WHO PESTICIDE EVALUATION SCHEME

50 YEARS OF GLOBAL LEADERSHIP

World Health Organization

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CONTENTS


WHOPES
anniversary
50 YEARS OF GLOBAL LEADERSHIP

WHOPES
FOREWORD

By Lorenzo Savioli

Renewed interest by the international community and Member States in control of malaria vectors and the emergence of vector-borne diseases as a consequence of ecological changes and natural disasters in recent years have significantly increased the use of pesticides for vector control and personal protection. This in turn has further increased the role and responsibilities sought from the WHO Pesticide Evaluation Scheme (WHOPES) in supporting national programmes and other stakeholders in the selection and safe and judicious use of public health pesticides.

The limited capacity of countries where vector-borne disease are endemic to carry out safety and efficacy assessments of public health pesticides, from one side, and the time- and cost-saving investment seen by pesticide industry in using WHOPES recommendations and quality standards to facilitate registration and use of these products in disease endemic countries, has made WHOPES a global leader in standard setting and evaluation of public health pesticides.

Established in 1960 with the approval of the World Health Assembly, the Scheme has evolved during the past 50 years to better respond to the needs of Member States and other stakeholders. The reorganization of the Scheme in 1996 and its evolution since then have included improved communication, greater transparency, intensified collaboration with stakeholders and intensified support to countries.

The establishment with the Food and Agriculture Organization of the United Nations of joint programmes on development of pesticide specifications (in 2001) and on sound management of pesticides (in 2007) are key strategic actions of the Scheme that have resulted in complementary, harmonized and coordinated guidance to Member States and other stakeholders in these areas. It is hoped that this collaboration will stimulate and ensure collaboration between agriculture and health sectors at national level to ensure optimized use of national resources for sound management of pesticides. There is immense scope for further collaboration with other sectors, including the environment, industry and nongovernmental organizations.

Strengthening capacity of Member States for judicious use of public health pesticides and their life-cycle management, and increased harmonization of registration procedures and requirements as well as information exchange and work-sharing are priorities on the WHOPES agenda. This agenda includes capacity strengthening for monitoring and evaluation of vector and public health pest control operations based on principles of integrated vector management.

The Global Collaboration for Development of Pesticides for Public Health has provided a forum for coordination and collaboration among different partners and stakeholders, which has to be further expanded and strengthened.

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World Health Organization Pesticide Evaluation Scheme
50
WHOPES
Celebrates Fifty Years

WHOPES

1. INTRODUCTION

The WHO Pesticide Evaluation Scheme (WHOPES) will celebrate its fiftieth anniversary in 2010. Formally established in 1960 – under the name WHO Programme for the Evaluation and Testing of New Insecticides – it was one of the main activities of the Vector Control unit, then part of the Division of Environmental Health.

The principal function of WHOPES has been to promote and coordinate the testing and evaluation of pesticides of interest to public health, including chemosterilants, pathogens, and hormone-like compounds, as well as repellents and attractants. Originally set up to support the Malaria Eradication Campaign and other disease control programmes of WHO, it progressively extended its responsibilities to include public health aspects of other uses of pesticides, such as the control of nuisance insects, rodent control, aircraft disinsection and personal protection.

The Scheme began as a collaborative effort with the chemical industry, research and government institutions, and regulatory agencies, to identify new insecticides of potential value for controlling vector-borne diseases, in response to the challenge of insecticide resistance, and subsequently embraced concern with environmental contamination. Since the early 1960s WHOPES has supported field research units in several countries in testing the effectiveness of insecticides, and their formulations, against major disease vectors and in assessing their safety, and has collaborated with WHO programmes and endemic countries in the design and evaluation of large-scale field trials of the epidemiological impact of insecticide application in public health programmes.

In its present form, WHOPES comprises a four-phase evaluation and testing programme concerned with the safety, efficacy and operational acceptability of public health pesticides and the development of specifications for quality control and international trade. It functions through the participation of representatives of governments, manufacturers of pesticides and pesticide application equipment, WHO Collaborating Centres and other research institutions, as well as other WHO programmes, notably the Programme on Chemical Safety.

WHOPES collects, consolidates, evaluates and disseminates information on the use of pesticides for public health. Its recommendations facilitate the registration of pesticides by Member States.

Today, the main objectives of WHOPES are to:

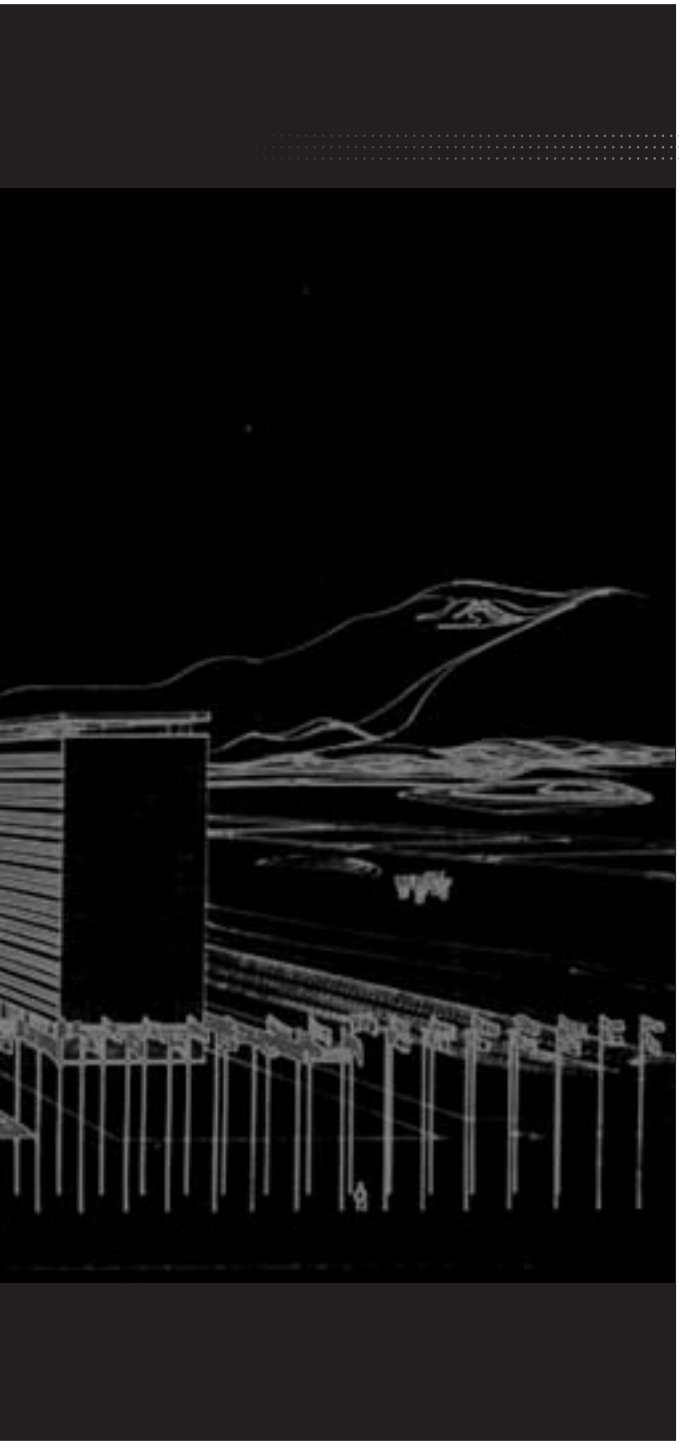
- facilitate the search for alternative pesticides and application methodologies that are safe and cost-effective; and
- develop and promote policies, strategies and guidelines for the selective and judicious application of pesticides for public health use, and assist and monitor their implementation by Member States.

The new requirements of the current scaling-up of campaigns for the control of vector-borne diseases, particularly malaria, are placing growing demands on WHOPES, making a review of its history and an analysis of the way in which it has adapted to changing demands particularly relevant. These increased demands and the broadening of collaboration with industry also offer the opportunity to accelerate the evaluation and testing of new compounds – and possibly to develop pesticides specifically adapted to the needs of vector-borne disease control, thus reducing dependence on compounds originally developed for agricultural use.

The history of WHOPES shows a clear evolution from its original objective of developing safe and effective insecticides for public health campaigns to development of the broader capacity to address the health implications of the management of pesticides from production right through to disposal. This broader approach has been made possible by the establishment of working partnerships to harmonize actions throughout the United Nations system (particularly FAO, the Food and Agriculture Organization of the United Nations) and industry.

Four main periods can be identified in the evolution of WHOPES:

- establishment and growth of the programme;
- contraction and stagnation between the early 1970s and 1982;
- reformulation from 1982 to 1996; and
- reorganization and renewed expansion from 1996 to the present.



WHOPES

2. ANTECEDENTS

From the time of WHO's creation, there was a clearly perceived need not only to use pesticides for the control of vector-borne diseases and to ensure their quality and safety but also to understand – and provide guidance to Member States on – the health implications of other uses of pesticides. During the first 12 years of WHO's existence, as resistance among vectors and pests became apparent and led to the development of new products, the Organization took on an increasingly prominent role in evaluating and testing new pesticides and in dealing with the problems of pesticide use in general. Establishment of the first WHO Programme for the Evaluation and Testing of New Insecticides in 1960 was preceded by a series of resolutions from the World Health Assembly, and by recommendations from WHO Expert Committees on insecticides and on malaria, which addressed the various problems of insecticide use and later formed the basis for the Programme's specific mandate.

The huge toll taken by malaria and other vector-borne diseases on military operations in tropical areas during the Second World War, as well as the extent and severity of the outbreaks that followed demobilization and the period of reconstruction of war zones, focused the attention of health authorities on the urgent need to control these diseases. Significant progress had been made in malaria control since the beginning of the 20th century but had been slow and dependent on detailed knowledge of the local epidemiology of the disease. Although some pesticides, such as Paris green and pyrethrum extracts, were used for the control of malaria and other vector-borne diseases before the War, it was the research motivated by the war effort that brought insecticides – notably DDT – to the forefront in disease control.

The discovery in 1939 of the insecticidal effect of DDT led to its use during the Second World War, but it was the later observation, in 1943, of its residual action that ushered in a new era, showing that "the control of malaria in vast rural areas has now become economically and technically feasible" (WHO, 1948).

Even before the official creation of WHO, the Interim Commission formed to prepare for the first World Health Assembly appointed an Expert Committee on Malaria. In its second session, the Expert Committee recommended that a subcommittee on insecticides be established to specify international norms for insecticides and their formulations and to encourage both the development of appropriate equipment and research and exchange of information (WHO, 1948).
Following the establishment of WHO, the First World Health Assembly (WHA) requested that a small committee be formed, comprising three experts with broad knowledge of insecticides and their use and representing the more important national insecticide committees (WHO, 1973a). This small committee was to set up panels of experts, each with two or three members, on the following subjects:

- chemistry of insecticides
- disinsection of aircraft
- mechanical devices for disinsection
- other dusting or vaporization devices
- dusting by aircraft
- insecticide application in houses.

In 1949, the Second WHA asked countries to require that all insecticide containers be properly packaged and labelled. The Fourth WHA, in 1951, and the subsequent meeting of the Executive Board (June 1951), stressed the need to prevent the toxic hazards of using insecticides in agriculture and health and requested countries to develop adequate regulations; WHO was requested to assist countries and to collect, validate and disseminate information in collaboration with the International Labour Organization (ILO) and FAO (WHO, 1973a).

The WHO secretariat responded to the WHA requests by setting up an Expert Panel on Insecticides and organizing the meetings of Expert Committees to address the different issues; Secretary of the Panel was Mr J.W. Wright, a WHO staff member in the Malaria Section of the Division of Epidemiology. In 1955, in response to a request by the WHA, WHO established a Division of Malaria Eradication to lead and coordinate a global programme of eradication; the Insecticides unit was transferred to the Division of Environmental Health. Later, as the Insecticides unit broadened its activities to embrace the needs of other vector-borne diseases, it evolved first into an independent section of Vector Biology and Control and then a full Division, finally merging with the newly created Division of Control of Tropical Disease in 1990. At present, WHOPES is part of the Department of Control of Neglected Tropical Diseases (NTD). Throughout these developments, the evaluation and testing of pesticides has remained one of the principal functions of the different units dealing with vector control in WHO.

As one of its earliest tasks, the Expert Committee on Insecticides undertook the definition of insecticide specifications, starting with DDT in its first session (10–15 May 1949) (WHO, 1950) and continuing with more precise specifications for DDT, chlordane, methoxychlor and hexachlorocylohexane (HCH) in its

second session (4–11 October 1950) (WHO, 1951); in its third to seventh sessions, the Committee also drew up specifications for aerosols and equipment (WHO, 1952a, 1952b, 1955, 1956a, and 1957) and, starting in 1956, the periodic publication of specifications for pesticides (WHO, 1956c).

The question of the safe use of pesticides had been addressed by the Expert Committee as early as its second session in 1950, and by the WHO secretariat, which consolidated available information, publishing a monograph on the subject in 1953 (Barnes, 1953), and convened a Study Group on Toxicity of Pesticides (6–13 June 1956) (WHO, 1956b). The Expert Committee on Malaria in its seventh session (15–23 September 1958) stressed the necessity for adequate protection when using toxic insecticides such as dieldrin, as well as the need to advise vector-borne disease programmes on the selection of insecticides and application techniques (WHO, 1959).

