REPORT OF THE SEVENTH MEETING OF THE GLOBAL COLLABORATION FOR DEVELOPMENT OF PESTICIDES FOR PUBLIC HEALTH

GCDPP

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1. INTRODUCTION

The seventh meeting of the Global Collaboration for Development of Pesticides for Public Health was held at the Centre International de Conférence de Genève in Geneva, Switzerland, on 24–25 June 2010.

Dr Hiroki Nakatani, Assistant Director-General for HIV/AIDS, Tuberculosis, Malaria and Neglected Tropical Diseases in the World Health Organization (WHO), opened the meeting and read a message[1] from the Director-General. WHO is celebrating the 50th anniversary of the WHO Pesticide Evaluation Scheme (WHOPES), established in 1960 by the Director-General, with the approval of the World Health Assembly, to evaluate pesticides for the control of vector-borne diseases and to prepare quality standards for the guidance of Member States. During those 50 years, WHOPES has consolidated its position as a cross-cutting programme of WHO, now based in the Vector Ecology and Management Unit of the Department of Control of Neglected Tropical Diseases, to support United Nations agencies and WHO programmes and to assist Member States in implementing vector control programmes safely and judiciously.

During the past 10 years, more than 40 pesticides have been evaluated for public health use, and more than 70 submissions for WHO specifications and quality standards for public health pesticides have been reviewed. WHOPES has also produced documentation and guidelines to support Member States in vector management. The testing and evaluation of insecticide-treated nets (ITNs) has been particularly important, providing a simple, practical, cost-effective weapon against malaria and other vector-borne diseases.

WHOPES has strengthened its collaboration with the Food and Agriculture Organization of the United Nations (FAO) to ensure complementary, harmonized, coordinated guidance and support to Member States and stakeholders in managing pesticides throughout their life-cycle.

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[1] The full message is available on the WHO website at: http://www.who.int/whopes/WHOPES_50_anniversary_DG_speech.pdf.

The emergence and re-emergence of vector-borne diseases, which may be aggravated by climate change in many parts of the world, calls for greater attention to these conditions, which account for about 17% of the estimated global burden of communicable diseases. As pesticides are still the most important element in the integrated approach to vector control, greater vigilance and better management of insecticide resistance is necessary, particularly in the control of malaria and dengue, as the number of potential replacement insecticides is rapidly shrinking. In particular, the successes achieved with the use of pyrethroid-treated mosquito nets are in danger if alternative insecticides are not developed in the near future.

Even if safety is an important consideration in the recommended use of pesticides, inappropriate use may result in adverse acute or chronic effects on humans and the environment. Yet, a significant number of countries in tropical and subtropical regions of the world do not have adequate national regulatory frameworks or the human or financial capacity to regulate the availability, sale and judicious use of pesticides. Furthermore, the availability of substandard, illegal and counterfeit products is increasing in many countries, posing additional health risks and straining their limited regulatory and enforcement capacity.

In May 2010, the Sixty-third World Health Assembly recommended establishing or strengthening capacity to regulate pesticides, with strong commitment from WHO to work with all stakeholders on the sound management of these chemicals. WHO will continue to support WHOPES in strengthening its collaboration with other agencies of the United Nations, such as FAO and the United Nations Environment Programme (UNEP), nongovernmental organizations and the pesticide industry to mobilize resources to strengthen national capacity. These efforts will require increased investment in research and development of new strategies of vector control and personal protection, in close collaboration with partners that include research institutions and academia.

Dr Nakatani welcomed the participants, recognizing the importance of the Global Collaboration for Development of

Pesticides for Public Health as a consultative group to WHOPES, with its broad constituency of experts from diverse backgrounds and functions, including government-supported agencies, manufacturers of pesticides and pesticide application equipment, United Nations agencies, WHO collaborating centres and research institutions.

2. COMMEMORATION OF 50 YEARS OF GLOBAL LEADERSHIP IN STANDARD-SETTING AND EVALUATION OF PUBLIC HEALTH PESTICIDES

Dr Lorenzo Savioli, Director of the WHO Department of Control of Neglected Tropical Diseases, reviewed the history of WHOPES since its establishment in 1960 and presented a document[2] on this topic. He reviewed the rapid spread of use of DDT and other residual insecticides for the control of malaria and other vector-borne diseases during the early 1950s, the increasing demand for technical advice and the response of WHO, which set up the Expert Panel on Insecticides in 1949. After the launching of the global malaria eradication campaign, increased use of insecticides and the emergence of insecticide resistance created a demand for replacement insecticides. WHO responded by establishing a programme for evaluating and testing new insecticides in 1960, which evolved into WHOPES in response to the changing requirements of Member States. The programme has progressively expanded its functions to other public health uses of insecticides, the impact on public health of other uses of pesticides and judicious use of pesticides and other control agents in integrated vector management.

Since its beginning, the programme has been a collaborative effort between WHO, industry, research institutions and

[2] *WHO Pesticide Evaluation Scheme: 50 years of global leadership*. Geneva, World Health Organization, 2010 (WHO/HTM/NTD/WHOPES/2010.2). Available at http://whqlibdoc.who.int/publications/2010/9789241599276_eng.pdf.

Member States. Although it has gone through several periods of reorientation, WHOPES maintains as its priorities:

- strengthening the capacity of Member States for judicious use and life-cycle management of pesticides and minimizing risks to human health and the environment;
- harmonizing registration procedures and requirements and exchanges of information and work;
- facilitating the development of alternative pesticides and innovative technology;
- broadening its scope to include evaluation of the full range of public health pesticides;
- maximizing coordination, collaboration and networking; and
- strengthening the capacity of the Scheme within the WHO department of Vector Ecology and Management.

In order to mark the event, a plaque was presented as a memento to selected institutions and individuals, in recognition of their contributions to the work of WHOPES. The institutions that received this award were: the Institut de Recherche pour le Développement, France; the Wallon Agricultural Research Centre, Gembloux, Belgium; the Indian Council of Medical Research, India (conferred in absentia); Imperial College at Silwood Park, United Kingdom; the United States Centers for Disease Control and Prevention, United States of America (USA); the London School of Hygiene and Tropical Medicine, United Kingdom; the Universiti Sains Malaysia, Malaysia; the Center for Medical, Agricultural, and Veterinary Entomology, United States Department of Agriculture, USA; FAO; UNEP Chemicals, Switzerland ; and CropLife International, Belgium. The individuals who received the award were: Professor Mir S. Mulla, University of California, Riverside, California, USA; Professor Graham Matthews, Imperial College, Ascot, United Kingdom; Professor Mark Coosemans, Institute of Tropical Medicine, Antwerp, Belgium; Mr Alan Hill, York, United Kingdom (conferred in absentia); and Dr Kathryn Aultman, Bill and Melinda Gates Foundation, USA.

3. PESTICIDES FOR VECTOR CONTROL

3.1 Emerging and re-emerging vector-borne diseases

Dr Ron Rosenberg, United States Centers for Disease Control and Prevention, addressed the challenge of controlling emerging vector-borne diseases. He defined 'emerging diseases' as those that quickly move from obscurity to epidemic threat. All classes of pathogens—viruses, protozoa, bacteria, fungi and helminths—can become emergent. The mechanisms for emergence include changing economics, demography or behaviour, as for example in the case of tick-borne encephalitis; rapid movement of people and goods, e.g. severe acute respiratory syndrome (SARS); selection pressure, such as when a pathogen that is already common in humans mutates to become drug resistant or more pathogenic; and changing ecology or climate, as in the case of Lyme disease. In other cases, a pathogen endemic in one area is transported to a naive geographical location. Increasingly common, however, is the jump of a pathogen from animals to humans. During the past 25 years, we have begun to recognize how dangerous zoonotic transmission can be: HIV, SARS, avian influenza, *Escherichia coli* H157:O7 and a variety of Hanta viruses are sobering examples. Although any pathogen can emerge, single-stranded RNA viruses are disproportionately represented because of their remarkably high mutation rates and ubiquity (of the preceding examples, only H157:O7 is not an RNA virus).

Of the more than 1400 known species of human pathogen, more than 90 have been discovered since 1987, and more than half of these are RNA viruses. Rapid global movement of people and goods and increasing human manipulation of and encroachment on the environment appear to accelerate the emergence, with an average of three emergents annually over the past 50 years. Most emerging pathogens are recognized only after long delays, as it is difficult to diagnose the unknown.

