended that sprayers fitted with a red CFV are used, however instructions below also cover those without. The spray tip should be kept 45 cm from the surface being sprayed to give a swath width of 70 cm. An area of 19 m² should be covered in one minute. It is recommended that sprayers are calibrated before use to ensure they are delivering the correct flow rate.

This is conducted as follows:

Sprayers with 1.5 bar CFV
Fill sprayer with 7.5L water. Pressurise to 4 bar (58psi). Spray into a measuring cylinder for exactly 1 minute. This should deliver 550-570ml.

Sprayers without 1.5 bar CFV
Fill sprayer with 10L water. Pressurize to 4 bar (58psi). Spray into a measuring cylinder for exactly 1 minute. This should deliver 760 -790ml.

Applying product using a sprayer fitted with a red CFV
Dilute one 150 g sachet of SumiShield 50WG in 7.5 litres of water and apply to 250 m² wall surface. Pressurize sprayer to 4 bar (58 psi). During spraying the valve will cut off spray if the pressure drops below 1.5 bar, if this happens re-pressurize sprayer.

Applying product using a sprayer without red CFV fitted
Dilute one 150 g sachet of SumiShield 50WG in 10 litres of water and apply to 250 m² wall surface. Pressurize sprayer to 4 bar (58psi). During spraying do not let pressure drop below 1.6 bar (25 psi).

For additional information on application methods see WHO – Indoor Residual Spraying Manual (second edition) 2015.

Easily transported and mixed — one 150g sachet per sprayer.

Handling

Use only in well ventilated areas. Wash hands thoroughly with soap and water after handling and before eating, drinking, smoking.

Storage Recommendations

- Keep out of reach of children.
- Keep away from food, drink and animal feeding stuffs.
- Store only in original sachets in a safe place at temperatures not exceeding 35C.
- Diluted insecticide should never be kept, even overnight; a fresh dilution should be prepared as necessary.

Consumer Acceptance

During village scale trials in Cote d`Ivoire a survey was conducted of householder experiences of Pirimiphos-methyl 300CS compared to SumiShield 50WG. There was virtually no odour detected after SumiShield applications which resulted in people more readily accepting this product being sprayed in their homes. However there was a significant dislike of the odour of Pirimiphos-methyl after spraying homes which could result in refusals. (See Fig A.)

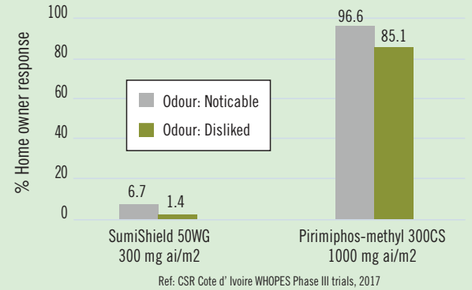
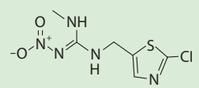


Figure A: Cote d'Ivoire — Homeowner preference survey of SumiShield 50WG and Pirimiphos-methyl 300CS

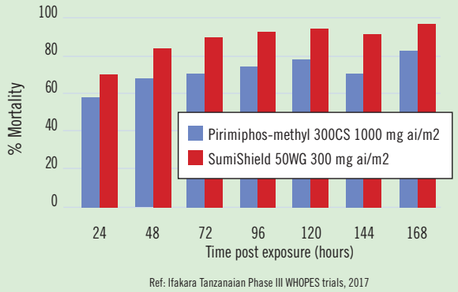
Technical specifications

Active Ingredient: Clothianidin	50.0% (w/w)
Other Ingredients:	50.0%
Total	100.0%



Nitroguanidine (neonicotinoid) IRAC
MoA Group 4A Neonicotinoids
IUPAC: (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine

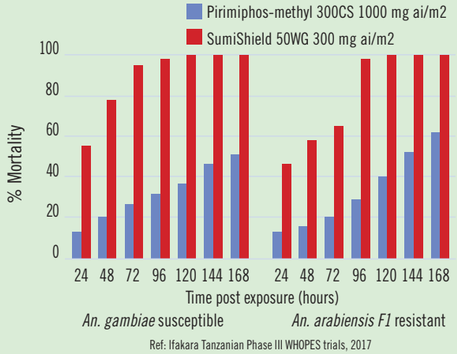
Biological efficacy



Ref: Ifakara Tanzanaian Phase III WHOPES trials, 2017

Figure 1: Tanzania — Comparative efficacy in WHO cone bioassays vs. *Anopheles gambiae* (Each data point represents total combined mortality averaged over 8 months).