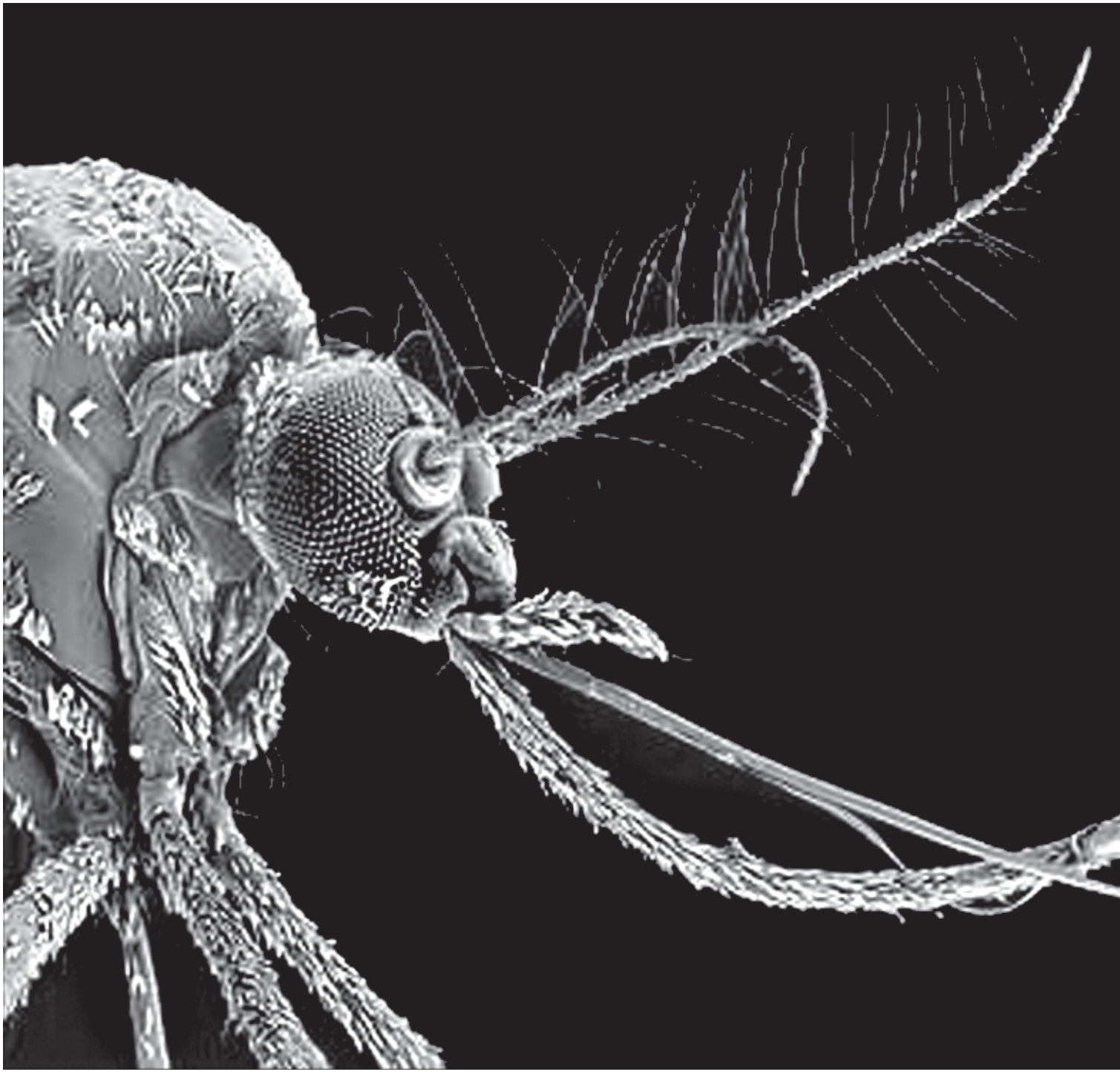
The problem of vector resistance to pesticides had been of particular concern since it was first reported in ***Anopheles sacharovi*** in Greece in 1951 (Livadas & Georgopoulos, 1953). The fear of insecticide resistance acted as an incentive to speed up control campaigns in order to eliminate the parasite before available insecticides lost their effectiveness. Reports of insecticide resistance in anophelines increased dramatically between 1955 – when the Global Malaria Eradication Campaign was launched – and the early 1960s, although this was in many cases simply the recognition of a phenomenon that had developed earlier in response to large-scale agricultural use of insecticides. Insecticide resistance was reviewed during the seventh session of the Expert Committee on Insecticides (10–17 July 1956) (WHO, 1957) and became the focus of the eighth session (18–23 November 1957) (WHO, 1958), which standardized the methods for testing physiological resistance and bioassays for determining the residual killing effect of sprayed surfaces.

While insecticide resistance was being recognized in an increasing number of areas, replacement of DDT with an alternative insecticide continued to be viewed as the only solution to the problem. Nevertheless, as the malaria eradication campaign was the main consumer of insecticides and indoor application of insecticides the principal tool for vector control, the strict requirements for safety, effectiveness and residual effect of a candidate insecticide meant that the search had to continue: the only available alternatives were dieldrin, which was too toxic and likely to select quickly for resistance, and HCH, which had too short a residual effect and showed cross-resistance with dieldrin.

In 1956, the 17th session of the Executive Board, alarmed by the report of insecticide resistance from Haiti which jeopardized the eradication of malaria from the Caribbean, requested WHO to stimulate and coordinate research on resistance and on development of new insecticides (WHO, 1973a). In response, the Organization established the Comprehensive Programme on Insecticide Resistance and Vector Control in 1958.

In 1959, a team sent to the Skala area of Greece to carry out tests on three organophosphorus insecticides concluded that the residual effect of these substances did not come up to expectation, possibly because the doses applied were lower than had been originally proposed. The team was then transferred to Lagos, Nigeria, where it was given the title Insecticide Testing Unit and placed under the supervision of the Division of Environmental Sanitation.

Strengthening of the collaboration between the Vector Control unit and industry, vector control programmes and research institutions culminated in the creation of the WHO Programme for the Evaluation and Testing of New Insecticides in 1960; the study of the nature of insect resistance and its implications remained as the second task of the unit (WHO, 1962a).



WHOPES

3. THE WHO PROGRAMME FOR THE EVALUATION AND TESTING OF NEW INSECTICIDES

The WHO Programme for the Evaluation and Testing of New Insecticides was established with the approval of the World Health Assembly in response to requests from disease control programmes, Member States and the Director-General; it was met with an encouraging response from the chemical manufacturing industry. During its first 6 months, the Programme initiated a study on more than 20 new insecticides (WHO, 1960; WHO, 1971a). The functions of the Programme were defined as follows:

- to encourage the production of effective substitute insecticides and investigate new methods of using chemicals under different environmental conditions;
- to stimulate studies of the chemical and physical characteristics of pesticides and establish specifications for pesticides used in public health;
- to study the toxicity to persons handling pesticides or living in treated premises;
- to work on the improvement of the spraying and dusting apparatus used in malaria eradication and other vector control programmes and develop specifications;
- to review the existing specifications for pesticides and to develop specifications and laboratory methods for examining and testing new chemicals and for improving current laboratory methods for materials in use; and
- to advise on the disinsection of aircraft.

1960–1970:
ESTABLISHMENT AND GROWTH OF THE PROGRAMME

ESTABLISHMENT AND GROWTH OF THE PROGRAMME

3.1 1960–1970: establishment and growth of the Programme

As its origins indicate, the Programme's main objective was to find new compounds that would overcome the problem of insecticide resistance, looking in particular for a replacement of DDT. From the outset, the Programme gave high priority to the evaluation of potential toxic hazards to persons handling insecticides and to the inhabitants of treated houses (WHO, 1962b). Although the Director-General's report (WHO, 1960) did not mention the environment, the problem of environmental contamination started to acquire increased importance and to create government concerns soon after establishment of the Programme. By 1970, in response to these concerns, the Programme's objectives included the desirability of recommended compounds not giving rise to further environmental contamination.

3.1.1 Concerns with the environment

As early as 1957, the ***New York Times*** reported on the unsuccessful efforts of a group in Nassau County to get DDT banned in New York State; their campaign was based on observations of a continuous decrease in the number of birds and on studies of the thinning of birds' egg shells. Then, in 1962, Rachel Carson published her book ***Silent Spring***, which rapidly became a best-seller and brought the issue of environmental contamination into public discussion.

During the 1960s, the work of Dr Charles F. Wurster and other scientists extensively documented the severe effects of DDT and other persistent insecticides on birds (McDaniel, Wurster & Wurster, 1965) and the widespread distribution of insecticide residues throughout the world. Residues were shown to accumulate in the liver and adipose tissue, particularly in predator species (birds, fish and mammals) at the top of the food chain – notably the bald eagle and the peregrine falcon in the USA. In1970, Norway and Sweden forbade the use of DDT; bans in the USA and several other countries followed during the 1970s and 1980s, including the United Kingdom in 1984.

These concerns contributed to the progressive broadening of the scope of the insecticide evaluation programme to include other methods of vector control. By 1963 it was decided to introduce a new class of compounds, chemosterilants, into the evaluation programme; testing procedures were developed and by September 1963 five potential chemosterilants had been tested, with particular focus on their toxicity to humans. This was part of the overall effort to develop effective methods for genetic control of vectors, which concentrated on the mass production and release of sterile males (also produced by the mating of members of different species of the same complex, cytoplasmic incompatibility, meiotic drive, translocations, etc). Much of the work was hampered by difficulties in rearing the large numbers of males, reliably separating the sexes, estimating natural population size and the density of liberation points, and mating competition between released males and males of the natural population.

Another major search for alternative control measures concentrated on the potential use of mosquito pathogens and predators. During the late 1960s, much effort was devoted to the study of Mermithidae nematodes, pathogenic fungi, viruses and bacteria; in the 1970s this culminated in the discovery and subsequent extensive testing of ***Bacillus thuringiensis israeliensis*** and ***Bacillus sphaericus***. The search for predators also yielded an extensive array of candidates ranging from the larvivorous mosquito, ***Toxorhynchites brevipalpis***, to various species of fish.

In 1967 the Programme was expanded to include the evaluation of rodenticides, because of the need for effective acute poisons arising from the development

of resistance to anticoagulants in many areas. Candidate compounds were evaluated by WHO Collaborating Centres in Denmark, the United Kingdom and the USA.

From the outset it was recognized that the Programme should provide not only for the development of new products but also for the evaluation of established pesticides. It therefore considered compounds such as parathion (designated OMS-19). Parathion was immediately rejected because of its high toxicity. However, other fairly toxic insecticides advanced through the different stages of evaluation; one such was dichlorvos (OMS-14), on the grounds that it could be applied as a fumigant under carefully controlled conditions.

The continued use of DDT, which remained the backbone of the malaria eradication campaign, posed serious problems. Debate, started outside the control of the scientific community, was rife with political overtones. Until 1971, the only comprehensive reports on the health effects of prolonged occupational exposure to DDT alone related to formulators in the USA, who had been exposed, over periods of 10–20 years, to doses originally as high as 35 mg/man-day (later reduced to about 18 mg/man-day). Even at the lower exposure level, the mean DDT concentration in fat was 30 times the average for the general population, indicating a 450-fold greater contamination. However, no specific complaints or medical findings that could be attributed to DDT exposure were found on clinical examination; moreover the general health record of these workers showed a pattern of ordinary ailments indistinguishable from those experienced by individuals comparable in every way other than exposure to DDT (WHO, 1973b). Hayes (1971) reviewed the evidence on DDT toxicity to humans and wildlife, and Galley (1971) examined the contribution of DDT used in public health programmes to environmental pollution, concluding that its use for indoor residual spraying posed no insignificant threat to any species and no threat to the inhabitants of sprayed houses.
To investigate the potential hazard of DDT use in the field, WHO sponsored two studies: one in Brazil by the Biological Institute of Saõ Paulo and the other in India in collaboration with the Indian Council of Medical Research (WHO, 1973b).

The Brazilian study included the periodic clinical examination of:

- 202 spraymen of the malaria eradication campaign who had been exposed to DDT for 6 or more years;
- 77 spraymen who were exposed to DDT for 13 years from 1947 to 1959; and
- 78 men who lived in houses sprayed indoors with DDT every 6 months.

The control group consisted of 406 men whose age distribution and socioeconomic level were similar to those of the exposed groups. A survey of illness requiring medical care during the 6 months preceding each clinical examination showed no differences between the exposed and unexposed groups over a 3-year period.

The Indian survey analysed 44 blood samples from men who had sprayed DDT indoors for 5 or more years and from 27 controls, as part of the feasibility study, followed at the end of the 1971 spraying season by the examination of 104 spraymen and 103 controls in Gujarat State. There were no differences in cardiovascular indices but neurological tests showed that knee reflexes were brisker in the exposed group, slight tremor was more often present, and performance in a timed Romberg test was poorer. No sensory changes were found, nor were there any significant differences in other reflexes, vibration sense, or coordination. There were no differences in weight, haemoglobin levels, blood sugar, or urine analysis. On the basis of these results, 20 men were selected for re-examination by a neurologist. From these follow-up examinations it was concluded that the differences found at the first examination were not real or else that parameters had returned to normal within the few months between the two examinations. The signs were in any case not dose-related, since they showed

no correlation with serum DDT levels. Body loads of DDT found in exposed spraymen were similar to those found in formulators in the USA. No effects of exposure were found, even in spraymen with more than 15 years' exposure.

These studies were difficult to carry out elsewhere, and the study of mortality was even more problematic as certification of cause of death was subject to errors in most countries and non-existent in many. Attempts to find groups exposed only to DDT for more than 5 years in other countries failed: turnover of spraymen was generally high and the extent of areas being sprayed was often reduced, either because the campaign had advanced into the consolidation phase or, to a lesser extent, because there had been a change of insecticide following the development of resistance.

In 1969, the Twenty-second WHA (WHO, 1973a) had also reacted to the potential impact of insecticides on the environment and recommended that WHO stimulate and intensify research on alternative methods of vector control. The Programme undertook a thorough review of the subject which was presented to the Twenty-third WHA in 1970, and extended its mandate to include evaluation of attractants, repellents and chemosterilants, establishing a Field Research Project on Vector Genetics and Control in India (WHO, 1970).