The more than 500 known arboviruses fall into three major families: flaviviruses, bunyaviruses and alphaviruses. During the past 5 years, we have seen continent-wide resurgences of dengue (flavivirus), epidemic Rift Valley fever (bunyavirus) in Africa, pandemic chikungunya (alphavirus) in the Indian Ocean region, the spread of West Nile virus (flavivirus) across North America, the introduction of Usutu (flavi) to Europe and an outbreak of Zika (flavi) in Micronesia. There are no commercially available human vaccines against any of these viruses nor any curative therapy.

There are not only are multiple species of vector but also multiple mosquito genera. Notably, all arboviruses appear to be zoonotic. Some, such as those that cause dengue and chikungunya, have adapted to predominantly human–human transmission, while others, such as West Nile and Rift Valley, still depend on animal–human transmission.

The role of vectors in abetting emergence is unusually complex and poorly appreciated. Vectors serve as a bridge between animal reservoirs and humans that often have no direct contact; they may also bridge ecological niches, e.g. forest to village to city, and they may increase the opportunities for viral mutation, pathogen amplification or transformation. Vectors may also increase the opportunities for emergence without increased pathogenicity to humans. For example, a single nucleotide mutation during 2006 in the 12 000-base genome of chikungunya increased the replication and dissemination of the virus in *Aedes albopictus*, which in many areas had supplanted *Ae. aegypti*. The virus did not become more pathogenic to humans but became more rapidly transmitted in more places, causing more disease. Similarly, a single base mutation in West Nile virus increased transmission to humans by increasing its virulence to birds, which in turn infected more culicine mosquitoes.

The emergence of new pathogen threats will certainly continue at the current or a higher rate, and most will be RNA viruses, many of which will be vector-borne. It is unlikely that there will soon be a means of predicting which viruses have emergent potential. The practical hope will be to detect animal or human outbreaks early and move to contain them before they spread. In the absence of vaccines or drugs, that containment must be directed against the vector. Too little attention is being paid to this beneficial aspect of insecticide development. The advantage of insecticides over highly specific control strategies, such as the development of transgenic mosquitoes or sterile insect releases, is that they are broadly efficacious. In developing, testing and delivering insecticides, it is also necessary to consider the inevitable need, beyond *Anopheles*, for broad-based pesticides and targeted delivery systems.

3.2 Malaria elimination: role of vector control

Dr Brian Greenwood, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, recalled that, in October 2007, Melinda and Bill Gates challenged the malaria community to extend their ambition from achieving control of malaria as a public health problem to one that encompassed elimination of malaria within the foreseeable future. This challenge was initially met with scepticism in many quarters, but it stimulated scientists to evaluate more carefully the situations in which elimination of malaria (interruption of local transmission) might be feasible within the next 5–10 years and to consider how to adapt malaria research to this new goal.

The first malaria eradication programme (1955–1969) is generally considered to have been a failure, as the malaria parasite was not eradicated; in many ways, however, it was successful, as the threat of malaria was eliminated from large areas of the globe. As the world contemplates a new malaria elimination or eradication programme, it is useful to review some of the successes and failures of the first programme to ensure that its mistakes are not repeated.

Many reasons have been identified for the failure of some aspects of the campaign: an unrealistic objective, which was not marketed properly; an overly ‘vertical’ programme; premature interruption of control; too great a reliance on a single measure, indoor residual spraying (IRS); biological and social resistance to IRS with DDT; little iterative research; and limited involvement of scientists in endemic countries. The sense of failure led to a considerable decline in donor support for malaria control during the 1970s and 1980s, even though the epidemiological reality pointed to the need for continued malaria control, and endemic countries, with the support of WHO, demanded higher priority for malaria control in international health, concretized in the Amsterdam Declaration of 1992.

Before the announcement of the Bill and Melinda Gates Foundation on malaria eradication in 2007, WHO had been supporting malaria elimination activities in Europe, North Africa, the Middle East and the newly independent states with considerable success, but this effort had not received much publicity and was not widely known by the malaria community. There had been increased political commitment to malaria control in endemic and industrialized countries, with a considerable increase in funding for malaria control from donors such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, the United States President's Malaria Initiative, the World Bank and some bilateral donors, to a level of US$ 2 billion per year. Furthermore, some reasonably effective tools (e.g. artemisinin-based combination therapy and long-lasting insecticide-treated nets [LLINs]) had become available. During the past few years, transmission has probably been interrupted in several countries, and, in 2010, Morocco was officially declared free of malaria by WHO.

After the Seattle meeting in 2007, the Global Health Group at the University of California, led by Sir Richard Feachem, established the Malaria Elimination Group,[3] which has produced two important documents on the factors to be considered by a country considering elimination and which has provided advice to countries that have decided to set out on this course. MalERA[4], a group led by Professor Pedro Alonso at the University of Barcelona, has been asked by the Bill and Gates Foundation to review the malaria research agenda with increasing focus on elimination. Several working groups, including one on vector control, have been established and will present their findings in a series of papers later this year.

It is highly likely that vector control will play a key role in any new elimination programme. Two situations can be envisaged. The first is that of countries in which the propensity for malaria transmission is naturally low because of the paucity of vectors

[3] www.malariaeliminationgroup.org.
[4] http:malera.tropika.net.

or their relative inefficiency as transmitters of malaria. Many of the countries likely to achieve malaria elimination in the near future fall into this category. In some of these countries, the main malaria vectors are not well characterized and bite and rest outdoors and so are not well controlled by the vector control measures currently most widely used: ITNs and IRS. In these countries, more imaginative vector control tools may be needed to take into account the local epidemiological situation.

The second situation in which elimination may be contemplated is that of countries in which there are effective vectors but for which strong control has been achieved by widespread deployment of conventional methods such IRS and ITNs. Sustaining this success will require management of the problem of resistance to the insecticides used in these two tools. It is likely, however, that in areas with high vectorial capacity, IRS and ITNs alone will not be sufficient to stop transmission, even when effective insecticides are used, and that an additional tool will be needed, which might be an entirely new form of vector control, such as genetically modified mosquitoes, or might involve use of a complementary tool such as a vaccine with transmission blocking properties.

Malaria control, especially in Africa, currently largely depends on effective treatment of cases with artemisinin-based combination therapy and prevention of infection with IRS and ITNs. Ensuring high, equitable coverage with these tools requires special skills, which may not necessarily be those of biologists. As the focus turns to elimination in areas where this may be feasible and in areas where generally effective control measures appear to be failing, the skills of entomologists, parasitologists and social scientists will increasingly be needed. Recent success in malaria control should not be an excuse for reducing the training of entomologists and parasitologists but rather the reverse: malaria elimination will require more malaria entomologists than ever before.

The new focus on elimination has excited the malaria community, and it is appropriate that attention should be given to defining areas where this is a feasible option in the short to medium term and to the research agenda that will be needed to achieve it. It is essential, however, that enthusiasm for elimination not detract from the need to control malaria and to find ways of doing this better in the large areas of the malaria-endemic world where elimination is not yet an achievable goal.

4. PARTNERSHIPS FOR PESTICIDE MANAGEMENT AND DEVELOPMENT

4.1 Code of conduct on the distribution and use of pesticides: joint FAO/WHO programme on sound management of pesticides

Dr Mark Davis, FAO, introduced the *International code of conduct on the distribution and use of pesticides*,[5] which was one of the first voluntary codes of conduct adopted in a broad framework of support for increased food security while at the same time protecting human health and the environment. It was adopted in 1985 by the FAO Conference at its Twenty-third Session, thus making it one of the first frameworks to guide countries in the management of chemicals. The Code established voluntary standards of conduct for all public and private entities engaged in, or associated with, the distribution and use of pesticides, and since its adoption has served as the globally accepted standard for pesticide management.

The Code, and its supporting technical guidelines, has helped countries to put in place or strengthen pesticide management systems. The number of countries without legislation to regulate the distribution and use of pesticides has greatly decreased; awareness of the potential problems associated with pesticide use has grown significantly; involvement in various aspects of pesticide management by nongovernmental organizations and the pesticide industry has been strengthened; and many more successful integrated pest management programmes have been implemented in developing countries.

[5] *International code of conduct on the distribution and use of pesticides* (revised). Rome, Food and Agricultural Organization of the United Nations, 2003. http://www.fao.org/docrep/005/Y4544E/y4544e00.htm.

Today, following revisions in 1989 and 2002, the Code provides a solid foundation to guide governments, pesticide manufacturers and traders, nongovernmental organizations, pesticide users, policy-makers and legislators in the management of pesticides ‘from the cradle to the grave’. It is a carefully and comprehensively considered document that in 12 articles addresses every aspect of pesticide management.

