

# REPORT OF THE TENTH **WHOPES** WORKING GROUP MEETING

**WHO/HQ, GENEVA**  
**11—14 DECEMBER 2006**

**Review of:**  
**SPINOSAD 0.5% GR AND 12% SC**  
**LAMBDA-CYHALOTHRIN 10% CS**  
**K-O TAB 1-2-3®**  
**INTERCEPTOR®**



**World Health  
Organization**

Control of Neglected Tropical Diseases  
WHO Pesticide Evaluation Scheme

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**CONTROL OF NEGLECTED TROPICAL DISEASES  
WHO PESTICIDE EVALUATION SCHEME**

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## 1. INTRODUCTION

The tenth meeting of the WHOPES Working Group, an advisory group to the WHO Pesticide Evaluation Scheme (WHOPES), was convened at WHO headquarters in Geneva, Switzerland, from 11 to 14 December 2006. The objective of the meeting was to review the reports of testing and evaluation of the following four products: (i) spinosad 0.5% GR (granule) and 12% SC (suspension concentrate) of Dow AgroSciences, France, for mosquito larviciding; (ii) lambda-cyhalothrin 10% CS (slow-release capsule suspension) of Syngenta, Switzerland, for indoor residual spraying against malaria vectors; (iii) K-O TAB 1-2-3<sup>®</sup> (an insecticide treatment kit) of Bayer Environmental Science, France, for treatment of mosquito nets for malaria prevention and control; and (iv) Interceptor<sup>®</sup>, alpha-cypermethrin long-lasting (coated) insecticidal mosquito net of BASF, Germany, for malaria prevention and control.

The meeting was attended by 11 scientists (see Annex 1: List of participants). Dr Mir S. Mulla was appointed as Chairman and Dr Purushothaman Jambulingam as Rapporteur. The meeting was convened in plenary and group sessions, in which the reports of the WHOPES supervised trials and relevant published literature and unpublished reports were reviewed and discussed (see Annex 2: References). Recommendations on the use of the above-mentioned products were made.

The meeting also reviewed the results of laboratory studies on the deltamethrin long-lasting (coated) insecticidal mosquito nets of Netto Group (Thailand), Hiking Group Shandongtex Genfont (China) and Tianjin Yorkool (China), as part of the requirements for extension of WHO specifications for deltamethrin long-lasting (coated) insecticidal mosquito net (LN), as well as the reports of the WHOPES multi-centre study to develop simple and reliable method to determine the bioefficacy of pyrethroid-treated nettings, and made recommendations for further action.

## 2. REVIEW OF SPINOSAD 0.5% GR AND 12% SC

Spinosad is a natural product produced by fermentation technology that employs the bacterium *Saccharopolyspora spinosa* (Actinomycetales) from which it is obtained by extraction and purification of the whole broth. Spinosyns A and D are present in the isolated spinosad, in proportions of 65–95% and 5–35%, respectively,<sup>1</sup> together with traces of spinosyn-related compounds and other materials derived from the fermentation and purification process.

The two main spinosyns (A and D) are closely related structurally. They represent more than 85% of technical spinosad and are responsible for most of its insecticidal activity. They differ only in the presence of an additional methyl group attached to the bridging carbon of the indacene moiety in spinosyn D.

Spinosyns A and D have very low vapour pressures, making them essentially non-volatile. Spinosyns A and D are weak bases. Spinosyn A has rather low, and pH-dependent, water solubility, with that of D even lower. As may be expected for weak bases, the water solubility decreases with increasing pH in both cases. Both spinosyns are resistant to hydrolysis in sterile, buffered water, with no detectable hydrolysis at pH 5 and increasing but very slow hydrolysis at pH 7 and pH 9. Aqueous photolysis of A and D at pH 7 was rapid, with a half-life of less than one day.

Spinosad acts as a nicotinic agonist. It alters the function of nicotinic and GABA-gated ion channels, depolarizing insect neurons and resulting in neuron excitation. Spinosad has shown no cross-resistance with existing insecticides and can be rotated with all other classes of currently used mosquito larvicides.

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<sup>1</sup> WHO specifications and evaluations for public health pesticides – Spinosad. Available at <http://www.who.int/whopes/quality>.

## 2.1 Safety assessment

The FAO/WHO Joint Meeting on Pesticide Residues (JMPR) assessed the toxicity of spinosad in 2001 (JMPR, 2001).

Spinosyn A is rapidly absorbed from gastrointestinal tracts and is distributed relatively evenly in the organism. It is metabolized mainly via glutathione conjugation and excreted mainly in the faeces. After a single dose, about 90% is excreted within 24 hours. Limited information on spinosyn D is available, which indicates a similar pattern of disposal.

Spinosad has low acute toxicity by oral ( $LD_{50} > 5000$  mg/kg), dermal ( $LD_{50} > 5000$  mg/kg) and inhalation routes ( $LC_{50} > 5$  g/m<sup>3</sup>), does not cause dermal sensitization in Buehler or maximization tests, is only slightly irritating to the eye and is non-irritating to the skin. In studies in mice and rats, spinosad did not induce tumours. Spinosad did not induce point mutations in bacteria or murine lymphoma cells, or chromosomal aberrations or unscheduled DNA synthesis in vitro or micronuclei in mice in vivo. Spinosad at low-to-moderate doses showed no teratogenicity, neurotoxicity or reproductive impairment.

Spinosad has the potential for bioaccumulation; it is photolabile, but resistant to hydrolysis. It is moderately toxic to fish, practically non-toxic to birds, and highly toxic to honeybees.

The WHO Programme on Chemical Safety is of the view that the use of spinosad as a mosquito larvicide poses no undue threat to the health of users or to the environment. However, it notes that

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