Following a WHO consultation on "the place of DDT in operations against malaria and other vector-borne diseases" (WHO, 1971b), all outdoor use of DDT – which had never been recommended as a larvicide because of the huge potential impact of such use on the selection of resistance – was proscribed. However, the consultation recommended that use of DDT by programmes of malaria control and eradication should continue, provided that there was strict compliance with the norms for protection of operators and the public and avoidance of environmental contamination (including disposal of contaminated containers and washing of equipment).

3.1.2 Organization of the Programme

Since the Programme ran as a collaborative effort of governments and research institutions, its executive authority was the Meeting of Directors of Collaborating Centres which took place annually (or as required if new submissions or problems required attention). The meeting reviewed evaluation results and decided on which compounds should advance to the next stage of evaluation or be removed from the scheme or whose study should be extended at a particular stage.

Insecticides were submitted for evaluation by industry or research institutions and each was given a code number that protected its identity during the testing and evaluation. This code consisted of the prefix OMS followed by a number, allotted sequentially as each compound was incorporated into the Programme. Thus malathion, the first insecticide submitted for evaluation in 1960, was OMS-1. When older compounds were later included in the Programme, they too were numbered in this way, so that DDT became OMS-16 and dieldrin OMS-18.

The structure of the Programme was described by Wright (1971) and is summarized in Figure 1. Seven laboratories served as WHO reference centres, performing the investigations required for the early stages of evaluation under controlled laboratory conditions. Compounds that met all the criteria of effectiveness and safety in the laboratory were then field-tested on progressively larger scales at six WHO field research units in six different countries.

3.1.3 Stages of the Programme

The Programme originally consisted of six stages (later extended to seven), the first three in the laboratory and the subsequent three (later four) in the field.

Stage I, performed at the University of Illinois, Chicago, USA, consisted of the establishment of

dosage–mortality curves for susceptible and resistant mosquitoes and houseflies from laboratory colonies. At this stage the potential of the candidate insecticide for selecting resistance in Culex and housefly was estimated by subjecting 25–50 generations of these species to selection pressure with the insecticide. A preliminary assessment of biodegradation was also undertaken at this stage.

When chemosterilants were added to the Programme, responsibility for their Stage I evaluation was assumed by the Entomological Research Division (ERD) of the Agricultural Research Service, United States Department of Agriculture (USDA), Gainesville, Florida.

Stage II extended the entomological evaluation of candidate compounds by measuring their direct effects on a number of insect species in three different laboratories:

- The Tropical Pesticides Research Unit (TPRU), Porton Down, England, assessed the physical properties of the insecticide and its residual effectiveness on different types of building materials with a range of sorptive capacity, using Anopheles stephensi as the standard test insect.
- The USDA laboratories in Gainesville made a preliminary evaluation of the effectiveness of the insecticide against mosquito larvae and adults, houseflies, body lice, fleas, ticks and bedbugs.
- In Savannah, GA, USA, the Technical Development Laboratory (TDL) of the United States Centers for Disease Control (CDC) undertook broader testing of effectiveness against mosquito larvae and adults, adult houseflies and Triatoma. From 1967, this laboratory also made the preliminary assessment of effectiveness of rodenticides as they were included in the Programme.

This stage also included determination of the mammalian toxicity of the compounds at the Medical Research Council (MRC) laboratories in Carshalton, England, which studied the oral and dermal toxicity and neurotoxicity of each compound, based on the data supplied by the manufacturer and, when required, the cumulative effect of repeated doses.

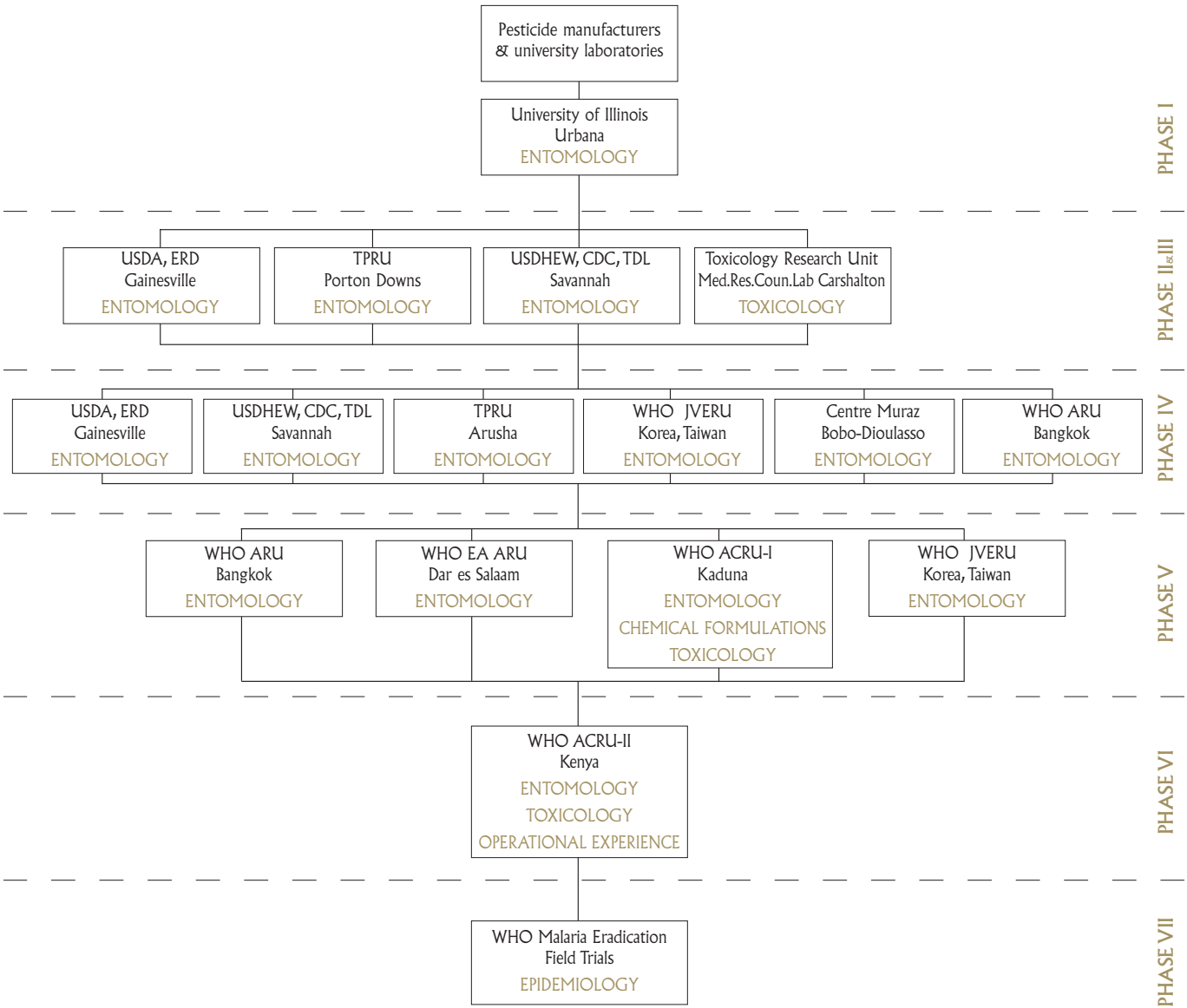
In **Stage III,** simulated field trials were performed at the laboratories in Gainesville and Savannah. These trials consisted of the study of the contact and fumigant effect of sprayed surfaces of various materials on adult mosquitoes, the larvicidal effect in small containers and drums, and the effect of dusts on lice and fleas. When appropriate, pre-flood applications were tested in the field.

Stage IV was the first in which a compound was tested on natural populations of target vectors and also the first in which spraymen and other people were exposed to the insecticide as it would eventually be used. Subjects were closely monitored under the guidance and supervision of the Carshalton laboratory, particularly with regard to the use of protective measures and for potential toxic effects, including dermatitis and severe lacrimation. At the same time, the Porton Down and Savannah laboratories studied the formulations and the establishment of analytical procedures. The actual tests depended on the target vector to be studied and are shown, together with the other field trials, in Table 1.

The following field research facilities collaborated in Stage IV field trials:

- Anophelines: Arusha in United Republic of Tanzania; Bobo-Dioulasso in Burkina Faso (then Upper Volta), and Savannah, GA, and Gainesville, FL, in the USA.
- Other larval and adult mosquitoes, with emphasis on *Aedes aegypti*: Savannah and Gainesville.
- Houseflies: Danish Pest Infestation Laboratory and Istituto Superiore di Sanità in Rome, Italy.
- Ticks: the Gainesville laboratory field station in North Carolina.
- Fleas: National Institute of Communicable Diseases in Delhi, India.

Figure 1. Structure of the evaluation programme and roles of collaborating laboratories[a]



[a]Adapted from Wright, 1971

– ***Simulium***: Office de la Recherche Scientifique et Technique d'Outre-Mer (ORSTOM) laboratory in Bobo-Dioulasso, Burkina Faso, and the New York State Museum and Science Service, USA.

In addition to the Collaborating Centres, the Programme established a number of field research projects in various countries, which carried out field trials in Stages IV and V, namely:

– ***Anopheles*** Control Research Unit (ACRU-I), Kaduna, Nigeria;
– ***Anopheles*** Control Research Unit No. II (ACRU-II), Kisumu, Kenya;
– ***Aedes*** Research Unit (ARU), Bangkok, Thailand;
– East Africa ***Aedes*** Research Unit (EAARU), Dar es Salaam, United Republic of Tanzania;
– Japanese Encephalitis Vector Research Unit (JEVRU), Taipei, China (Province of Taiwan);
– Japanese Encephalitis Vector Research Unit (JEVRU), Seoul, Republic of Korea.

Stage V consisted of trials of operational applications of insecticide on a small scale, such as a full village. On this scale it was possible not only to study in detail the impact on a relatively isolated vector population but also to identify operational problems, monitor spraymen and inhabitants of sprayed houses for toxicological effects, and observe nuisance effects such as unpleasant smell. This stage was carried out mainly by the WHO Field Research Units:

– In addition to entomological evaluations, ACRU-I at Kaduna undertook detailed toxicological vigilance: spraymen, handlers of insecticides and occupants of treated houses were examined before, during and after spraying for clinical signs or symptoms, and their exposure was determined (e.g. by measuring cholinesterase activity when organophosphorus or carbamate compounds were used). It should be noted that later experience in El Salvador and the Islamic Republic of Iran showed that determination of cholinesterase activity, while very useful as a warning of overexposure to organophosphorus compounds, was of little value for carbamate exposure. Safe use of carbamates depends on the provision of facilities for – and supervision of – frequent washing of face and hands and for maintaining proper standards of personal hygiene; minor complaints, from which recovery is rapid, serve as early indications of overexposure (WHO, 1967).
– The Gainesville and Savannah laboratories carried out trials on mosquitoes, body lice and ticks, as well as houseflies in Georgia and ***Aedes aegypti*** in the Caribbean, and did several studies on aircraft disinsection.
– The Filariasis Research Unit in Rangoon, Burma (now Yangon, Myanmar) studied measures for the chemical control of Bancroftian filariasis.
– The ARU studied ultra-low-volume application (ULV) of insecticides in Bangkok. ULV was also evaluated in Ethiopia in a biotope where ***Aedes simpsoni*** is an important vector of yellow fever.
– In both China (Province of Taiwan) and the Republic of Korea, JEVRU investigated compounds of potential use against larvae of ***Culex tritaeniorhynchus*** in rice fields. This evaluation was complicated by the widespread use of pesticides in rice paddies in both countries.

Stage VI was, until 1970, the final stage in the testing of insecticides by WHO and was run by the disease control programmes of the Organization after joint assessment, with the Vector Biology and Control unit, of the results of the evaluation at all previous stages. The epidemiological trials aimed at the control of malaria were particularly demanding. These trials required demonstration of the interruption of transmission in a large area by application of the insecticide on full operational scale; evaluation required comparison with a control area, measuring epidemiological and entomological indicators over a period of 1–2 years.

Trials of three insecticides for the control of malaria were conducted during the 1960s:

- malathion (OMS-1) by the Malaria Field Research Project in Rakai, Uganda;
- dichlorvos (OMS-14) by the Malaria Field Research Project in Kankiya, Nigeria; and
- fenitrothion (OMS-43) also by the Malaria Field Research Project in Kankiya.

Only malathion was considered to have passed this stage and therefore to be suitable for use in malaria eradication campaigns.

3.1.4 Revision of the stage structure

Between 1964 and 1965, a Stage VI trial of fenitrothion at a target dose of 2 g/m² active ingredient every 3 months was conducted in an area of 15 000 houses in Kankiya (Kano State, northern Nigeria). The result was a dramatic reduction in house-frequenting ***An. gambiae*** and ***An. funestus***, although infections in infants indicated continued transmission. It was then decided to prolong the trial, with three additional rounds of treatment at 2-month intervals. Although entomological results remained very good there were still a few infected infants. On the basis of these results, fenitrothion was deemed unsuitable for malaria eradication.

The toxicological evaluation was based on medical investigation of every neurological complaint and, because fenitrothion is an organophosphorus compound, on the testing of cholinesterase levels by tintometer. Only one sprayman had minor complaints, which disappeared after his withdrawal from work. Cholinesterase measurements, by contrast, gave rather erratic results, particularly during the seventh spraying round; this round had to be interrupted as many spraymen showed significantly lowered cholinesterase levels, which were attributed to the higher skin absorption of the most recent batch of water-dispersible formulation.

A number of operational problems had been evident from the outset. Some early batches of the insecticide product lost their suspensibility too quickly; this was reported to the manufacturer. A subsequent batch retained good suspensibility but rapidly eroded the tips of sprayer nozzles. Two further batches, although solving the spraying problems, were associated with greater lowering of cholinesterase levels, prompting the decision to test spraymen every morning to select those able to work. In the final round, a considerable number of spraymen failed to meet the required cholinesterase levels, and it was therefore decided to terminate the trial until a satisfactory fenitrothion formulation could be provided by the manufacturers (Vandekar, 1980).