The central role of FAO in pesticides management is largely a reflection of the fact that most pesticides are used in agriculture. Nevertheless, pesticides have always also been used in the health sector to control disease vectors, such as mosquitoes carrying malaria and dengue fever, sandflies transmitting leishmaniasis and plague-transmitting rodents. Similarly, it is the health sector that is concerned with the potential and actual toxic effects of pesticides to both people who have been directly exposed and those indirectly exposed through contaminated food or water.

FAO and WHO have collaborated for as long as the Code of Conduct has been in place. The two organizations have consistently worked together to prepare pesticide hazard information sheets, recommend maximum residue limits for pesticides in agricultural produce, determine technical specifications for pesticide formulations and improve the overall management of pesticides.

In 2007, a memorandum of understanding was signed between FAO and WHO for the joint development and implementation of the Code of Conduct. Both WHO and FAO established a panel of experts to support the Code, which meet annually in the Joint Meeting on Pesticides Management to discuss policy and technical issues and offer guidance to FAO and WHO on more effective approaches to pesticide management.

Today, the Code stands alongside the Basel, Rotterdam and Stockholm conventions, the Montreal Protocol and the Strategic Alliance for International Chemicals Management as one of the pillars of chemicals management. The Code is unique in the comprehensive life-cycle management approach that it has recommended for 25 years, and it comes as no surprise that international efforts to develop management strategies for chemicals in sectors other than agriculture and health are emulating the Pesticides Code of Conduct in their approach.

Several factors differentiate pesticides from other chemicals. They are designed to be toxic to living organisms, and they are intentionally dispersed in the environment and applied to food crops and in peoples' homes. There are over 900 active ingredients for pesticides, which are formulated into tens of thousands of products, and they are used by more people than any other group of hazardous materials. Pesticide users are often poor, poorly educated and poorly equipped to use them without causing harm to themselves, other people and the environment.

Twenty-five years after adoption of the Code, much remains to be done. Legislation in many countries is outdated and incoherent with modern practices and technology. Few developing countries have the capacity to evaluate and register the pesticides that are suitable for their needs while keeping risks at acceptably low levels. As a result, highly hazardous pesticides continue to be used. Countries need guidance on reducing reliance on these chemicals and replacing them with less hazardous pest management options. Few developing countries or countries with economies in transition have the technical, human and financial capacity to operate laboratories that allow them to test pesticides for compliance with the specifications that FAO and WHO have set for pesticide quality, or to test food for pesticide residues. Most countries do not have the infrastructure to take pesticide containers out of circulation and to dispose of waste pesticides safely.

It is, therefore, necessary to continue strengthening national capacity to: reduce the risks of highly hazardous pesticides; introduce non-chemical controls through integrated pest or vector management; use less hazardous pesticides; and improve pesticide application with better personal protection. These goals can be achieved through legislation, regulation and enforcement, registration and quality control, and post-registration controls.

FAO and WHO will increase their efforts, through closer collaboration between themselves and other strategic partners, including UNEP, other intergovernmental organizations, civil society and the private sector, to help countries to implement the Code more effectively. The sustainability of such efforts requires not only financial and human resources in the short term but also continuity in the provision of support to countries to ensure that they take ownership of the issues.

Pesticide management is not an end in itself but must be contextualized with sustainable intensification of crop production in the agricultural sector and reduction of vector-borne disease transmission in the health sector. These objectives remain our two organizations' goals, and, where pesticides play a constructive role in their achievement, they must be managed effectively. That is the role of the International Code of Conduct on the Distribution and Use of Pesticides.

4.2 Integrated vector management and capacity-building

Dr Michael Macdonald remarked on the considerable increase in global investment in malaria control during the past 10 years, 68% of which is for vector control, mainly through extension of the use of IRS and distribution of ITNs, which has reached 307 million (192 delivered and 115 in active tender) since 2008. This progress is nevertheless threatened by the development of resistance to pyrethroids, which are the basis of ITNs and of most current IRS. Pyrethroid resistance, first detected in West Africa, is now being found in southern and East Africa, particularly in Ethiopia, Malawi and Zambia. The sustainability of current achievements, essential for progress towards elimination, requires timely monitoring and mitigation of insecticide resistance and the ability to complement or replace interventions threatened by resistance.

The proposal that integrated vector management be used for rational decision-making on the optimal use of resources for vector control has not only a sound theoretical basis but is increasingly supported by field experience. WHO issued guidelines for integrated vector management in its document

Global strategic framework for integrated vector management,[6] which lists five key elements: advocacy, social mobilization and legislation; cross-sector collaboration; an integrated approach; evidence-based decision-making; and capacity-building.

For integrated vector management, capacity must be built to gradually achieve, consolidate and maintain gains; manage insecticides in a safe, judicious and environmentally compliant manner; use new tools, including personal protection; manage insecticide resistance; and monitor and adapt to climate change. These objectives are pursued through:

- training handbooks, in collaboration between WHO, the United States Centers for Disease Control and Prevention and the United States Armed Forces Pest Management Board;
- support for national training and programme development, including the Corporate Alliance on Malaria in Africa, e.g. in Angola;
- workshops on best practices in pesticide management, e.g. in Kenya; and
- an inventory and network of national training and research institutes, e.g. 27 institutions for entomology and vector control identified in 18 countries in Africa.

Malaria elimination will require not only a massive increase in investment but also the development of human resources to improve resistance monitoring and management and new tools and systems to attain and sustain elimination.

4.3 Collaboration with international instruments: the Stockholm Convention and the Strategic Alliance for International Chemicals Management

Dr Agneta Sundén Byléhn, UNEP Chemicals, Geneva, recalled that negotiations for the Stockholm Convention on Persistent

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6 *Global strategic framework for integrated vector management*. Geneva, World Health Organization, 2004 (WHO/CDS/CPE/PVC/2004.10).

Organic Pollutants were initiated in the mid-1990s. Since then, UNEP has intensified its cooperation with WHO and FAO to assist countries in identifying more sustainable alternatives to pesticides containing persistent organic pollutants, including the 'drins', termiticides and, not least, DDT. The mandate to draw up the Treaty clearly stated that none of its measures should adversely affect public health; therefore, the use of DDT in disease vector control was given special status, as this is considered an acceptable purpose. Nevertheless, the Treaty imposes certain requirements on Parties that use DDT.

The cooperation between UNEP and WHO emphasizes working towards a win–win situation in implementation of the Convention, with strengthened disease vector control and less DDT. In that spirit, UNEP collaborates with WHO and FAO to promote both integrated vector management and integrated vector and pest management by distributing guidance materials, holding subregional workshops involving government officials responsible for public health, the environment and agriculture, and establishing projects in countries that still use DDT or may need to revert to DDT for disease vector control. UNEP Chemicals and WHOPES have furthermore collaborated to enhance pesticide management capacity through technical advice and training. UNEP is examining options for disposing and recycling ITNs at the end of their life.

Recently, UNEP has been cooperating in more general pesticide management with FAO in the framework of the Strategic Alliance for International Chemicals Management, adopted in 2006, and the International Code of Conduct. UNEP contributes mainly to the environmental dimension and has established an expert group to provide science-based advice on environmental issues linked to chemicals, including the protection of wildlife, ecosystems and ecosystem services (especially water), environmental resources and environmental influences on the behaviour of chemicals. The expert group will first discuss pesticides identified as priorities at a meeting held in 2009 with people responsible for pesticide management in developing countries and countries with economies in transition.

UNEP is also engaging experts to update a review on endocrine disruptors prepared by the International Programme on Chemical Safety. This work represents a vision of the future, as it involves exposure to multiple chemicals. This issue has gained in importance with increased understanding of biochemical receptors and the additive and sometimes synergistic effects of multiple chemicals. In recent studies in Denmark, 2-year-old children were found to have additive risks after exposure to multiple chemicals, including pesticides, with anti-androgenic and -oestrogenic effects, and similar additive effects have been found in wildlife. Endocrine disruptors like phthalates and brominated flame retardants occur in many commonly used products, such as infant feeding bottles and textiles. Newborn infants have hundreds of such chemicals in their blood after exposure in utero.

Exposure to multiple chemicals also directly affects vector control, increasing pressure for developing resistance. Pesticides, like antibiotics, are important for combating disease, and loss of effectiveness will have grave consequences for public health and economic growth. As it is difficult and costly to develop new active ingredient, it is necessary to explore whether more can be done to preserve the effectiveness of existing pesticides.