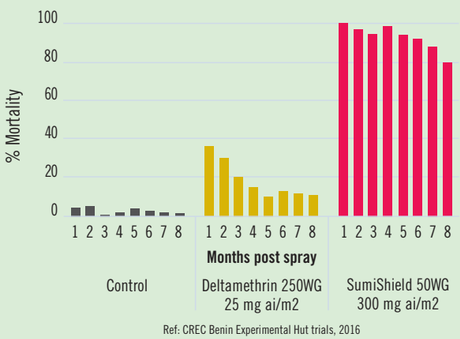
In WHOPES Phase III trials conducted in Tanzania the efficacy of SumiShield 50WG was compared to Pirimiphos-methyl 300CS in houses using the WHO cone tests. Mortality counts at different times post-exposure were combined and averaged. Fig 1. shows the data 8 months post-spray which demonstrates that SumiShield 50WG out- performed Pirimiphos-methyl 300CS and gave good mortality even at 8 months post-treatment



Ref: Ifakara Tanzanian Phase III WHOPES trials, 2017

Figure 2: Tanzania — Efficacy of Pirimiphos-methyl 300CS and SumiShield 50WG in WHO cone tests on mud baked bricks 8 months after spraying.

In WHOPES Phase IIIh trials the residual performance of SumiShield 50WG in Tanzania on mud baked bricks was compared to Pirimiphos-methyl 300CS using the WHO cone test. Fig. 2 shows the mosquito mortality at 8 months post-spray over time against both susceptible *An. gambiae* and resistant *An. arabiensis* strains. SumiShield 50WG significantly out-performed Pirimiphos methyl 300CS against both mosquito strains.



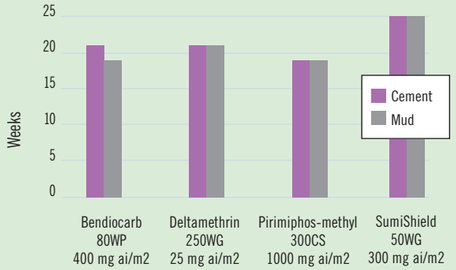
Ref: CREC Benin Experimental Hut trials, 2016

Figure 3: Benin — Mortality of free flying wild pyrethroid resistant *An. gambiae* in experimental huts

3. Trials were conducted in Benin by CREC who evaluated SumiShield 50WG vs. Deltamethrin 250WG in experimental huts against free flying wild *An.gambiae* which were pyrethroid resistant. Mortality at 120 hours post exposure was recorded every month up to 8 months. Fig. 3 shows that SumiShield 50WG significantly out-performed the deltamethrin based product and still gave 81% mortality at 8 months compared to 11% mortality for deltamethrin. In this example there was no cross resistance to pyrethroids.

Figure 4: India — Residual efficacy in weeks that >80% mortality was achieved in WHO cone bioassays vs. lab strain *An. culicifacies*

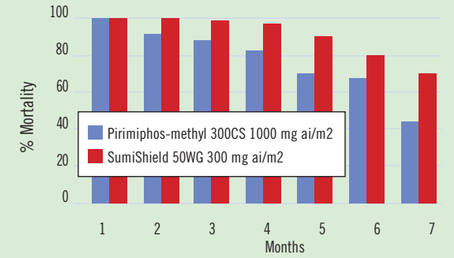
Phase II WHOPES trials were conducted by NIMR in India. Fig. 4 shows the number of weeks that four IRS products managed to achieve 80% mortality of *An. culicifacies* on two surfaces (cement & mud). SumiShield 50WG was superior to all three other commonly used IRS products and gave at least 80% kill for at least 25 weeks.



Ref: NIMR India Phase II WHOPES trials, 2017

Figure 5: Residual activity of SumiShield 50WG and Pirimiphos-methyl 300CS in WHO cone bioassays against *An. culicifacies*

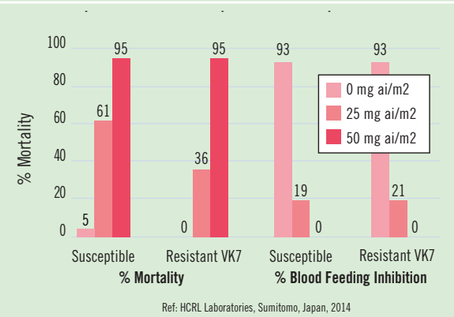
NIMR, India also conducted WHOPES Phase III trials. Fig 5 shows a comparison of SumiShield 50WG vs. Pirimiphos-methyl 300CS in the field using WHO cone bioassays against *An. culicifacies*. SumiShield 50WG again delivered better results than Pirimiphos methyl 300CS and was effective up to 6-7 months post-spray.