This trial was the main reason for the Division of Malaria Eradication demanding that the toxicological and operational evaluation should not end with the "village-scale trial" but include a large-scale operational trial (new Stage VI), allowing formulation, operational and toxicological problems to be solved before the candidate product was submitted for epidemiological evaluation in a new Stage VII.

The new Stage VI involved advanced operational and toxicological evaluation in an area with up to 25 000 inhabitants, living in several thousand houses, with operations being conducted under field conditions that resembled those in a real campaign. It was intended to allow analysis of the stability and performance of the commercially produced formulation, its suitability for application by locally employed spraymen using conventional equipment, its entomological effectiveness and its safety. The first Stage VI trial under the new protocol was undertaken by ACRU-II, in Kisumu, Kenya.

Stage VII was then defined as epidemiological evaluation in an area of about 3000 square miles and 100 000 inhabitants, in order to minimize the effect of transient populations on malaria incidence. The evaluation consisting of careful epidemiological and entomological studies in certain key index villages

in the sprayed area and in an adjacent unsprayed area. If the insecticide were shown to be capable of interrupting malaria transmission in this trial, it could then be recommended for use by malaria eradication programmes whenever a new insecticide was required for that purpose.

In 1967, ACRU-II in Kisumu undertook a Stage VI trial of fenitrothion (originally OMS-43 but now reformulated by a different manufacturer and designated OMS-223), and a Stage VII trial was proposed of propoxur (OMS-33), which had passed Stage VI trials in El Salvador and in the Islamic Republic of Iran (Vandekar et al., 1967). It was not easy, however, to find a suitable site of the prescribed dimensions for testing OMS-33. The old-style Stage VI trials had been carried out in countries (El Salvador, Islamic Republic of Iran) that were conducting national malaria eradication campaigns and therefore did not limit evaluation of their insecticide trials to entomological, operational and toxicological observations, but continued with their routine epidemiological evaluation of the study areas, thus effectively comparing the effects of OMS-33 with those of their normal malaria control activities (DDT with or without mass drug administration). Other Central American countries, seeing the obvious benefits of OMS-33 spraying, did not want to wait for WHO to conduct a Stage VII trial before using it in their campaigns.

A meta-analysis of the results of the various trials of OMS-33 yielded sufficient accumulated evidence of the epidemiological impact of propoxur spraying in various eco-epidemiological situations for its use in malaria eradication to be recommended (Wright et al., 1969). In fact, no trial was conducted with any pesticide in strict accordance with the definition of Stage VII, although an area with 100 000 inhabitants continued to be the Stage VII ideal (Wright, 1971).

3.1.5 Criteria for advancement through the Programme stages

The criteria for acceptance at the different stages of the Programme were detailed by Wright (1971) and are given in the Annex of this present publication.

In terms of insecticidal effect, criteria for advancement through Stages I to III were very specific. By contrast, the decision on whether a chemical would be rejected on toxicological grounds was based on its projected use (e.g. larvicide or adulticide), the extent to which human populations might be exposed, the insect involved, the dosage and application method, the formulation and the stability of the product.

Acceptance of compounds on entomological grounds was based on mortality data without consideration of other possible properties, such as excito-repellency. The original idea of finding a replacement for DDT dominated the expectations for new insecticides, so that any candidate chemical was required to possess the properties that, at the time, were considered to be responsible for the success of DDT.

Even had repellency and irritability of DDT and other insecticides been included as a subject of evaluation during the 1960s, it was never considered that these characteristics could make a positive contribution to disease control by diminishing human–vector contact or by denying the vector daytime resting in houses. In fact, repellency and irritability were almost always considered as shortcomings, since the campaigns were conceived as a war on the vector and therefore required high mortality and reductions in density.

Although not specifically included in Wright's description of the evaluation scheme, acceptance at Stage V depended on obtaining a reduction of more than 70% in biting density. This was contested in El Salvador particularly, where spraying with an effective insecticide, such as propoxur, could kill all the vectors entering sprayed houses – and thus affect transmission – yet have no effect on the biting density of the main vector, An. albimanus, a highly zoophilic mosquito.

3.1.6 Pesticides tested and evaluated

During the first 10 years of the Programme, 43 manufacturing companies in 8 countries submitted their newly synthesized materials, and 5 universities and institutes in 3 countries contributed groups of chemicals of novel structure.

Table 1. Tests performed at the field stages of the Programme[a]

Target insect	Stage IV	Stage V	Stage VI
Adult mosquitoes	Experimental huts	Village	Several thousand houses
Mosquito larvae	Single ponds, streams or containers	Populated area of several acres or several city blocks	A large area (several square miles) of country or in an entire city
Houseflies	Single barns or chicken houses	Group of barns or in a village	In large areas
Reduviid bugs	Single houses	Village	In several thousand houses
Simulium	Single streams or part of a stream	River basin or group of streams	Over a large area of many square miles
Lice	Small group of people	Infested village	Over a large population
Bedbugs	Single houses	Infested areas	Large-scale trial
Fleas	Single burrows or animal nests	Confined area	Over infested community
in a large area			
Ticks	Naturally infested plots	Several acres	Over a large area

[a]Adapted from Wright, 1971

Wright's review of the Programme up to the end of 1970 (Wright, 1971) indicated that almost 1400 compounds passed through Stage I, 1265 of which were insecticides and the rest rodenticides, synergists and growth-inhibiting compounds. Progress of the insecticides through the Programme is illustrated with Figure 2, which shows that only 305 of the 1265 compounds moved into Stages II and III; 50% of the remaining 960 were rejected for insufficient insecticidal activity, 40% were too hazardous, and 10% were withdrawn by their suppliers. Only 82 insecticides advanced into Stage IV, half of them active against anophelines and half against other insects of public health importance; again, the commonest reason for rejection was insufficient insecticidal activity (50%), followed by withdrawal by suppliers (30%) and potential hazard (20%).

The rate at which the Programme grew is also discussed by Wright (1971), who indicates that between 1962 and 1966 the number of compounds entering the Programme was between 160 and 200 per year; in 1967, however, the number dropped to 60 and remained between 50 and 70 until 1970. The large number of compounds in the early years may well have been due in part to the inclusion in the Programme of insecticides that had already been in use for many years; for example, DDT was included as OMS-16, dieldrin as OMS-18, gamma-BHC (lindane) as OMS-17, and parathion as OMS-19. Subsequent lower numbers represented more realistically the rate of development of new insecticides by industry and research institutions.

It is interesting to see a general shift from organophosphorus to carbamate insecticides in the period reviewed by Wright; were the analysis to continue to the present day, it would indicate a shift to pyrethroids, starting in the 1980s.

1970–1982:
CONTRACTION AND STAGNATION

50 YEARS OF GLOBAL LEADERSHIP

3.2 1970–1982: contraction and stagnation

In 1969, the World Health Assembly recognized that many countries could not expect to achieve malaria eradication in the foreseeable future with the human and technical resources available, and that they should therefore pursue programmes of long-term malaria control. This was seen as a radical change in strategy, and many bilateral and multilateral agencies, such as the United States Agency for International Development (USAID) and the United Nations Children's Fund (UNICEF), whose support had been critical at the start of the malaria eradication effort, decided that they could not continue to support control programmes indefinitely. A similar attitude was adopted by many governments: with no promise of early eradication, they found it difficult to continue preferential support for the fight against malaria over a number of pressing and more acute health problems.

In addition, the so-called "oil crisis" of the early 1970s resulted in considerable increases in the price of DDT and other insecticides, and of their transport, resulting in a further reduction in insecticide consumption and a continued increase in the cost of developing new compounds.

As a consequence, the 1970s began with a reduction in antimalaria activities; this led a number of pesticide manufacturers to lose interest in supporting the WHO evaluation scheme, since the malaria control campaigns were the main consumers of insecticides in the public health sector.

3.2.1 First attempts at simplification

By 1972, the Expert Committee on Insecticides (WHO, 1973b) had recognized that there had been a continuous decline in the number of new compounds submitted to the Programme over the previous 5 years: only 38 were received in 1971and 50–60 annually during 1967–1970, compared with 150–200 during 1962–1966. The Expert Committee viewed this tendency with concern and encouraged the Programme to accelerate the evaluation process so as to provide satisfactory alternatives to DDT as soon as possible.

As was discussed earlier, the Programme was finding it difficult to conduct a Stage VII trial that was in strict accordance with the definition, while the position taken by some Central American countries – to proceed to large-scale use of propoxur on the basis of the results of a relatively small trial in El Salvador rather than wait for a Stage VII trial – was gaining support.

Critics considered the proposed Stage VII trial to be expensive for a process that yielded results whose extrapolation to other areas might not be entirely obvious. It was felt that smaller trials in countries that were interested in finding alternatives to their current practices and that represented a range of ecological areas would provide much more useful information. Moreover, the pesticide industry and many users were beginning to feel that the seven-stage programme was unnecessarily cumbersome and slow.

The Expert Committee on Insecticides (WHO, 1973b) therefore endorsed the steps already taken to accelerate evaluation of compounds with potential for anopheline control – making the first observations on safety in a somewhat enlarged Stage IV, extending the trials at Stage V, and amalgamating the work of Stages VI and VII.

3.2.2 Broadening of involvement in pesticide toxicology

At the same time, the toxicological expertise of the insecticide evaluation programme was increasingly in demand: continued development of resistance among

agricultural pests and the extension of monocultures required an ever-growing use of insecticides, some of them highly toxic. The Expert Committee on Insecticides (WHO, 1973b) asked the Programme to address the "health aspects of pesticides not directly associated with vector control".

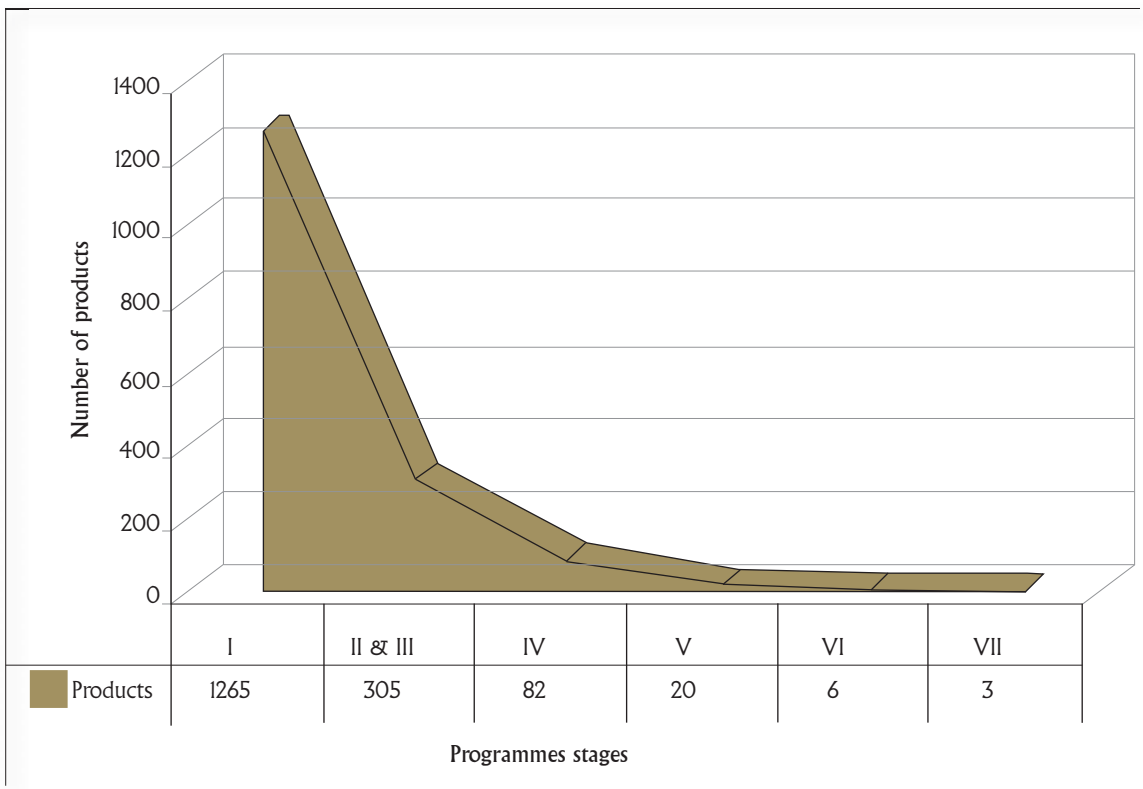
The Programme was already contributing basic information for the issue of "data sheets" on each pesticide. These were produced by WHO in response to a 1966 request from the Expert Committee of Insecticides (WHO, 1967); later, they became a joint effort with FAO and included general information and notes on use, as well as recommendations on control for regulatory authorities, precautions to be taken in use, and guidance on medical treatment for cases of intoxication. These modifications of the data sheets were endorsed by the Expert Committee (WHO, 1973b).

Importantly, the early 1970s saw the elaboration of a "Classification of Pesticides by Hazard", which aimed to distinguish between the more hazardous and less hazardous forms of each pesticide, taking into account the physical state of each formulation and its percentage content of active ingredient (WHO, 1975).

3.2.3 The epidemic of poisoning with malathion

The general contraction of the malaria control budget was followed by a dramatic epidemic in the Indian

Figure 2. Number of insecticide products passing through different stages of the Programme for the testing and evaluation of new insecticides (1960–1970)[a]



[a]Adapted from Wright, 1971

subcontinent in 1975–1977, which mobilized important external support and a rapid resumption of antimalaria operations, in both India and Pakistan.

In 1976, tragedy struck in Pakistan, where malathion was being used in the malaria control programme. Malathion was considered to be one of the safest insecticides, with an oral LD_{50} in rats of 2000 mg/kg (compared with 113 mg/kg for DDT) and a dermal toxicity similar to that of DDT. Nevertheless, there was an epidemic of poisoning: out of 7500 spraymen, 2800 were poisoned and 5 died.