The Code of Conduct assists countries to address the adverse effects of pesticides, and UNEP is envisaging using the Code of Conduct as a model for managing other types of chemicals used in other sectors and products through implementation of the environmental component of the Strategic Alliance for International Chemicals Management. The Alliance was established after recognition of a growing gap between the capacity of developing countries to manage chemicals and the increasing production and use of chemicals in those countries. The Alliance also recognizes a lack of coherence in the management of risks between sectors. The collaborative work to promote integrated vector and pest management has shown that win–win situations can be created for public health, the environment and agriculture by intersectoral collaboration and better understanding of the issues and the potential for complementary, synergistic benefits from coordinated and joint efforts.

Work on the issues associated with the presence of chemicals in common products has shown how little control there is and how little the producers of the products know about the chemicals in the production chain. Pesticides used in public health are also used in agriculture, in much greater volumes. Experience with e.g. DDT has shown the importance of the development of resistance in disease vectors due to agricultural uses, including for non-food crops. Agriculture is not, however, the only source of resistance pressure, as pesticides are also used in consumer products such as construction materials and furniture, from which they can be released. They also find their way into the environment during production, formulation and repackaging.

With these issues in mind, the international community might consider the need and benefit of advice on risk management, release reduction and other measures during the production of pesticides and pesticide-containing materials, in order to reduce exposure of humans and the environment, including disease vectors.

4.4 Partnership and coordination: keys to success

Dr Kate Aultman, Bill and Melinda Gates Foundation, said that the key to success is partnership and coordination among multinational agro-chemical companies, mid-range industries and small innovators, even those with little capacity for research and development; public health practitioners, including programmes such as national programmes for malaria control; national regulatory authorities; multilateral organizations, including United Nations agencies and the WHO Roll Back Malaria programme; academic institutions; and product development partnerships. The Global Collaboration for Development of Pesticides for Public Health is a good example of collaboration in the development of vector control products.

Through collaboration, these partners can address cross-cutting issues that impede innovation in vector control, which include market concerns, like how to scale-up, deliver and finance the use of vector control products, policies for optimal use and procurement issues. Additional benefits of coordination are information exchange, establishing expectations and managing competition. Joint efforts can provide investment for new products, after predicting and quantifying the public health impact and validating estimates against actual data.

The main result of collaboration is a common vision of ‘success'. The efficacy of vector control products is based on simple measures of entomological impact, mortality and repellency. Another vision of success, such as interruption of transmission or reduced biting pressure, will lead to more refined, more useful definitions. In the field of drugs against malaria, success is defined as a drug that results in radical cure and prophylaxis after a single dose. A common vision of success will allow definition of a target product profile, which will set clear benchmarks for the performance of candidate products and provide a simple, concrete basis for comparison. The Bill and Melinda Gates Foundation is working with grantees to define target product profiles, with the end-points of efficacy (phases 1, 2 and 3), safety (depending on route of application) and effectiveness, including in the community. Other features are cost, acceptability, deliverability and environmental soundness.

A common vision of success in vector control will also allow definition of the tools required to achieve it. Experience with malaria vector control in Africa highlighted the role of exophilic vectors, which are poorly controlled by indoor interventions such as IRS and the use of LLINs. Analysis of the effects of new products on the basis of vector behaviour and ecology should highlight gaps to be filled by new products.

The Gates Foundation has initiated a project to support coordination, known as the Vector Control Development Network, a virtual network for coordination and integration, run by a staff of five to seven people. A few partners are now involved, but it is expected to grow and will eventually be open to all. Its goal is to identify the effect of vector control products on disease transmission; the initial focus is vector control, but other elements of the transmission cycle will be added. The Network will achieve its goals by sharing data and designing interactive tools and shared models. The main objectives include:

- estimating the ability of candidate products to reduce transmission;
- drawing up concrete target product profiles;
- defining the optimal, minimal set of products for elimination or eradication within specific epidemiological, environmental and political contexts;
- supporting communities in preparing investment proposals and guiding product development; and
- setting a common vision for vector control.

The underlying premises of the Network are that the bionomic traits of vectors (behaviour, ecology and physiology, including resistance) are the main determinants of the effectiveness of products, and that bionomic traits are stable and fixed and associated with the taxa of the vector (including species, sibling species and chromosomal forms). Nevertheless, the composition of vector communities must be clarified, including 'species' richness, diversity and their roles in supporting pathogen transmission.

The project should also contribute to the development of new products for vector control, as the Global Collaboration for Development of Pesticides for Public Health and WHOPES have done for 50 years.

5. CHALLENGES AND MANAGEMENT OF NEW PUBLIC HEALTH PESTICIDES

5.1 Development of new public health pesticides

Mr Egon Weinmueller, BASF, on behalf of the CropLife vector control industry, introduced the 'CropLife Vector Control Project Team', consisting of representatives of the main pesticide industries: BASF, Bayer CropScience, Bestnet, Clarke Mosquito Control, Dupont, Sumitomo Chemical/Valent Biosciences, Syngenta, Tana Netting and Vestergaard Frandsen. The objectives of the team are to act as an authorized representative of the industry to negotiate with international or local authorities on all matters affecting the activities of its members; to build and defend a positive image of the industry; to establish a common position of the industry on issues affecting public health and to work with international and national regulatory authorities to ensure harmonized regulation for public health insecticides.

The team has helped to increase the speed of recommendation of products by WHOPES; to harmonize the position of industry, including regulatory frameworks and insecticide resistance management; and to share responsible stewardship policy (quality monitoring and improvement, disposal, training, code of conduct, safe use, integrated vector management). It has also participated in several Roll Back Malaria working groups, such as that on vector control.

Industry supports and promotes the principles of integrated vector and insecticide resistance management, for which alternatives to DDT will be required. More information about resistance status and transmission season will be needed to guide the choice of intervention, and all potential interventions must be evaluated for their effect, so that decisions are based on evidence. Local capacity to implement integrated vector management successfully and maintain it in the long term remains a challenge. Guidelines for the management of resistance have been published by the public health team.

Currently, 12 insecticides are recommended for use in IRS. New formulations have been shown to be effective for 6–12 months and are under further development or being marketed. Decisions on their use depend on many factors.

LLINs are a cost-effective alternative to or complement other integrated vector management tools. They are simple to use, and high coverage can ensure protection at community level similar to that of IRS. Research on the combination of LLINs and IRS shows excellent complementarity, but the experience is limited, and more operational research is needed. Industry is undertaking such studies.

The main challenge for industry is finding new molecules with unique modes of action for public health needs. Currently, only companies conducting research and development for crop protection can do this effectively, as the development of new active ingredients and improved formulations is expensive and not a priority. The market for public health insecticides is more limited in size and opportunities than crop protection uses, and there is therefore no financial incentive, the main incentive being social responsibility. Nevertheless, new partnerships are evolving, such as the Innovative Vector Control Consortium.

New formulation techniques (micro-encapsulation, resin coatings, controlled release products) raise optimism about the possibility of improving the residual efficacy of IRS and larviciding. Research is under way to improve the durability of LLINs and on the use of combinations of active ingredients on nets to improve their efficacy against resistant insect strains. Cooperation with other funding sources will be needed to accelerate research and development in vector control.

There has been some innovation in stewardship and packaging, but insecticide application has remained unchanged for 50 years. For instance, compression spraying, when done correctly, continues to be reliable, but there is room for improvement.

Industry is strongly committed to managing quality, product stewardship, safe use of pesticides, integrated vector management and resistance management. The vector control industry has scaled up its efforts to develop new public health insecticides for vector control.

Regarding the regulatory environment, WHOPES is recognized as a regulatory system that issues guidelines for product testing and evaluation, recommendations for the use of products in different interventions and publication of product specifications. Industry supports WHOPES as a transparent reference framework for public health products. Nevertheless, as recommendations for the use of innovative products can take more than 3 years, more flexibility and acceleration of the process are needed, with greater transparency in the development of new guidelines and in evaluation. WHOPES committees will require more resources to cope with the increased workload and to hold more technical advisory committee meetings. Industry should be allowed to comment on and review the acceptability of studies conducted according to good laboratory practice for WHOPES. Particular consideration should be given to the re-evaluation of older products when new or improved protocols are established.

In order to bring new products onto the market, transparency, consistency, speed and universal acceptance of harmonized data are needed. Industry adopts high international standards to satisfy the requirements of the European Union, the USA, FAO/WHO and local jurisdictions. The time and resources needed to meet local registration requirements vary widely, however, leading to duplication of studies, high costs and delays before even WHOPES-recommended products can be used in local markets. A separate, harmonized public health regulatory work-sharing model (hosted by the Stockholm Convention secretariat) is under discussion, which should make local registration faster and easier. There is a risk that older chemical processes for crop products will be phased out as being too expensive to support from a regulatory perspective, reducing the options for public health.