Ref: NIMR India Phase II WHOPES trials, 2017

Figure 6: Effect of low doses of SumiShield 50WG on mortality and blood feeding inhibition of *An. gambiae* 24 hours after exposure to sublethal deposits on cement plates

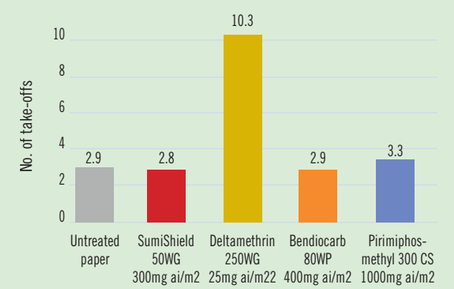
The question is often asked `If mosquitoes take a bit longer to die will they still take a blood meal ?` or `As the insecticide dose drops below target application rate will mosquitoes be able to take a blood meal ?` Fig. 6 shows that in trials conducted at HCRL labs in Japan using SumiShield 50WG even at 50 mg a.i./m^2 (1/6th of the target dose) blood feeding was totally inhibited and nearly all those mosquitoes subsequently died. This effect was very similar whether the mosquitoes were insecticide resistant or not. Even at 25 mg a.i./m^2 most blood feeding is inhibited.



Ref: HCRL Laboratories, Sumitomo, Japan, 2014

Figure 7: Contact irritancy of insecticide deposits. Number of take-offs in three minutes (susceptible *An. gambiae*)

One of the most important attributes for any IRS product is non-irritancy (repellency) so that mosquitoes will unknowingly rest on a treated surface as long as possible and so pick up a lethal dose. Some insecticides such as deltamethrin have a high contact repellency which is not ideal for an IRS. Therefore Sumitomo decided to develop SumiShield 50WG as a single active product since clothianidin is non-repellent. This is clearly shown in contact irritancy tests (Fig. 7). Mosquitoes were exposed to standard doses of four products and the number of flight take offs recorded over 3 minutes. The results show SumiShield 50WG to have a very low contact irritancy to mosquitoes and deltamethrin the highest.



Mammalian Toxicity

*87% of countries failed to rotate the class of insecticides used last year.**

Mammalian Toxicity

Acute oral LD50: LD50 is 3900mg/kg body weight (bw) for male rats and 4700mg/kg bw for female rats.
Skin and eye: Slight (barely perceptible) transient skin irritation and an eye irritant for rabbits.
Inhalation LC50 (4h): for male and female rats >2.3mg/L
Other: Not mutagenic. Not oncogenic in rats and mice. Not teratogenic in rats and rabbits.

Clothianidin is moderately toxic through oral exposure, but toxicity is low through skin contact or inhalation. Since contact of householders will be via treated walls the product should not cause any significant risk. While clothianidin may cause moderate eye irritation, it is not a skin sensitizer. Clothianidin does not damage genetic material nor is there evidence that it causes cancer in rats or mice; it is unlikely to be a human carcinogen.

Aquatic life

United States EPA assessment report (2003) states that clothianidin should not present a direct acute or chronic risk to freshwater and estuarine/marine fish, or a risk to terrestrial or aquatic vascular and nonvascular plants. Consistent with the majority of pesticide products clothianidin is considered to be toxic to aquatic invertebrates if disposal of wastes according to disposal instructions are not followed.

Clothianidin is practically non-toxic to selected test bird species that were fed relatively large doses of the chemical.

Birds

According to the EPA, clothianidin is practically non-toxic to selected test bird species that were fed relatively large doses of the chemical on an acute basis.

* UNITAID Malaria Landscape Report 2014

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"SumiShield 50WG is very special. It is the first example of a brand-new mode of action product for IRS. And more than that, the product has an excellent performance profile — it lasts a long time, throughout the main malaria transmission season."
–Dr. Sarah Rees, IVCC Portfolio Manager