A thorough investigation, with the collaboration of WHO and CDC, concluded that the main cause of this poisoning was iso-malathion, present in the formulation as an impurity and almost certainly produced during storage of the malathion. The quantitative correlation found between iso-malathion content and the toxicity of many field samples of malathion was confirmed by an examination of mixtures of pure compounds. Comparative studies involving the addition of known amounts of iso-malathion to technical-grade malathion indicated that other active substances were present; these were identified (trimethyl phosphorothioates) and shown to behave like iso-malathion in potentiating the toxicity of malathion (Baker et al., 1978; Aldridge et al., 1979).

The investigation also showed that the operators handling and spraying the insecticide had not observed the elementary precautions despite clear handling directions and package labels. It became obvious that large-scale vector control programmes, particularly in tropical countries, would require continuous improvement of specifications: every factor identified as a potential cause of problems could be translated into limits to be imposed on the insecticide specifications before procurement and reflected in guidelines for handling and using the products.

The deterioration of malathion during storage was considered to be largely the result of substandard formulation. The ban on DDT in the USA and other industrialized countries and increasing public concern about environmental contamination in many countries had led to a generalized shift to malathion, then viewed as the only suitable substitute. This rapid growth in the demand for malathion, couple with expiry of the patent, led to an increase in the number of manufacturers – and this proliferation of sources, in turn, contributed to changes in formulation, which could affect stability in tropical storage conditions. The fact that a similar situation could apply to any of a growing number of pesticides clearly underlined the need to insist on compliance with specifications.

This poisoning epidemic in Pakistan also highlighted the necessity of refining specifications for insecticide formulations, introducing strict procedures for testing the effects of storage under varied environmental conditions.

In cooperation with industry and governments, the Programme paid increased attention to the testing of new formulations and methods of application, setting up Collaborating Centres in Burkina Faso (then Upper Volta), Côte d'Ivoire, the United Kingdom and the USA to complement the WHO field research units in Indonesia and Nigeria. Testing was designed to select formulations with considerably improved performance and stability, while also proposing improved packaging that reduced hazards in handling and use. To address these issues, the second report of the Expert Committee on Vector Biology and Control (WHO, 1978) was devoted to chemistry and specifications of pesticides.

3.2.4 Growing perception of the need to review the evaluation programme

During the 1970s, the increasing number of malaria campaigns that shifted their focus from eradication to control contributed significantly to disillusion with vertical programmes, which were considered to have ignored the social and economic origins of ill health and given rise to major inequalities in health care and to inappropriate and costly services. From this grew the concept of "primary health care", which was formally defined in 1978 at the WHO/UNICEF Conference at Alma-Ata in the Soviet Union (WHO/UNICEF, 1978).

Primary health care was adopted as the strategy for health development at the WHA in 1979 (WHO, 1985a). The need for equitable distribution of health resources and for attention to be focused on the point of contact between the individual and the health services was stressed, as were the essential role of intersectoral collaboration and community participation in strengthening individual and community self-reliance. The concept of integrated vector control, which also arose during the 1970s, fitted with the principles of primary health care and aimed to reduce the dependence of vector control programmes on the exclusive use of insecticides, while developing practical methods of environmental management and searching for biological and genetic methods of control. A joint initiative had already seen WHO, the United Nations Environment Programme (UNEP) and FAO setting up a Panel of Experts on Environmental Management for Vector Control (PEEM), devoted to project support and evaluation, while the WHO/UNDP/World Bank Special Programme for Research and Training in Tropical Diseases (TDR) supported the development of alternative methods of disease control. The Programme collaborated with both these bodies in identifying pesticides of biological origin and supporting field trials for their evaluation.

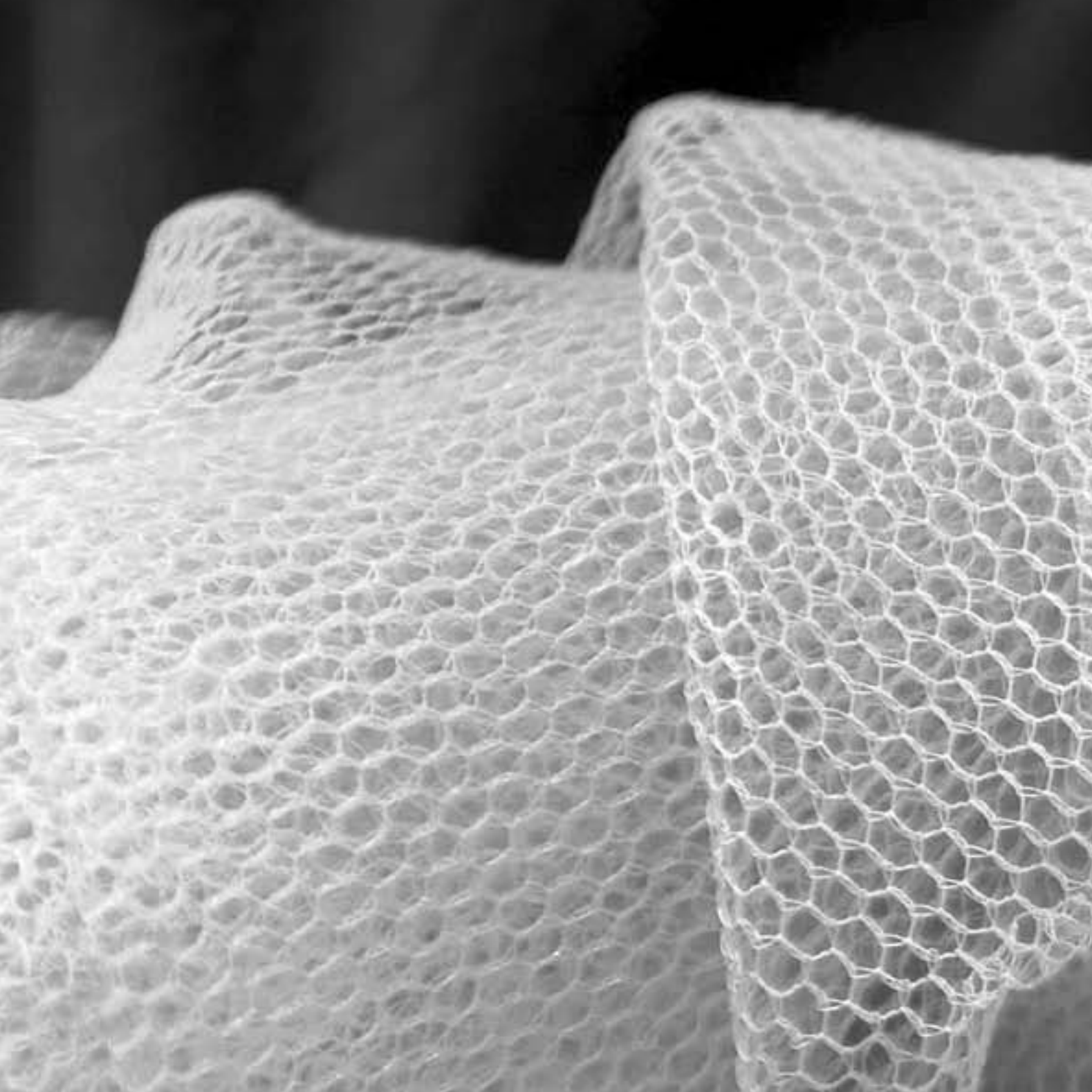
Budgetary constraints on WHO continued during the 1970s as the WHA opposed any increase in the regular budget, and action programmes became increasingly dependent on extrabudgetary funds. Activities controlled from the centre were particularly affected and, as a result, field research units directed by the evaluation programme began to be transferred to national control; this prompted concerns about the future of field trials. It was felt that there should be close liaison between Collaborating Centres and WHO regional offices in testing new application methods and in responding to national and regional needs rather than to those of a centrally directed global programme.

The doubts raised during the 1970s over the use of very large-scale field trials to "demonstrate" that an insecticide was able to "interrupt" malaria transmission in one particular area led to a demand for better understanding of the mode of action of pesticides and of the relationship between actual killing of insects and other effects – such as irritability, repellency and deterrence – which, depending on the circumstance, could favour or hamper transmission. Much greater demand was placed on detailed studies of vector behaviour towards sprayed houses and surfaces, highlighting the value of experimental house studies (Stage IV) and entry and exit observations in Stage V. This also reflected a changing view of the aim of control activities, from the simple "military" concept of "war" and its emphasis on vector mortality (as exemplified in the criteria of acceptance for advancing through the evaluation stages) to a wider understanding of vector control, requiring characterization of the available insecticides and practical recommendations for every potential use. It was argued that the final objective of the Programme should not be an epidemiological trial ("one size fits all") but specifications for different proven uses (to be modified as knowledge increased).

These concerns about the ability of the Programme's elaborate seven-stage protocol to respond to all the needs of public health programmes using insecticides also demanded that ways be found to expedite the screening of new compounds and ensure their field testing with minimal delay. At the same time, the cost of developing and producing new compounds was continuing to rise as a result of the need to reduce environmental contamination by industrial residues, while projected demand was falling as vector control programmes explored ways of reducing their dependence on insecticides. Countries were continuing their efforts to modify vector control programmes in line with the primary health care strategy and increasingly trying to incorporate community participation into vector control activities. The Programme was consequently being asked to recommend types of insecticide that would be appropriate in their efficacy and manner of application for use in integrated programmes that incorporated environmental and biological methods of vector control.

1982–1996: REFORMULATION

50 YEARS OF GLOBAL LEADERSHIP



3.3 1982–1996: reformulation

3.3.1 Review of 1982

In November 1982, WHO convened a Meeting of Directors of WHO Collaborating Centres on the Evaluation and Testing of New Insecticides with the specific purpose of analysing in depth the working of the Programme (WHO, 1982). Focusing on the need to bring the Programme into line with the vector control needs of Member States, the meeting deemed it essential to:

- review relations with the chemical industry to ensure a steady flow of new compounds for evaluation;
- give special attention to the manner of organization of field trials of new compounds or new formulations in collaboration with governments, industry and WHO Collaborating Centres; and
- consider methods of facilitating community participation in vector control, taking careful account of the feasibility of developing some of the most promising suggestions received from the field – appropriate technology must be working technology.

The Programme was renamed the WHO Pesticide Evaluation Scheme (WHOPES) and reorganized into four phases (see Table 2). A new requirement was introduced that all candidate compounds should previously have been tested for pesticidal action by their manufacturers and that some information be available on their physical, toxicological and environmental properties. This information, to be provided by manufacturers to WHO and the Collaborating Centres, would be of immense value in guiding decisions about the potential of each compound for control and in designing the necessary testing programme.

It was considered essential that manufacturers supply not only these basic data but also the test material, while the final recording of data would be the responsibility of WHO.

The importance of operational evaluation of biological agents and of the development of specifications and guidelines for their use was also emphasized, with particular attention to ***Bacillus thuringiensis israeliensis***.

Field testing should continue to be done, in collaboration with national institutions and control programmes, by WHO Collaborating Centres, mainly the Vector Biology and Control Research Unit at Semarang (Indonesia) and the Research and Reference Centre on Vector Biology and Control at Maracay (Venezuela), but also – in collaboration with industry and the country concerned – in other suitable locations and through regional inter-country programmes.

One of the main differences between WHOPES and the original Programme was that the compounds might now be tested against several vectors by various methods of application requiring different formulations. Decisions on advancing through the phases of the Scheme were therefore based on compound/vector/use and it would be possible for a compound to be in more than one phase at the same time; moreover, the observation of serious toxicity could result in the testing of a compound being terminated at any time. Testing of biological agents was also supported by TDR.

The final phase of the Scheme – Phase 4 – thus became the development of specifications for the active ingredient and for appropriate formulations for the types of application found to be effective. It required information on physical and chemical properties and collaborative development of analytical methods and was to be conducted by WHO Collaborating Centres

and by WHO in consultation with industry. Analytical procedures were to be standardized in collaboration with the relevant international organizations (WHO, 1984).

To encourage the collaboration of industry, a meeting on Insecticide Requirements for Public Health was held in 1983 (cited by WHO, 1990a, and by Gratz & Jany, 1994), attended by 60 representatives of 33 of the world's major pesticide producers. At the same time, the cost of insecticides — and its possible reduction by the use of appropriate formulations — was explored at an Interagency Consultation on Impact on Human Health and the Environment of Small-scale Formulation of Pesticides for Local Use, which considered both chemical and biological products (WHO, 1983).

Industry responded favourably to the revised Scheme as well as to the efforts to address common problems, as recorded in the Director-General's report on the work of WHO for 1984–1985, which noted that "industry is submitting more compounds and with higher insecticide activity".

The Programme called a consultation of clinicians from poison centres, government pesticide registration specialists, epidemiologists and representatives of the pesticide industry in November 1985 to discuss the development of guidelines for the prevention of pesticide poisoning (WHO, 1986).

Despite this progress, vector control programmes continued to struggle with declining resources and

Table 2. Phases of the WHO Pesticide Evaluation Scheme (WHOPES) in 1982[a]

1	Laboratory tests	Active ingredient and formulations	Pesticidal efficacy; persistence; effects on non-target organisms	Spectrum of resistance; selection	Toxicological review and/or tests	Collaborating Centres
2	Small-scale trials	Formulations	Efficacy; effects on field non-target organisms	Recording of physical properties	Safety observations	Collaborating Centres
3	Village-scale and larger field trials	Formulations	Efficacy; effects on non-target organisms; epidemiology estimate of survey	Recording and testing of physical properties	Safety observations or survey	Member States and/or Collaborating Centres; manufacturers; WHO
4	Specifications	Active ingredient and formulations	Collaborative studies on analysis and physical properties			Manufacturers; Collaborating Centres; WHO

[a] Source: WHO, 1982

deteriorating epidemiological situations, endeavouring to cope with pressing problems in what was called a "fire-fighting" strategy.