Innovation and the development and deployment of new vector control products and solutions will occur only with cooperation from all parties. More, broader resources are needed for harmonization and greater speed to market.

5.2 Country perspective in China

Dr Qiyong Liu, Professor and Director, Department of Vector Biology and Control, National Institute for Communicable Disease Control and Prevention, State Laboratory for Infectious Diseases Prevention and Control, Chinese Centre for Disease Control and Prevention, said that pesticides were first used in China in the 1950s. Their use has increased continuously since then, against both vectors of disease and other pests. The production and application of public health pesticides increased sharply after the mid-1980s, from only mosquito coils to more than 50 pesticides formulations with 98 active ingredients, including pyrethroids, organophosphates, carbamates and some heterocyclic compounds. Now, 2343 products have been registered by 786 pesticide manufacturers.

The health administration was responsible for public health pesticides before 1997, but in May of that year responsibility was shifted to the Ministry of Agriculture and merged with the management of agrochemicals. The Institute for the Control of Agrochemicals has since been in charge of registration and pesticide management. Pesticides are carefully regulated in China through a programme of premarket assessment, which includes inspection and control of product quality, safety and efficacy, packaging, transport, storage and use. Many standards, guidelines and other technical norms have been established to regulate pesticide registration, production and application. The public health sector plays a leading role in application and management, with technical support from the Chinese Centre for Disease Control and Prevention.

Because of the variety of climate zones and geography in China, there is a wide diversity of public health pests. In addition, climate and environment changes may be contributing to the spread of the geographical distribution of many pests towards the north, as well as to an increase in the duration of exposure. Moreover, rapid urbanization is contributing to pest infestation in China. All these factors are increasing demand for public health pest management, especially for pesticide products.

In response to these trends, safety and security have become priorities in society's core concerns. These concerns have been addressed by various international agreements, such as the Stockholm Convention on Persistent Organic Pollutants. The abuse of pesticides can result in serious problems of pesticide resistance.

The response to these challenges has been an innovative, comprehensive strategy for sustainable management of public health pests. The main issues addressed in the strategy are: sustainable development of public health pesticides, including innovative ingredients and formulations; sustainable application of available public health pesticides, with a well-organized programme for surveillance of pesticide resistance and strengthening of qualified human resources; and sustainable administration of public health pesticides, with updating of the relevant laws, regulations and technical standards, to increase market supervision, promote international cooperation and harmonize registration with good laboratory and manufacturing practice.

5.3 WHO regional perspectives

5.3.1 WHO African Region

Dr Birkinesh Ameneshewa, WHO Regional Office for Africa, discussed the challenges posed by increasing use of pesticides in countries of the WHO African Region, both at individual and household level and by governments and partners, to control vectors as part of the comprehensive disease control strategy and against nuisance insects. Pesticides continue to be one of the main strategies against vector-borne diseases, and it is expected that their use will continue to increase as vector control expands. Knowledge, awareness and general capacity for appropriate, safe, judicious use of pesticides in order to minimize their negative impact on human health and the safety of the environment is, however, scarce at all levels. Many countries that have increased the use of pesticides for the control of malaria and other vector-borne diseases during the past few years have invested little, if anything, in creating the conditions and developing the required capacity for their safe management and judicious use. There are a number of constraints and gaps in the pesticide management cycle throughout the continent.

First, quality control of public health pesticides is lacking. Although many countries have legal provisions for enforcement of quality control, their capacity for enforcement is not yet adequate. Some countries have quality control laboratories, but most lack adequate, appropriate equipment, supplies, logistics and well-trained staff in order to perform the required chemical and physical analysis according to WHO specifications. Moreover, post-registration monitoring and quality control of pesticides are seldom practised.

In many cases, pesticide registration does not follow the recommended procedures and checks, owing to a lack of well-equipped laboratories, expertise, guidelines and financial resources to conduct risk assessment of products under local conditions. Even when an effort is made to ensure proper registration of pesticides, enforcement is weak due to shortages of manpower and expertise, and periodic reviews of registered pesticides are almost never conducted.

Procurement and importation also pose a number of problems. In many cases, there is no coordination between the ministry of health that procures the pesticide and the authorities conducting quality control and registration, which is often the ministry of agriculture. If quality has to be checked outside the country, there may be difficulty in timing procurement with the time of pesticide application. Tendering is typically long and time consuming and in some cases not transparent. Sometimes, partners do not adhere to national legislation, instructions are not available in local languages, and private companies provide limited post-import support to national vector control programmes in terms of capacity-building and safe management of the pesticides they sell.

The storage and transport of pesticides are not considered to be different from those of common health facility items. Information and knowledge about safe transport and storage are scarce, storekeepers and transporters are seldom given any training or guidelines on how to deal with pesticides, and there are no standardized licensing processes. As a result, pesticides may be transported with other types of goods, including food. Weak stock management systems encourage misuse and mismanagement of pesticides.

The disposal of waste pesticide does not comply with international standards in many countries, which have no local companies that can dispose of pesticide waste professionally. Limited training on the disposal of empty packaging and contaminated materials is given to personnel using pesticides. There are inadequate facilities, guidelines, expertise, awareness and knowledge for waste disposal and container destruction, even for emergency situations during storage and transport. The picture is worse with regard to obsolete pesticides, which in a number of countries are stored for years in huge quantities, with waste and empty containers, due to lack of capacity to dispose of them safely.

Monitoring of the efficacy of insecticides is generally lacking, although insecticide resistance is the most important threat to insecticide-based vector control methods. Judicious use of the currently available pesticides is of paramount importance in order to reduce the rate of emergence of resistance in insect vectors. Nevertheless, many countries lack the capacity, financial resources and personnel for systematic monitoring of vector resistance and consideration of actions that might prolong the effective life of the limited number of insecticides available for vector control.

Progress in the African Region will require analysis of each country's situation, so that the most appropriate capacity-strengthening interventions can be provided to ensure safe, judicious use of pesticides. This is a priority in the WHO African Region. Intensive advocacy about the importance of safe management of pesticides at all levels is critical.

5.3.2 WHO Eastern Mediterranean Region

Dr Abraham Mnzava, Regional Adviser, Vector Biology and Control, WHO Regional Office for the Eastern Mediterranean, recalled that the Region had 11% of the global burden of vector-borne diseases with only 8% of the population. The Region is threatened with emerging and re-emerging vector-borne diseases as a result of natural events, such as climate change, droughts and floods, and man-made factors, including uncontrolled urbanization, lack of appropriate policies for vector control and population movements.

The Region is, however, making good progress in implementation of integrated vector management, which is the Regional strategic approach for the control and prevention of vector-borne diseases. This progress is due to the scaling-up of universal access (36 million people protected with LLINs) and capacity-strengthening in medical entomology and vector control to ensure that ministries of health provide the necessary leadership and that control programmes can efficiently monitor and evaluate vector control. The interventions continue, however, to rely heavily on the use of insecticides, which are often also used against insect nuisances.

The efforts are likely to be compromised not only by the increasing development and spread of vector resistance to almost all classes of insecticide but also the absence of national strategies and resources to manage public health pesticides. For example, a regional strategy for the management of public health pesticides was prepared in 2003, but it was translated into plans of action in only a few countries, which are recent recipients of Bill and Melinda Gates and Global Environment Facility support. Other countries continue to face the challenges of managing public health pesticides.

A recent assessment illustrated the challenges faced by the countries of the Eastern Mediterranean Region.

Legislation and regulation of public health pesticides are lacking in some Member States, which lack a unified registration system for agriculture and public health pesticides and in which the ministry of health has limited participation in safety assessment and regulation of pesticides. In many countries, there is a lack coordination and regulation on the use of pesticides between different sectors, including municipalities; a general lack of re-registration schemes to ensure updating of national regulation on the basis of new information; inadequate regulation of household pesticide products and of the activities of professional pest control operators; limited access to scientific data; and inadequate enforcement of regulation and use of pesticides.

Procurement and quality control frequently pose problems, as there is often no national policy. Countries have limited capacity for quality control, lack policies for the procurement and quality control of pesticides in emergency situations and for donation of pesticides, lack criteria for use of brand as opposed to generic pesticide products and have limited capacity for adoption of the WHO procedure for the determination of equivalence. Furthermore, illegal traffic and the circulation of counterfeit and substandard pesticide products are frequent. Many countries lack the capacity for rational selection of vector control interventions and insecticides.

The storage, transport and distribution of pesticides also pose problems in some Member States that have limited facilities for safe storage, lack national guidelines and resources on safe transport of pesticides and have limited capacity for proper stockage and management.

