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REPORT OF THE SEVENTH WHOPES WORKING GROUP MEETING

WHO/HQ, GENEVA
2–4 DECEMBER 2003

Review of:
VECTOBAC WG
PERMANET
GOKILAHT-S 5EC

WORLD HEALTH ORGANIZATION
COMMUNICABLE DISEASE
CONTROL, PREVENTION AND ERADICATION
WHO PESTICIDE EVALUATION SCHEME (WHOPES)

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1. INTRODUCTION

The seventh meeting of the WHOPES Working Group, an advisory group to the WHO Pesticide Evaluation Scheme (WHOPES) was convened at WHO headquarters, Geneva, 2–4 December 2003. The objective of the meeting was to review the reports of the testing and evaluation of VectoBac® WG (Valent BioSciences, USA) for mosquito larviciding, PermaNet® (Vestergaard Frandsen, Denmark) for malaria prevention and control, and Gokilaht®-S 5EC (Sumitomo Chemical Co., Japan) for space spraying against mosquitoes.

The meeting was opened by Dr L. Savioli, Coordinator, Strategy Development and Monitoring for Parasitic Diseases and Vector Control. In his remarks, Dr Savioli emphasized the need for the development of novel vector control strategies, as the number of available tools is rather limited at the present time. He further noted that WHOPES is playing a critical role in the development of vector control agents and their formulations.

Dr Morteza Zaim, Scientist in charge of WHOPES, presented the objectives of the meeting as well as an overview of the Scheme to the participants and noted that WHOPES recommendations are intended to expedite registration of public health pesticides by the Member States. He noted the close collaboration of WHOPES with the Programme on Chemical Safety (PCS) and mentioned that no public health pesticide is considered by the Scheme for field testing until the safety assessment has been carried out by PCS. Dr Zaim also noted that the reports of the WHOPES Working Group Meetings are a consolidation of the available information on pesticides evaluated by the Scheme and an excellent resource for pesticide registration authorities and national control programmes. He further emphasized that every effort is made to ensure that the reports are useful and widely available.

Dr Zaim briefed the participants on the new FAO/WHO procedure for developing pesticide specifications, by which the specifications are linked to the product of the manufacturer which provided the data package and the pesticide product for testing/evaluation. Details of the data package requirements and procedures for development of specifications are included in the *Manual for development and use of FAO and WHO specifications for pesticides*, 1st ed., published by the Food and Agriculture Organization of the United Nations (FAO) in 2002.

Dr H. Endo, Director, WHO Department of Communicable Disease Control, Prevention and Eradication, also attended the meeting and expressed his great interest in the proceedings and deliberations of the Working Group. Dr Endo made specific reference to the emergence and spread of vector-borne diseases, such as West Nile Virus, and reiterated, that in view of the occurrence of these types of epidemic, vector control research and the development of new strategies for vector control are attracting increasing attention. He emphasized the high priority that WHO is giving to vector biology and control as an important cross-cutting activity, despite the availability of only limited resources.

The meeting was attended by 11 scientists (see Annex, List of participants). Dr Mir S. Mulla was appointed as Chairman and Dr P. Jambulingam as Rapporteur. The reports of the WHOPES supervised trials and relevant published literature (see Section 6, References cited) were reviewed and discussed. Recommendations were made on the use of VectoBac® WG, PermaNet®, and Gokilaht-S® 5EC.

2. REVIEW OF VECTOBAC WG

VectoBac® is a bacterial larvicide. The active ingredient in VectoBac is composed of viable *Bacillus thuringiensis israelensis* (H-14) endospores and delta-endotoxin crystals.

Bacillus thuringiensis (*Bt*) is a facultative anaerobic, Gram-positive bacterium forming parasporal crystalline inclusions, which are toxic to certain invertebrates, especially species of insect larvae belonging to the insect orders of Coleoptera, Diptera and Lepidoptera. The parasporal inclusions consist of different insecticidal crystal proteins (ICP). A susceptible insect larva must ingest the ICP or spore–ICP complexes. The efficacy of the ICP depends on solubilization in the midgut, conversion of the protoxin to the biologically active toxin by proteolytic enzymes, specific membrane receptor binding by the C-terminal domain of the active toxin, and pore formation by the N-terminal domain, with subsequent lysis of the gut epithelial cells. Germination of spores and proliferation of vegetative cells into haemocoel may result in a septicaemia, contributing to the cause of death. Receptor binding by the ICP is the major determinant of host specificity. *Bacillus thuringiensis* has many subspecies that exhibit toxicity to a variety of insects. Over the past 50 years, most of the *Bt* products have been used for the control of agricultural pests. It was not until 1980 that a *Bt* subspecies, known as *israelensis* (*Bti*), was discovered and developed for use in mosquito and onchocerciasis control programmes.

2.1 Safety assessment

The human and environmental safety of *Bt,* including *Bti,* has been assessed by WHO (1999). The ICP spores and vegetative cells of the *Bti* subspecies, when administered by different routes, were found to be mostly non-pathogenic and non-toxic to various animal species. *Bti* has no adverse affect on birds, earthworms, fish, or numerous other non-target aquatic vertebrates in laboratory and field studies. A few species of aquatic invertebrates, however, are susceptible to *Bt. Bti* has little toxicity to non-target arthropods.

After the application of *Bti* to an ecosystem, the vegetative cells and spores may persist at gradually decreasing concentrations. The ICPs, however, are rendered biologically inactive within hours or days.

With the exception of case reports of ocular and dermal irritation, observations of occupational exposure have revealed no adverse health effects. Antibody titres to the vegetative cells, spores and spore–crystal complexes have been demonstrated in workers spraying *Bti* products; however, no adverse health effects were reported. *Bt* has no adverse effect on human health when present in drinking-water or food.

Owing to their specificity, *Bti* products are unlikely to pose any hazard to humans, other vertebrates, and non-target invertebrates, provided that they are free from non-*Bt* microorganisms and biologically active products other than the ICPs. They are safe for use in aquatic environments, including drinking-water and reservoirs, for the control of mosquitoes, blackflies, and larvae of nuisance insects.

The VectoBac WG formulation of *Bacillus thuringiensis* subsp. *israelensis* is a fermentation product, consisting of brownish fine-sized granules with loose appearance that disperse readily when mixed with water. VectoBac water-dispersible granule (WG) is non-toxic by ingestion, skin contact, or inhalation. The following are extracts from the Manufacturer's Material Data Safety Data Sheet and Label recommendations of the WG