The spread of dengue haemorrhagic fever at the beginning of the 1980s demanded new safe larvicides for use in drinking-water, as well as the evaluation of insecticides for space spraying applications. Moreover the introduction of Aedes albopictus from Asia into the Americas in the mid-1980s added further difficulties to the control of dengue. Community-based approaches to mosquito control, pursued in many countries, included the use of insecticides against peridomestic breeding of Aedes, mosquito nets impregnated with permethrin or other pyrethroids, and even mosquito coils (evaluation of which yielded somewhat mixed results). Promising results were obtained with the juvenile hormone analogue, methoprene, which was considered suitable for use in drinking-water.

Growing financial constraints continued to stimulate many vector control programmes to reduce their dependence on chemical pesticides, with the result that the Scheme increasingly included the evaluation and testing of agents of biological origin for efficacy, for safety for humans and the environment, and for their potential for inclusion in integrated vector control programmes. The Scheme thus collaborated in the evaluation of ***Bacillus thuringiensis israeliensis*** against mosquitoes and blackflies in a variety of ecological situations, particularly in areas where ***Simulium*** had become resistant to temephos, although the formulations remained rather unsatisfactory. It continued to search for safe formulations that could be adapted to local production, while screening and evaluating the efficacy, safety and environmental impact of ***Bacillus sphaericus*** and other biological agents, such as juvenile hormone analogues. The hormone analogues were tested in field trials in India (Pondicherry), central Java (Semarang) and Thailand (Bangkok), and eventually in field trials in 15 countries using pilot formulations prepared by commercial companies. Their efficacy against a number of mosquito species breeding in polluted waters was confirmed.

Two inhibitors of insect moulting derived from benzoylphenylurea — diflubenzuron and OMS-2017 — were tested against ***Ae. aegypti*** and ***Simulium*** larvae. Mermithidae nematodes were also tested. In addition to the development of specifications and guidelines for their use and large-scale production, the operational evaluation of biological agents explored the possibilities of "cottage" production and local use.

The new WHOPES was particularly concerned with the problems of insecticide resistance and cross-resistance of candidate pesticides with those already in wide use. It therefore designated the laboratories of the University of California at Riverside as a Collaborative Centre to study, as part of Phase II evaluation, resistance mechanisms and the spectrum of cross-resistance and to extend selection experiments to determine the likelihood of resistance development. Several WHO collaborating laboratories undertook the development of test kits for determining the biochemical and genetic nature of insecticide resistance in arthropods.

3.3.2 Review of WHOPES in 1987

Between 1982 and 1987, 35 compounds had been included in the Scheme, while 5 others had been announced but withdrawn by the manufacturers before samples were sent. The submitted compounds consisted of 2 organophosphates, 12 pyrethroids, 4 carbamates, 9 insect growth regulators, 1 hydrazone derivative, 3 insecticides belonging to new chemical classes, 2 rodenticides and 2 molluscicides.

Of the 35 compounds that started Phase 1 (tests on laboratory colonies), 24 were accepted for phase 2, of which 12 were accepted against adult mosquitoes, 24 against mosquito larvae, 6 against tsetse flies, 9 against house flies, 4 against fleas, 2 against ticks, 15 against bedbugs, 1 against lice, 2 against molluscs, and 3 against reduviid bugs.

At Phase 2 (tests on natural populations of vectors or intermediate hosts), 2 of the 24 compounds that passed Phase 1 were recommended for use against adult

mosquitoes as residual sprays, 7 against mosquito larvae, 9 against blackfly larvae, 2 against reduviid bugs, and 1 against molluscs.

Thus the progress of the evaluation and testing of these compounds through the collaborating institutions had followed the expected course up to the completion of Phase 2, but problems remained in setting up the field trials required for Phase 3. A Meeting of Directors of WHO Collaborating Centres was therefore convened in Geneva in November 1987 (WHO, 1988) to review the progress of WHOPES with the following objectives:

- speeding up the evaluation and reporting of new compounds in order to maintain the interest of industry in developing pesticides for public health use;
- broadening the scope of the evaluation scheme so that the main nuisance pests or humans and all vectors of human disease were included;
- concentrating efforts on those compounds that had already shown insecticidal activity when screened by manufacturers;
- organizing Phase 3, with the cooperation of industry, WHO and governments of countries where the field trials were to be carried out;
- reinforcing quality control of pesticides in developing countries; and
- providing users with efficient products that would be safe when transported, stored and used in accordance with instructions.

The revised Scheme included the possibility of using pesticides of higher toxicity in more dilute formulations. Since the toxicity of some formulated products may differ from that of the technical-grade material, testing of formulated products might be required.

The eighth report of the Expert Committee on Vector Biology and Control (WHO, 1984) had already noted that bendiocarb, a carbamate insecticide of relatively high mammalian toxicity, could be applied safely by modifying the conventional method of presentation and application. By supplying an 80% water-dispersible powder in preweighed sachets, each containing the required amount of pesticide for one pump-charge, the mixing of the material could be done with acceptable safety.

The network of WHOPES collaborating institutions had expanded and now consisted of:

- 10 Collaborating Centres
  - CDC, Atlanta, GA, USA
  - Division of Medical Entomology, Ministry of Health, Bangkok, Thailand
  - OCCGE, Bobo-Dioulasso, Burkina Faso
  - ORSTOM, Bondy, France
  - Medical Research Council, Toxicology Unit, Carshalton, England
  - USDA Insects Affecting Man & Animals Laboratories, Gainesville, FL, USA
  - Vector Control Research Centre, Pondicherry, India
  - Overseas Development Natural Resources Institute, Porton Down, England
  - Rodent Control and Demonstration Unit, Rangoon, Burma (now Yangon, Myanmar)
  - University of California, Riverside, CA, USA

- 5 associate laboratories
  - Virginia Polytechnic Institute, Blacksburg, VA, USA
  - Station de Phytopharmacie de l'Etat, Gembloux, Belgium

  - Centre de Recherche sur les Méningites et les Schistosomiasis, Nyamey, Niger
  - Universidade Federal do Rio de Janeiro, Brazil
  - Onchocerciasis Control Programme, Bouaké, Côte d'Ivoire

- 1 research institute
  - Institut Pierre Richet, OCCGE, Bouaké, Côte d'Ivoire.

It was agreed that large-scale field trials remained essential but that they had been losing momentum for a variety of reasons including, in the opinion of the Directors' meeting: the decision of Member States to revert to malaria control rather than malaria eradication, with the consequent perception of less need for new insecticides; the disestablishment, for technical and other reasons, of WHO field research units; and economic considerations.

To rebuild the capacity for the required large-scale field trials, more active participation by industry was deemed essential to make the setting up of field trials of the required size and technical detail economically feasible.

The report of the Directors' meeting (WHO, 1988) described the respective roles of industry, governments and WHO as follows:

Industry and WHO WHOPES staff are generally the ones who have the means and information to recognize potential candidate compounds that have shown promise at phases 1 and 2. In addition to the information collected in the WHOPES, industry may also have from their own laboratories and other research collaborators data concerning compounds with potential for a phase 3 trial against a certain vector. When such a compound is identified, suitable areas where trials could be conducted are tentatively selected. Some of these sites may be WHO Collaborating Centres. In other cases, industry representatives may have contacted the government representatives directly and made tentative proposals for field trials. It is expected that industry will contribute substantially towards the trial costs including the supply of insecticides.

WHO, both at the headquarters level through its VBC Division and at the Regions through the VBC advisers or regional entomologists, is able to participate in such trials in several ways, in addition to what has already been mentioned in the above paragraph. This may range from actual preparation of protocols (these should always be prepared or cleared through WHO); selection of trial and comparison areas; assisting the country concerned in obtaining suitable spray equipment and spare parts; providing consultants to assist in the organization and supervision of spray operations, safety and toxicological observations, and entomological operations. Many of these projects may require substantial funding. Data from trials are reviewed at appropriate intervals by all of the three agencies.

The governments, through their ministries of health, research institutes and other similar organizations, play a most critical role in the execution of the trials.

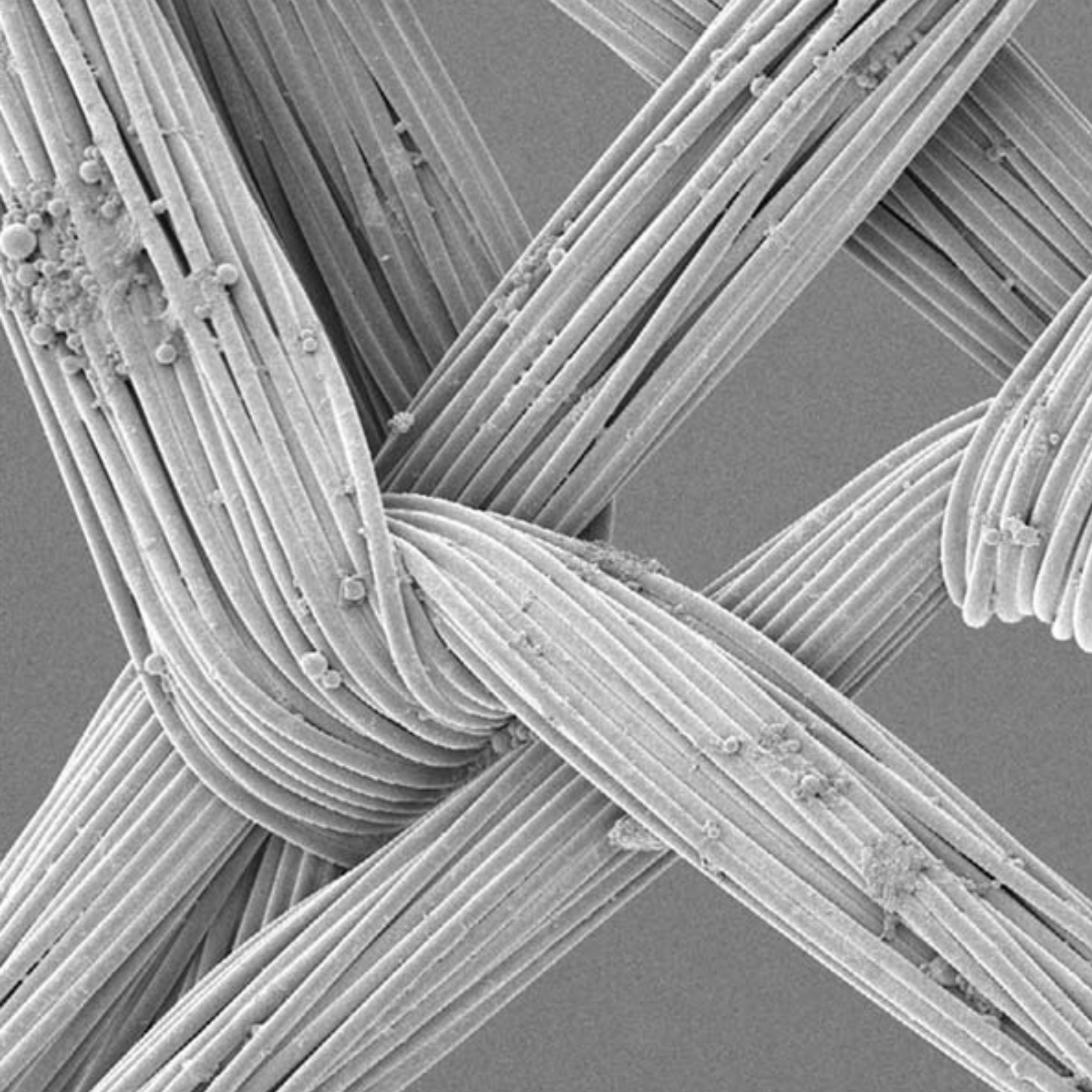
Suitable laboratory facilities, transport, personnel for spraying, as well as evaluation activities, must be available.

Despite these efforts, it was not easy to reverse the trend of declining investment in vector control by the international community; inevitably, there were serious repercussions on the capacity of countries to cope with the problem. Nevertheless, and perhaps as a reaction to the huge mobilization of international support to

contain the AIDS epidemic, malaria-endemic countries awoke to the possibility of calling for a global effort to combat malaria and other neglected diseases.

In response to this call, WHO convened a Ministerial Conference on Malaria Control in Amsterdam, Netherlands, in 1992, which agreed on a global strategy for malaria control; the conference issued the Amsterdam Declaration calling for a renewed global effort to address the worsening malaria problem in tropical countries (WHO, 1993b). The strategy was endorsed by the WHA in 1993, reviewed by the Economic and Social Council of the United Nations and endorsed by the General Assembly in 1994 (quoted in WHO, 2000).

1996–up to the present:
REORGANIZATION AND RENEWED EXPANSION
50 YEARS OF GLOBAL LEADERSHIP



3.4 1996 up to the present: reorganization and renewed expansion

Following endorsement of the malaria control strategy at the highest political levels and the demands of delegates from endemic countries, the WHA adopted, in May 1996, a resolution requesting that efforts be made to increase resources to intensify WHO's actions in malaria control, to reinforce the malaria training programme at country, regional and global levels, and to explore the possibility of establishing a special programme on malaria prevention and control (WHO, 1996a).

It was clear that accelerating the control of malaria, as well as that of other vector-borne diseases, required the development of new pesticides to cope with the spread of resistance. Insecticides — whether indoor residual spraying, impregnated mosquito nets or larvicides —remained the backbone of most vector control programmes, even if other measures were important in certain eco-epidemiological situations or as part of a developing integrated vector control programme. It was also recognized that the high cost of field trials remained a major obstacle to the rapid development of essential new pesticides or new formulations and that the call for industry to assume an important part of that cost required a revision of industry's participation in the whole process.