Pesticide application requires national guidelines for safety and effectiveness, which are lacking in many countries, with inadequate capacity for supervision of pesticide application and for coordinating applications in different sectors. Many countries have not adopted integrated vector management as a national policy for judicious use of pesticides, because of limited capacity for correct application, safe handling and use of pesticides and lack national quality standard and capacity for evaluating pesticide application equipment.

Monitoring and evaluation of vector control and pesticide applications are weak in many countries, which often lack the capacity to monitor cases of pesticide poisoning. Many countries have no capacity for recording and reporting insecticide use in public health, including that for nuisance control, for assessing the impact of pesticides on health and the environment, or for monitoring susceptibility of vectors and pests of public health importance to insecticides.

The disposal of obsolete pesticides and pesticide waste and containers is frequently inadequate owing to lack of resources. Few countries have schemes for safe disposal, and there is a general lack of capacity to prevent leaks of pesticides and poorly stored obsolete pesticides into the environment. Community awareness about pesticides use and hazards is generally lacking.

The lessons learnt from pilot countries in the Region and from other global efforts will be used to address the problems of managing public health pesticides in other countries of the Region.

6. INNOVATIVE TECHNIQUES FOR VECTOR CONTROL

6.1 Devising novel strategies against vector mosquitoes and houseflies

Dr Gary G. Clark, Research Leader, Mosquito and Fly Research Unit, Center for Medical, Agricultural and Veterinary Entomology, Agricultural Research Service, United States Department of Agriculture, reviewed the work of the Department of Agriculture, since the establishment, in 1932, of an entomological research laboratory with an initial focus on mosquitoes (including malaria vectors under conditions simulating those of South Pacific jungles) and other insects that affect humans and animals. The Agricultural Research Service was created in 1953.

Among the many accomplishments of research scientists at the laboratory are development of a new method for residual control of *Anopheles*; the broad-spectrum repellent *N*,*N*-diethyl-3-methylbenzamide (DEET); a mass-rearing technique for application of a sterile insect technique, including a trial in El Salvador for the control of *Anopheles*; and ultra-low volume pesticide spray systems to protect military personnel from mosquitoes. The laboratory also made major contributions to the development and registration of methoprene in a variety of biological control approaches (e.g. *Bacillus thuringiensis* var. *israelensis* and *B. sphaericus*) and permethrin-impregnated tents and uniforms for personal protection. The laboratory, in collaboration with industry and WHO, conducted the first evaluations of almost all the public health insecticides that entered the market in the last half of the twentieth century.

More recently, the programme developed ‘attract and kill’ and ‘push–pull’ approaches to vector control, evaluated spatial repellents, found new toxicants and used RNA interference to silence critical genes and other molecular techniques to control vectors. In addition, behavioural studies were conducted of the excito-repellency caused by new insecticides and the impact of sublethal doses of insecticides. While much progress has been made over the past eight decades, researchers have continued to explore microbial control of vectors (e.g. salivary gland hypertrophy virus in houseflies and baculoviruses in mosquitoes), a modern sterile insect technique for mosquito control and insecticide-treated covers for water-holding devices.

Recent and planned research activities include: the mating competitiveness of males carrying a dominant lethal mutation against a field strain of *Ae. aegypti*; the efficacy of insecticide-treated container covers against female *Ae. aegypti*; studies of nonchemical methods for disinsecting commercial aircraft; the response of *Ae. aegypti* to prallethrin and sumithrin insecticides; and studies of durable wall-lining against several mosquito and fly species.

The focus of the programme for the next 5 years will be a search for new larvicides, adulticides and RNA interference-based biopesticides; identification of chemicals responsible for attraction; improved repellents for use on clothing; improved products and techniques for aerosol and residual insecticide applications; and development of attractant–toxicant traps and 'push–pull' baited trapping systems.

6.2 New repellents, insecticides and application systems from the Deployed War-fighter Protection programme

Dr Graham B. White reviewed the work of the United States Armed Forces Pest Management Board and its initiative to discover, develop and validate novel pesticides for use against medically important arthropods, with emphasis on reducing risks of vector-borne diseases for deployed military personnel. With a budget of US$ 5 million annually, the Deployed War-fighter Protection research programme on disease-carrying arthropods, supports investigations by the Agriculture Research Service of the United States Department of Agriculture (see section 6.1) and awards competitive grants for projects by scientists in other organizations. During six cycles of competitive awards, over 40 grants have supported investigators in academia, industry and the military, targeting mosquitoes, phlebotomines, other flies and general vectors. The research has yielded products for patenting, licensing, regulatory approval and commercialization.

The main activities are devising novel insecticide formulations, application methods and personal protection systems. The products include molecular insecticides, autodissemination of pyriproxyfen by adult mosquitoes, new volatile pyrethroids, natural insecticides (β-damascone, citronellol, cyclemone A, geranyl acetone, melafleur and rosalva), chromene and piperidine toxicants. The adulticides and their applications that have been developed include an etofenprox space-spray formulation, new diesel-powered and silent back-pack sprayers, characterization of sprayers in the National Stock Number inventory, refinement of cage bioassays and the finding that thermal fog is more effective for adulticiding than ultra-low volume applications in desert environments.

Particular attention has been paid to the modes of action of mosquito repellents, which has revealed stereospecific positive orthosteric and negative allosteric activities of repellents on different sites of the odorant receptor complex. Novel interventions include a lethal ovitrap for dengue vectors, a folding portable insecticidal fly trap, volatile chemical inhibitors of mosquito biting, attractive toxic sugar baits for adult sandflies, rodent baits for systemic control of adult sandflies and feed-through control of larval sandflies.

It is envisaged that products developed within the Deployed War-fighter Protection initiative will be suitable for wider application against pests and vectors of public health importance. Moreover, ways have been found to expedite registration of new vector control products by the Environmental Protection Agency in the USA in order to encourage industry to develop and supply such materials.

7. INNOVATIVE RESPONSES TO THE SPREAD OF INSECTICIDE RESISTANCE

7.1 Innovative Vector Control Consortium product portfolios for insecticides and information systems and tools

Dr Robert Sloss, Innovative Vector Control Consortium, described the work of the Consortium, established in November 2005 with US$ 50.7 million from the Bill and Melinda Gates Foundation to encourage the development of new public health insecticides and information systems and tools for more effective use of existing and new control measures. The Consortium has two portfolios for the development of new public health products, one for formulating and finding new uses for existing products, and the other for finding new active ingredients.

One objective of the first portfolio is to develop a range of long-lasting (at least 6 months on all common surfaces) IRS formulations in order to maximize the number of classes of insecticide available for resistance management. They should include the four classes available for vector control and any agrochemical insecticides that could be re-purposed for vector control. The second objective is to develop LLINs containing an insecticide other than a pyrethroid. Two of the five projects for IRS formulations and use have come to the end of funding by the Consortium, and discussions are under way with WHOPES to determine the remaining requirements for their recommendation. The other three projects are in the stage of ‘proof of concept’. The development of LLINs containing alternatives to pyrethroids is proving difficult because of the safety profile and performance requirements for the nets. Nevertheless, three projects with promising results are at the ‘proof of concept’ stage.

The portfolio for development of new active ingredients for vector control with modes of action that are unaffected by known resistance mechanisms consist of three full projects: one for screening and optimization with Bayer, one for molecular design with the Liverpool School of Tropical Medicine, Bayer and the University of Liverpool and one for screening with

Syngenta. A ‘proof of concept’ screening project has been completed, and a molecular design ‘proof of concept’ project is active. Discussions are under way with other companies to increase the number of screening projects.

In the next 5 years, the Consortium will have tested all the options for potential re-purposing of current agricultural insecticides and developed them as products suitable for vector control. The screening programmes will be advanced through chemical optimization into the early phase of development to ensure that three new active ingredients suitable for vector control are available by 2020.

It is expected that the work of the Consortium will:

- give control programmes access to longer-lasting IRS formulations with different modes of action to manage resistance;
- allow use of one application per season with formulations other than DDT;
- lead to an overall reduction of programme costs due to fewer applications per season;
- provide long-lasting formulations for use with a new generation of active ingredients;
- supply chemicals with new modes of action for vector control from existing agrochemicals; and
- make ITNs that can be used in areas of high levels of pyrethroid resistance.

With respect to information systems and tools, the Consortium is undertaking five projects to provide information for decision-making in the field in order to reduce disease transmission. The systems projects will cover the data collection and management necessary for effective monitoring and evaluation of disease and the interventions to control it. The tools projects covers the generation of information necessary for effective vector management.

The ‘malaria decision support system’ brings the indicators of effective vector control together into one system, which can be adapted for the needs of a particular country or region. It makes it possible to determine the outcome of interventions in different environments and the operational challenges. It consists of a computer package for collating data on disease incidence, vector populations (including density and insecticide resistance) and interventions; the information is presented in a web-based, real-time geographical format. The infrastructure will be completed in 2010. It has been tested in countries and is ready for field testing. The system should be ready in mid-2010.

The aim of the 'dengue decision support system' is to provide information on all aspects of mosquito vectors and dengue to help control programme managers to implement, evaluate and refine locally appropriate disease prevention and control strategies. The system will allow standardized collection, management and analysis of data on vectors and dengue, which will be displayed in intuitive formats (e.g. maps, graphs, charts) to assist implementation of locally appropriate vector and dengue control strategies and evidence-based decision-making. A framework for the system has been prepared, and software for its operation is being developed. It is expected that the software will be ready in late 2010.

The Consortium is supporting development of a user-friendly computer model for simulating populations of *Ae. aegypti* and dengue virus transmission on the basis of data for specific situations, including climate, mosquito biology and behaviour, virus factors, human demographics and immune status. Various control interventions, such as insecticide space spraying, removal of mosquito development sites, insecticide-treated materials and vaccines, can be introduced into the programme so that the relative impact of individual or combined disease control strategies can be assessed. The new Windows™ version of the programme has undergone extensive evaluation in order to confirm full functionality. The goal is to make the programme freely available as a component of the 'dengue decision support system'.

The Consortium is funding development of a molecular biology kit that will allow scientists to identify mosquito species, infection status and the presence of insecticide resistance genes by detecting a gene or sequence of DNA. The kit will replace current individual tests and make it easier for vector control programme managers to obtain information. A number of the protocols have been published. Work will continue until the end of 2010 to identify novel markers of metabolic resistance in both *A. gambiae* and *Ae. aegypti* in a range of field strains. The next stage will be expansion of the project into new regions and new malaria vectors.

An insecticide quantification kit is being developed as a simple, cost-effective, user-friendly means for monitoring insecticide residues on insecticide-treated materials. Apart from carrying out bioassays in the field, the only way to check that protection is being provided by IRS or ITNs is to measure the actual amount of insecticide remaining. Currently, the insecticide concentration is measured by gas chromatography or high-performance liquid chromatography, which are expensive and require skilled staff and sophisticated facilities. The Consortium has developed kits for various insecticides (including pyrethroids and DDT); some are in the final stage of development and are being field-tested in Africa. The versatility of the test kits is being broadened in terms of both application and the products detected.

7.2 Threat to control of malaria caused by *Anopheles gambiae* of resistance to pyrethroids and the prospect for sustaining insecticidal control with alternatives such as indoor residual spraying and long-lasting insecticidal nets

Dr M. Rowland, London School of Hygiene and Tropical Medicine, London, said that pyrethroid resistance has become widespread among *A. gambiae* in West Africa, partly as a consequence of the use of insecticides in agriculture but increasingly as a result of scaling-up of LLINs and IRS. Recent observations in southern Benin, Burkina Faso and Bioko Island indicate that vector control with ITNs and IRS is being undermined by pyrethroid resistance. Research is under way to identify new insecticides to control pyrethroid-resistant mosquitoes and, if possible, reduce selection pressure for pyrethroid resistance.

A number of insecticides new to malaria control have been identified and evaluated in the field. The challenge for IRS is to make the insecticides long lasting and to make them more cost-effective, so that one application covers an entire transmission season. This can be achieved by advances in formulation technology. The challenge for LLINs is to make them long lasting but also to increase personal protection by excito-repellency. Combination products, particularly on nets, are a pragmatic way of improving protection of users and efficacy against resistant mosquitoes

The current situation is illustrated by:

- a fall in the malaria burden as a result of use of artemisinin-based combination therapy and subsidized or free distribution of ITNs, as exemplified by the evolution of morbidity in the Gambia, Kenya and Zanzibar;
- the known geographical distribution of the ‘knockdown resistance’ gene *kdr* (east and west), the esterase and the oxidase-based pyrethroid resistance mechanisms; and
- the finding in a *kdr*-resistant area of the Côte d'Ivoire that ITNs were protective against malaria.

Studies were conducted in experimental huts in the north of Benin, where *A. gambiae* M is susceptible to pyrethroids, and in the south, where it is resistant (*kdr* plus oxidases), and the results were compared with epidemiological data. These studies and those on the IRS campaign on Bioko Island show that pyrethroid resistance in *A. gambiae* M reduces the impact of ITNs and IRS. Thus, the scaling-up of LLINs and IRS is selecting for resistance, and strategies are needed for containing it.

The response to insecticide resistance remains dependent on alternative insecticides that are either new active ingredients (for which an average of 10 years should be expected between discovery and use), re-purposing or reformulating insecticides used in agriculture or combinations of existing products. Promising non-pyrethroid insecticides include chlorfenapyr (a pyrrole) and pirimiphos-methyl (an organophosphate); and a microencapsulated suspension at a dose of 0.5 or 1 g/m^2 showed good residual effect in bioassays in Benin.

Combinations are being tested, including treatment of LLINs with mixtures or 'mosaics' of pyrethroids plus a synergist or pyrethroids plus an agricultural insecticide.

7.3 Insecticide combinations for controlling insecticide-resistant malaria vectors

Dr Vincent Corbel, Institut de Recherche pour le Développement, Centre de Recherche Entomologique de Cotonou, Bénin, said that malaria vector control in Africa relies predominately on the use of residual insecticides in the domestic environment. ITNs and IRS are the cornerstones of malaria control programmes, and high coverage with either can dramatically reduce malaria-associated morbidity and mortality. The success of these tools has contributed to optimism that elimination of malaria as a public health problem on the African continent is feasible. Lack of insecticide classes for public health and the emergence of resistance to the majority of existing insecticides may, however, substantially reduce the contribution of vector control to malaria elimination.

Insecticide resistance management with mixtures, sequences, mosaics or rotations of unrelated compounds have been tested during the past few decades in Africa, India and South America with greater or lesser success. The dramatic increase in pyrethroid resistance of malaria vectors worldwide is therefore a cause for great concern, as malaria vector control is highly dependent on this class of insecticides, especially for ITNs.

Given the current lack of investment in the development of new public health insecticides, efforts have been made to design combination nets (e.g. mixtures and mosaics of various insecticides, repellents or synergists) and to promote resistance management based on combinations of different insecticide classes in the same setting (ITNs and IRS). The advantages of combining different insecticides is clearly to enhance the impact on vector populations, improve the perceived effects on domestic pests (e.g. *Culex pipiens quinquefasciatus*) and slow (or prevent) the selection of resistance genes. Recent field trials in several African countries (including Benin, Burkina Faso and Côte d'Ivoire) showed that 'two-in-one' treated mosquito nets were effective in killing pyrethroid-resistant malaria vectors, although some limiting factors, such as safety, cost-effectiveness and production capacity at factory level, remain to be addressed. Combinations of ITNs and IRS (such as insecticide-treated plastic sheeting and durable wall lining) have attracted interest as approaches to malaria elimination by maximizing the chances of interrupting transmission. Unfortunately, although trials were started in Cotonou in collaboration with WHO in 2001, only a limited number of studies (on Bioko Island and in Benin and Mozambique) are available. Determining the real benefit of using these interventions in combination for malaria control will require further entomological and epidemiological investigations.

Tests of ITN treated with carbosulfan alone showed a strong effect, but two-in-one mosaics were even more effective against pyrethroid-resistant mosquitoes with a much lower insecticide content on the nets.

With regard to 'combination' nets, only one product has so far been produced at factory level (Permanet 3.0*), a mosaic LLIN containing deltamethrin plus piperonyl butoxide (synergist) on the roof (polyethylene), designed to improving efficacy against pyrethrin-resistant mosquitoes. In comparison with Permanet 2.0 in Africa (Burkina Faso, Cameroon, United Republic of Tanzania) and Asia (Viet Nam), it had better performance in the pyrethrin-resistance area of Cameroon (metabolic) and Burkina Faso (*kdr* resistance), while no clear benefits were obtained in Viet Nam (metabolic resistant *A. epiroticus*) or the United Republic of Tanzania (susceptible *A. gambiae s.l.*). These contrasting results point to the need for further entomo-epidemiological investigations

The future of 'combination' nets will involve:

- ensuring that 'long-lasting' combination nets have comparable decay rates (efficacy) and respect target doses (quality control);

- developing suitable methods and criteria (WHO guidelines?) for testing and evaluating long-lasting combination nets (decision-making);
- investigating the safety (risk assessment) and regulatory issues involved for non-pyrethroids used in combination nets;
- providing more operational evidence that combination nets can enhance mass killing of mosquitoes and personal protection in an area of resistance; and
- keeping industry 'in the business' (research and development), given the absence of alternatives to pyrethroids for treatment of mosquito nets.