Indeed, 1996 marked a turning-point in the history of WHOPES, which became a truly collaborative scheme, in which partners found new opportunities for collaboration and for channelling their interests in the ultimate objective of improving disease control. The reorganization and renewed expansion of WHOPES included a review of criteria and procedures for testing and evaluation of public health pesticides; resource mobilization; improved communication and greater transparency; intensified collaboration with other stakeholders; critical needs assessment and development of guides, norms and standards for sound management of public health pesticides throughout their life cycle; and intensified country support. The steps in the reorganization process are outlined in the following paragraphs.

3.4.1 Informal Consultation on Evaluation and Testing of Insecticides

Following the recommendation of the World Health Assembly, WHOPES convened a consultation (7–11 October 1996: WHO, 1996b), with the following objectives:

- to review and update the methods and criteria for evaluation and screening of pesticides;
- to provide information to industry about pesticide requirements for public health;
- to draw the attention of industry to the problems faced in disease control, especially those caused by the spread of resistance;
- to stimulate the development of alternative chemicals and formulations for public health use; and
- to strengthen the relationship between WHO, industry and Collaborating Centres.

WHOPES proposed to develop standard methods and criteria for screening and for laboratory and field evaluation. These could be used by manufacturers to conduct trials, mostly in the laboratory; the results would be submitted to WHOPES for review and, if appropriate, be accepted as part of WHOPES requirements. After this review, plans would be made for complementary trials for full evaluation of the product.

The meeting also discussed the information on current use of public health pesticides and their future requirements.

3.4.2 Formalization of collaboration with partners

Although the respective responsibilities of industry, governments and WHO for the objectives of WHOPES had been defined at the Meeting of Directors of Collaborating Centres in 1987, the required collaboration was never formalized, surging only when it was needed during the evaluation process.

The need to mobilize all potential resources for evaluating and testing pesticides, in as wide a range of situations as their public health applications demanded, required the establishment of closer contacts with all relevant agencies. Any lingering reluctance to collaborate openly had to be abandoned; for its part, WHOPES recognized that it could not, as it might in the past, exercise a monopoly on the evaluation process, and strengthened its position as a coordinator of a public–private partnership – perhaps the first in WHO.

Establishment of the Global Collaboration for Development of Pesticides for Public Health (GCDPP) in 1997, with the advice of the legal department of WHO, thus served to strengthen WHOPES activities, facilitate the search for alternative safe and more cost-effective pesticides and application methodologies, and further promote the safe and proper use of pesticides and application equipment.

The GCDPP serves WHOPES in an advisory and resource-mobilizing role. Its specific objectives are:

- to advise on issues related to the development and use of pesticides and pesticide application equipment, within the context of WHO's global disease control strategies;
- to advise on the relative priority of activities within the mandate of the GCDPP;
- to promote harmonization of activities related to pesticide development and safe use; and
- to promote the highest quality of work through appropriate resource mobilization.

Manufacturers of pesticides and pesticide application equipment, national and government-supported agencies, regional and international organizations, universities and research institutions are invited to participate in the GCDPP; every effort is made to maximize the representation of all interested parties, while ensuring an appropriate balance of the particular fields of expertise essential to GCDPP's proper functioning. Leading scientists and officers in charge of vector control activities in the WHO regional offices are also invited to attend the meetings of GCDPP.

A biennial meeting takes place in Geneva, Switzerland (unless exceptional circumstances necessitate another venue) and informal consultations take place as required. Since its establishment, the GCDPP has met six times at WHO headquarters in Geneva. Terms of Reference, the list of members and reports of the meetings are available on the WHOPES web site (http://www.who.int/whopes/gcdpp/en/).

3.4.3 The WHOPES Working Group

Another important reform in 1996 was the establishment of the WHOPES Working Group. Scientists invited to the meetings of this advisory group participate in their individual capacity and are selected, largely from the WHO Panel of Experts on Vector Biology and Control, as required by the agenda of the specific meeting. The Working Group meets once a year to review reports of WHOPES-supervised trials, relevant published literature and unpublished reports and to make recommendations as to suitability for use in public health or requirements for continued evaluation; it may also suggest possible modifications of the product or its formulation.

WHOPES recommendations are intended to facilitate both registration of the evaluated products and their use by WHO Member States. A recommendation – or interim recommendation – concerning a specific product means that WHO has evaluated that product in laboratory and field trials and that the product has been found to meet the criteria and requirements of the Organization. Such recommendations do not imply any approval by WHO of the product in question (which is the sole prerogative of national authorities).

WHOPES publishes the reports of the Working Group meetings and makes the full text available for downloading on its web page (www.who.int/whopes). These reports all include a statement that a WHOPES recommendation does not constitute any assurance that the manufacture, distribution, sale and/or use of the product in question is in accordance with the national laws and regulations of any country, including, but not limited to, patent law. and that recommendations may not be used by manufacturers, suppliers or any other parties for commercial or promotional purposes.

During the period 1997–2009, more than 50 pesticide products were reviewed by meetings of the WHOPES Working Group (Figure 3). Among these products were: 11 for indoor residual spraying; 12 for use as mosquito larvicides; 3 for space spraying; 10 for conventional treatment of mosquito nets (including long-nets); 16 long-lasting insecticidal nets for WHO interim or full recommendations; and 2 mosquito repellents. The studies were carried out in 22 countries with the participation of more than 27 institutions.

3.4.4 Cooperation with FAO in a joint programme for the development of pesticide specifications

WHO specifications for public health pesticides are developed with the basic objective of promoting, as far as practicable, the manufacture, distribution and use of pesticides that meet basic quality requirements. They are regarded as a global benchmark of product quality.

Procedures for establishment of these specifications were instituted by WHO in 1953, and the first edition was published in 1956 (WHO, 1956). A corresponding process for crop protection products was initiated by FAO in 1963. The separate processes in WHO and FAO continued in parallel until 2001, at which point the two organizations agreed to develop specifications for pesticides jointly, thus providing unique, robust and universally applicable standards for pesticide quality. This joint programme was based on a Memorandum of Understanding signed by WHO and FAO in 2001 and as a follow-up to the recommendations of the Sixteenth WHO Expert Committee on Vector Biology and Control, which dealt with chemistry and specifications of pesticides (WHO, 2001).

The Manual on development and use of FAO and WHO specifications for pesticides (FAO, 2002) was the first publication of this joint programme and superseded all previous manuals and guidance documents published by either organization on this subject. The first revision of the manual was published, available only from the Internet, in 2006 (FAO/WHO, 2006). The manual provides standard processes, unified requirements and procedures, harmonized definitions and nomenclature, technical guidelines and standards applicable to pesticides for use in agriculture and public health. The FAO and WHO specifications for pesticides based on this manual are developed through the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS) and published on the web sites of both organizations.

WHO specifications for technical material, developed under the new procedure, do not necessarily apply to nominally similar products of other manufacturer(s) or to those whose active ingredient is produced by other procedures of manufacture. The scope of the specifications can be extended to similar products but only when the JMPS is satisfied that the additional products are equivalent to those that formed the basis of the reference specification.

Unless otherwise stated, WHO specifications for formulations developed under the new procedure encompass the products of all formulators legitimately able to certify that their products contain only active ingredient sourced from a manufacturer to whom the WHO specification for technical material applies. Buyers and/or regulatory authorities should demand such certification and ensure both that it is valid and that the products fully comply with the physical and chemical requirements of the WHO specifications.

Both the text of the specifications that follow the new procedure and those (full and interim) based on the old procedure, together with WHO analytical methods, may be accessed from the WHOPES web site (www.who.int/whopes/quality).

Between 2002 and 2009 more than 75 submissions were reviewed by the JMPS for development of WHO specifications for public health pesticides under the new procedure (see Figure 4).

3.4.5 Life cycle approach to pesticide management and expanding collaboration with FAO

The threats posed to the health of the population by the inappropriate use of pesticides have been an important concern of WHOPES since its early years. The safe use of pesticides was considered by the WHO Expert Committee on Insecticides and Vector Biology and Control, as well as by the expert committees on every vector-borne disease, and has been the subject of specific Study Group Meetings. WHOPES has also collaborated with FAO in the development of guidelines for the disposal of waste pesticides and for preventing the accumulation of obsolete insecticide stocks (WHO, 1983, 1985b and 2001; FAO, 1995 and 1996).

Critical aspects of public health pesticide management were reviewed and discussed at a WHO Interregional Consultation held in Chiang Mai, Thailand, 25–28 February 2003 (WHO, 2003 and 2005), as well as at the fifth GCDPP meeting, held in Geneva, 25–26 September 2006 (WHO, 2006b). The two meetings recognized that capacity strengthening for sound management of public health pesticides was a matter of priority because of:

- the increased use of insecticides for vector-borne disease control and personal protection;
- the growing challenges of managing these chemicals under decentralized health systems;
- the diminishing arsenal of safe and cost-effective insecticides and the need to extend the useful life of existing products; and
- inadequate national regulatory frameworks and human and financial capacity to regulate availability, sale and use of public health pesticides.

Regulatory weaknesses allow the excessive and unsafe use of pesticides, leading to pollutants in food, drinking-water and the environment, and a significant risk to human health. Substandard, illegal and counterfeit pesticide products available on the market are also of great concern, undermining expected pesticide efficacy and performance and threatening human health and the environment.

In recommending pesticides for health and agricultural use, respectively, WHO and FAO have a unique position within the United Nations system. Close collaboration between the two organizations, through their headquarters, regional offices and country representatives, is essential if they are to provide unified, coordinated and consistent advice on sound management practices to their Member States and to other stakeholders. In March 2007, FAO and WHO therefore signed a Memorandum of Understanding on cooperation in a joint programme on sound management of pesticides and established the FAO/WHO Joint Meeting on Pesticide Management (JMPM).

The International Code of Conduct on the Distribution and Use of Pesticides, originally adopted in 1985 by the FAO Conference and revised in 2002 (FAO, 1985 and 2003), promotes sound pesticide management practices that minimize potential health and environmental risks. The Code of Conduct describes the shared responsibility of many segments of society, including governments, industry, trade and international institutions, and serves as a framework for management of all pesticides, including those intended for agricultural and public health use.

Development of joint guidance documents to support Member States in implementing the Code of Conduct and in management of pesticides throughout their life cycle was given high priority by JMPM. The WHO guidelines, relating to public health pesticides, have been collected together on a separate page on the WHOPES web site to ensure easy access (http://www.who.int/whopes/recommendations/who_fao_guidelines/en/index.html). These guidelines

cover procedures for safe and effective application of insecticides for vector control, as well as WHO specifications for pesticide application equipment.

Periodically, WHO published specifications for pesticide application equipment. The first edition of ***Equipment for vector control*** — providing information on a wide variety of equipment that could be used for the dispersal of pesticides — was published in 1964 (WHO, 1964). The document included detailed specifications for the sprayers and dusters considered most important for vector control operations. Further editions have been published since that time (WHO, 1974 and 1990b).

In 2006, WHOPES published (and made available on its web page) ***Equipment for vector control: specification guidelines*** with the objective of standardizing the development of specifications for major equipment used to apply pesticides for the control of vectors (WHO, 2006a). The specifications guidelines are also intended to assist national authorities in selecting equipment of assured quality for the application of pesticides for vector control activities. They contain the minimum required standards advocated by WHO and reflect technological advances in the field; they therefore supersede earlier WHO specifications for such equipment.

The test methods described in the document are intended to assess whether equipment will function for a minimum of 3 years with routine maintenance according to the manufacturer's guidance.

Manufacturers are requested to provide warranties for their equipment, any certification required by national authorities regarding materials used in the construction of the equipment, and details of tests carried out for compliance with national or international specifications. If problems occur with equipment that is claimed to meet the published WHO specifications, feedback to WHO on the performance of the equipment will be welcomed and will be used in future revisions of the guidelines. Manufacturers are responsible for supplying operating and maintenance manuals in appropriate languages and, where necessary, for helping to train local staff in the proper use, routine maintenance and correct storage of equipment.

At the request of industry, WHO no longer tests application equipment for compliance with WHO specifications. Any national programme that wishes to have a specific item of equipment evaluated will be responsible for arranging a test with a recognized laboratory equipped to evaluate pesticide application equipment (e.g. a WHO Collaborating Centre).

Since 2006, WHOPES has developed and published detailed guidelines for efficacy testing of public health insecticide products with the aim of harmonizing procedures used by different laboratories and institutions and generating comparable data for the registration and labelling of such products by national regulatory authorities (see http://www.who.int/whopes/guidelines/en/). Similarly, in collaboration with the WHO Programme on Chemical Safety, it has developed generic risk assessment models for use of insecticides in public health.

A database for monitoring and publishing information on the global use of insecticides for vector-borne disease control has been developed by WHOPES; this database is unique and serves as a reference for sound management of public health pesticides. The fourth edition of ***Global insecticide use for vector–borne disease control*** was published in 2009 (WHO, 2009).

3.4.6 Intensified country support

Since its establishment, WHOPES has, through its normative functions, supported Member States in the safe and effective use and application of public health pesticides, including issues related to quality control of pesticides and application equipment; the last edition of these guidelines was issued by GCDPP (WHOPES/GCDPP, 2006).

In implementing the recommendations of the fifth meeting of GCDPP (WHO, 2006b), i.e. supporting Member States in "establishment of national regulatory frameworks as well as capacity strengthening on sound management of pesticides based on a critical needs assessment", WHOPES has jointly organized, and participated in, several regional and national workshops to promote sound management of public health pesticides.

The Scheme also increased its efforts to mobilize resources and in 2007 received a grant from the Bill and Melinda Gates Foundation to support 12 vector-borne disease endemic countries, mostly in Africa, in:

- facilitating the establishment of national regulatory frameworks and optimizing the registration of public health pesticides;
- strengthening country capacities for sound management of pesticides, including their judicious use to reduce the health and environmental impact of pesticide use/application; and
- reducing the trade in substandard pesticide products.

These activities have been carried out in the participating countries through strong multi-stakeholder collaboration, and in close cooperation with FAO and UNEP, to ensure complementary, harmonized and coordinated guidance to the responsible bodies at national level and to all stakeholders on sound management of pesticides.

WHOPES has been closely involved in capacity strengthening for vector control and sound management of public health pesticides through participation in WHO regional initiatives. It has also initiated the capacity strengthening of selected institutions for testing and evaluation of public health pesticides; this is currently ongoing in India, Malaysia and Viet Nam.

Figure 3. Number of pesticide products reviewed by Working Group meetings of the WHO Pesticide Evaluation Scheme, 1997–2009 (IRS = indoor residual spraying; L = larviciding; SS = space spray products; CTN = conventional treatment of mosquito nets; LN = long-lasting insecticidal mosquito net; RP = mosquito repellents)

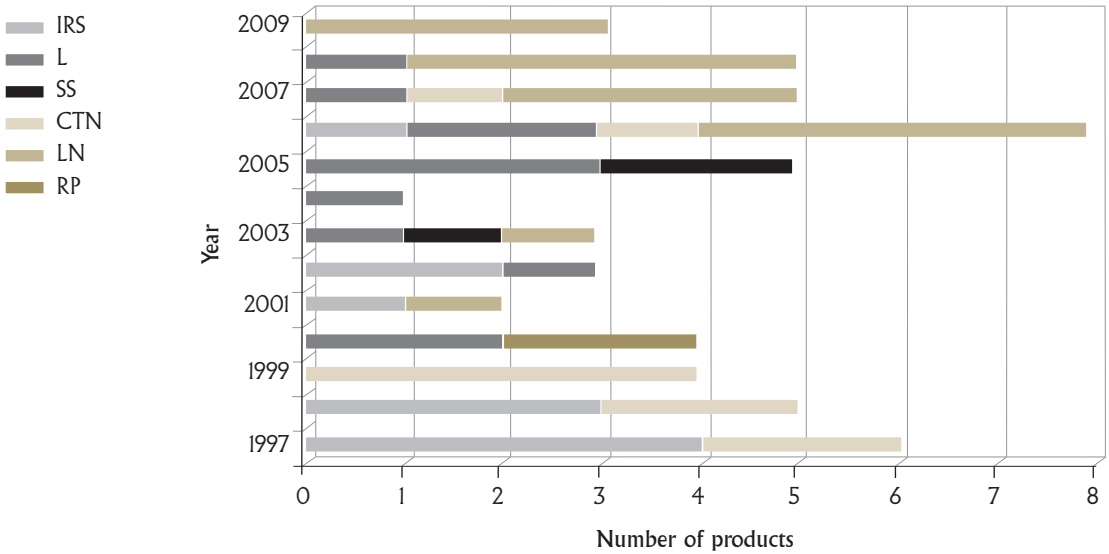


Figure 4. Number of submissions considered by the FAO/WHO Joint Meeting on Pesticide Specifications for development of WHO specifications for public health pesticides under the new procedure, 2002–2009

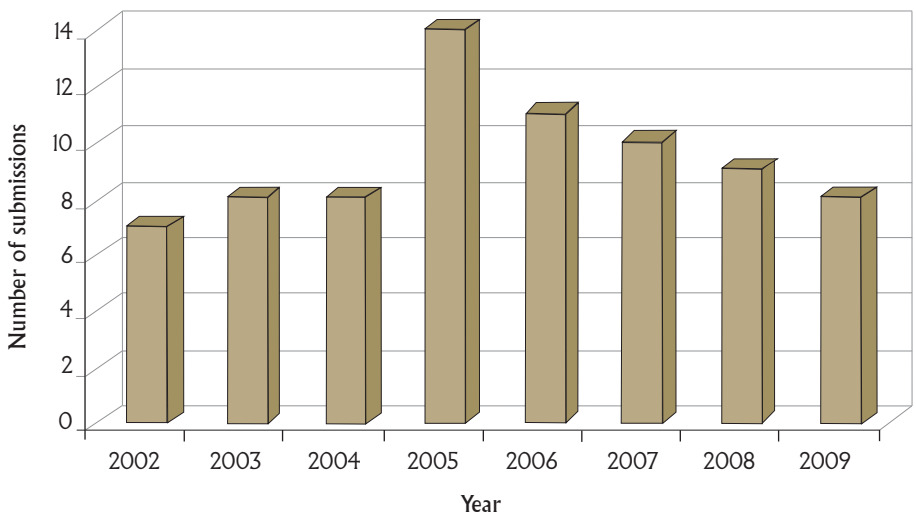
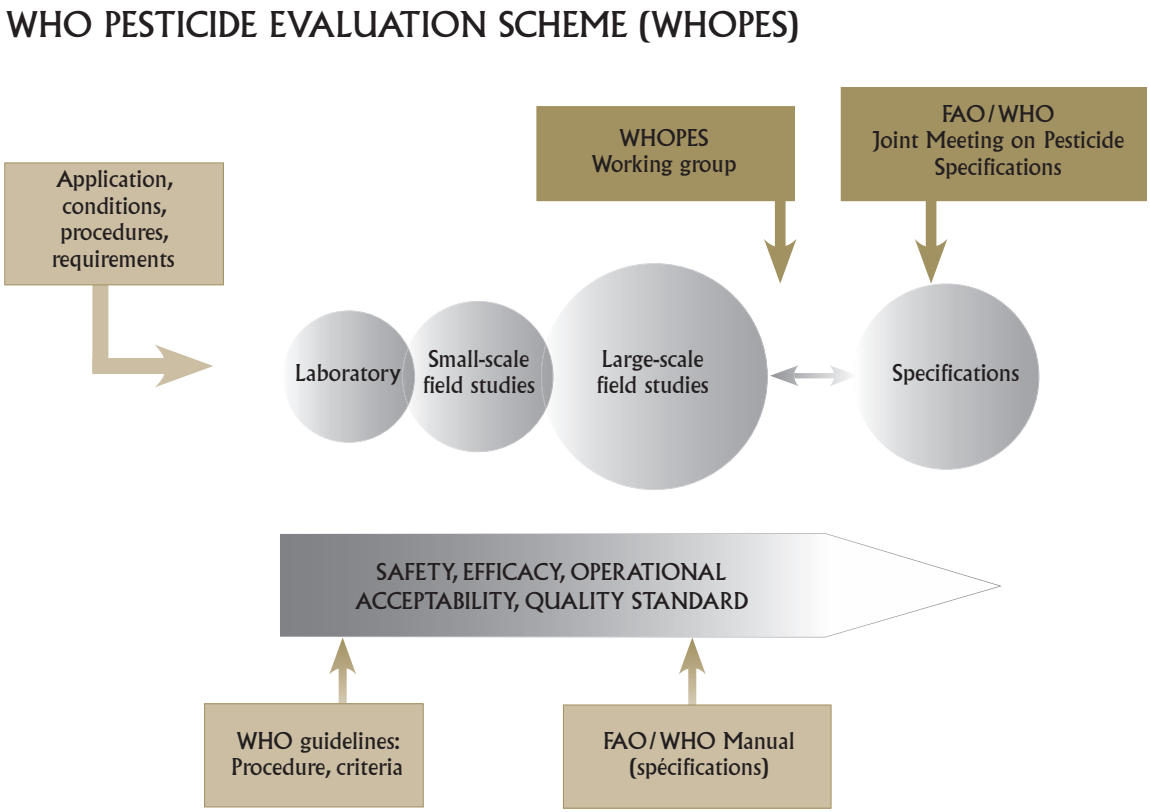
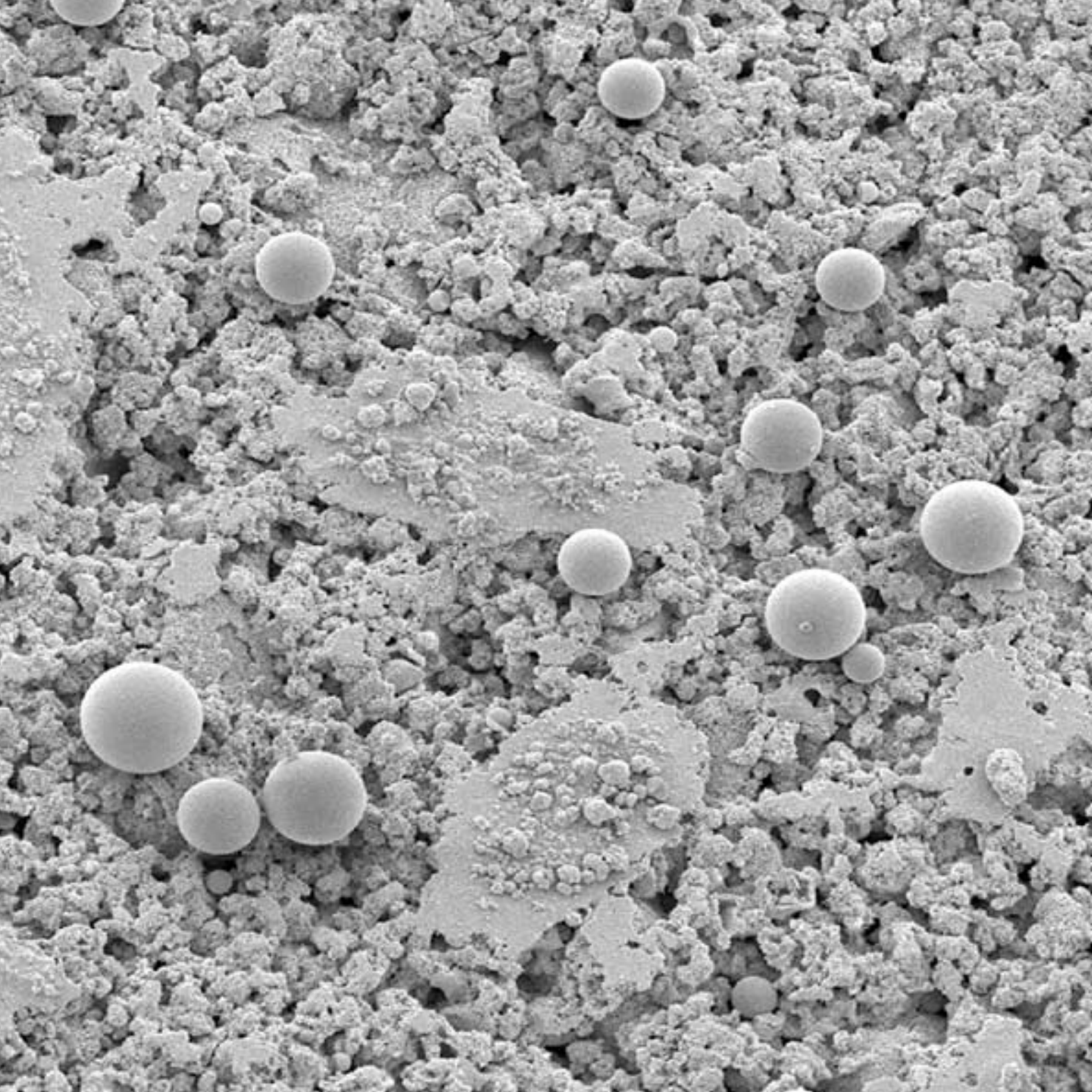


Figure 5. Schematic presentation of current WHOPES process





WHOPES

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ANNEX

Criteria used by the WHO programme for the evaluation and testing of new insecticides*.

Stage I, II and III

Stage I

Insect	Type of treatment	Exposure period	Criteria for acceptance
Adult mosquitoes	Residue	1 hour	24-hour mortality of 50% at 16 µg/cm²
Larval mosquitoes	Larvicide	24 hours	50% kill at 0.1 ppm
Adult houseflies	Topical application	24 hours	24-hour mortality of 50% at 1 µg/fly

Stage II

Insect	Type of treatment	Exposure period	Criteria for acceptance
Adult and larval mosquitoes and adult houseflies			
Adult mosquitoes	Residue	1 hour	70% 24-hour mortality for 8 weeks
	Space sprays	30 seconds	96% mortality at concentration 0.005–0.01%
		Momentary	LC_{90} = 0.05% or less
Larval mosquitoes	LC_{95} determination	24 hours	Variable, dependent on toxicity of compound for mammals; normally 1.0 ppm or less
	Residual larvicide	24 hours	Kill of 95% for 6 weeks
Adult houseflies	Residue	1 hour	90% mortality for 4 weeks
	Residues on plywood	30 minutes	70% mortality for 1 month
	Space sprays	Momentary	LC_{90} <1%
	Baits	24 hours	90% mortality at concentration <0.005%
		1 hour	70% mortality at 24 hours
	Impregnated cords	1 hour	100% mortality for 2 months
***Triatoma*, lice, fleas, bedbugs and ticks**			
Adult and immature *Triatoma*	Residues on plywood	2 hours	70% mortality for 2 weeks
Adult lice	Powders on cloth	24 hours	90% mortality for 2 weeks
Adult fleas	Residues on paper	24 hours	90% mortality for 4 weeks
Adult bedbugs	Residues on paper	24 hours	90% mortality for 4 weeks
Ticks	Residues on paper	24 hours	90% mortality at 20 mg/m²

Stage III

Insect	Type of treatment	Exposure period	Criteria for acceptance
Adult mosquitoes	Residue (interior application)	1 hour	90% mortality for 8 weeks
	Residue (exterior application)	1 hour	70% mortality for 8 weeks
	Residual fumigant	12 hours	70% mortality for 6 weeks in ventilated huts
Larval mosquitoes	Residual larvicide drums	24 hours	70% or greater mortality for 8 weeks
	Small containers	24 hours	70% mortality 12 weeks
	Pre-flood (field)	24 hours	70% or greater mortality for 8 weeks
Adult lice	Sleeve (powder)	24 hours	90% mortality for 1 week
Fleas	Dust	24 hours	LC_{95} = 5%

* Source: Wright JW (1971). The WHO programme for the evaluation and testing of new insecticides. Bulletin of the World Health Organization, 44(1–3):11–22.

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