The possible combination of different interventions, such as IRS and ITNs or carbamate-treated plastic sheeting, which showed a significant protective effect in trials in Bioko and Mozambique, suggest that the future of combined interventions depends on:

- providing more evidence (with robust study designs) on the public health benefits of combining vector control interventions in areas of stable malaria transmission;
- conducting social surveys of the acceptability of combined interventions (IRS plus LLINs);
- addressing the cost-effectiveness of using strategies similar to LLINs plus IRS (e.g. plastic sheeting, wall lining) for future decision-making (IRS replacement);
- developing durable wall lining with alternatives (non-pyrethroids) to increase the impact on pyrethroid-resistant malaria vectors (insecticide resistance management strategy); and
- strengthening the capacity of research institutions and universities in the southern hemisphere to test and evaluate vector control interventions.

Insecticide combinations may be urgently needed innovative tools to ensure more effective control of resistant malaria vectors and help developing countries to achieve the malariarelated Millennium Development Goal: a 75% reduction in the malaria burden by 2015.

7.4 New repellents and application strategies

Dr Ulrich R. Bernier, Mosquito and Fly Research Unit, Center for Medical, Agricultural and Veterinary Entomology, Agricultural Research Service, United States Department of Agriculture, recalled that the Department's research laboratory had received its first sample of insecticide, a natural pyrethrin mixture, in 1942. Since then, over 30 000 repellent and insecticide products have been evaluated, including DEET, permethrin-treated military uniforms and ultra-low volume insecticides.

The current objective of the Mosquito and Fly Research Unit is research on medically important biting and filth flies. Exploration of host odours has led to the identification of attractants and attractant blends and also to discovery of a class of compounds that impart a spatial effect, so that insects cannot detect host odours. In bioassays, these compounds inhibit the attraction of *Ae. aegypti* and *A. albimanus* mosquitoes and *Phlebotomus papatasi* sandflies to a normally attractive stimulus (e.g. human odours).

A review of Department of Agriculture's archives on previous testing of chemical families has resulted in models of chemical structures, from which predictions are made for the synthesis of new compounds. Bioassays will provide data to be fed back into the models. Exploration of over 30 000 chemical structures tested has led to the development of new topical repellents. Thus, 68 piperidine and carboxamide candidate mosquito repellents have been evaluated in a cloth patch assay for duration of repellency and minimum effective dose for repellency. The repellent efficacy of several of the compounds is comparable to or better than that of DEET. The studies are being extended to repellents against other arthropod species, including stable flies (*Stomoxys calcitrans*) and ticks (*Ixodes* and *Ambylomma*).

The United States Army and Marine Corps are using insecticide (mainly permethrin)-treated uniforms made of fire-resistant materials. Because of changes in the composition and construction of the fabric, permethrin is absorbed and retained less effectively, and the Marine Corps provides only factory-treated uniforms to its personnel. The construction of the Army uniform results in poorer efficacy of appropriate levels of permethrin, and new impregnates and combinations are being explored to provide better protection from mosquito and sandfly bites**.** Promising results are being obtained with attraction inhibitors that mask or cloak the presence of kairomones, resulting in anosmia. These are being tested in *Ae. aegypti*, *A. albimanus* and *P. papatasi*, as are release devices to obtain over 24-h protection.

7.5 Inclusion of spatial repellents in vector control

Dr Nicole Achee, United States Uniformed Services University of the Health Sciences, described the problems that have hampered progress in the control of arthropod-borne diseases, in spite of worldwide vector control. One element is the limited availability of effective active ingredients and appropriate application formats for global strategies.

Vector control is currently based mainly on the contact toxicity of insecticides and not their their spatial repellency, which causes the vector to move away from the treatment source without directly killing it. Spatial repellency prevents human–vector contact by creating a vector-free space around human hosts within a specified area. This phenomenon, identified in 1963 by de Zulueta and Cullen in Uganda, has not been given the attention it deserves. A switch to spatial repellency would have considerable immediate advantages over toxicity, including minimizing selection for insecticide resistance, reducing toxicity to mammals by use of doses below the 90% lethal dose and providing protection at a distance from the treated area, e.g. beyond indoor spaces. Moreover, the study of spatial repellency will have long-term benefits, such as the identification and development of new chemical active substances and new modes of action, and exploitation of as-yet-undescribed vector activity outside the home before, during and after host-seeking. This will stimulate the development of innovative products and enhance vector control.

Nevertheless, before spatial repellency can be recommended, clear evidence will be needed that spatial repellency is separate from irritancy and toxicity and that vector control with this approach will affect disease. It will therefore be necessary to establish a ‘critical path of development’ for spatial repellent products, by convening a meeting of academics, industry and global public health experts to discuss the role of spatial repellency in the reduction of arthropod-borne diseases. Furthermore, global health authorities must formally accept and recognize the development and use of spatial repellent strategies; the evidence required to support use of non-toxic chemical activity to reduce human–vector contact should therefore be the focus of research programmes and industry efforts, with identification of research gaps.

Studies are under way to determine the concentration of active ingredient present in the space around a spatial repellent treatment source, e.g. a sprayed house, how the concentration changes with distance and the behaviour that the concentration elicits in a vector: spatial repellent, contact irritant or toxicity. It should be determined whether spatial repellency diverts vectors to untreated spaces, which might increase the risks of non-users and shift rather than reduce disease transmission.

The overall goal of recently funded collaborative efforts between the SC Johnson Company and various academic partners is to demonstrate an effect of spatial repellent products on disease and to prepare a business plan for product marketing. These efforts, in combination with other research programmes on spatial repellency, will create opportunities and impetus for industry, academia and the private sector to seek, evaluate and develop repellent products in new chemical classes for use in sustainable vector control.

7.6 Application of near-infrared spectroscopy to medical entomology: age grading and species identification

Dr Robert Wirtz, United States Centers for Disease Control and Prevention, described developments in the application to entomology of near-infrared spectroscopy. This technique, which has been used to detect infested grain kernels, can be applied to measure the amount of near-infrared energy absorbed at specific wavelengths by biological materials. The absorption is affected by the biochemical composition of the organism, and different organisms can have different absorption spectra. The stretching and bending of mainly C–H, N–H and O–H functional groups can cause unique absorption of near-infrared energy, which can be used to identify different species or age groups.

This technique has been used in medical entomology for sexing tsetse pupae, identifying insect vector species and age grading. The technique can be automated, and its performance ranges from one specimen per minute with a manual scanning instrument, to one kernel or pupa per second with an automated scanning and sorting instrument, up to more than 100 kernels per second with high-speed sensing and sorting instruments. Research is under way to produce smaller, less expensive instruments (near-infrared laser clusters) to increase precision (near-infrared spectroscopy microscopy) and achieve better discrimination (dispersive near-infrared spectroscopy).

As near-infrared spectroscopy is not destructive, it has been used, in collaboration with the International Atomic Energy Agency, to sex tsetse pupae, with 98% success. This has allowed the irradiation and release of males and the return of females to the colony.

Recently, near-infrared spectroscopy was used to identify species of mosquitoes, allowing pairwise comparisons of near 100% accuracy between *A. gambiae, A. stephensi, A. albimanus, A. quadrimaculatus, A. dirus* and *A. freborni*. In an analysis of *A. gambiae s.l.* collected in the field and identified by molecular means, near-infrared spectroscopy identified *A. gambiae s.s.* and no *A. arabiensis* with 92% accuracy.

The technique is also used for age-grading insects. Determination of the age of flies resulted in three groups (< 4, 4–9 and ≥ 10 days); the results were independent of the preservation technique, and the accuracy was better than with pterin analysis. Application to colonized *A. arabiensis* permitted differentiation of two groups (< 6 and > 8 days) with 95% accuracy, with an intermediate group (6–8 days) of doubtful identification.

Research is under way to validate age-grading, identification of species and RNA preservation in the field; use of the technique for detection of filarial, malaria and arbo- infections in vector arthropods; identification of near-infrared spectroscopy target compounds and new instruments and dedicated funding. The goal is to develop small instruments for rapid identification of vector species, age and infectious status in order to evaluate interventions.

7.7 Delivering pesticides on target: the role of good-quality spray equipment

Professor Graham Matthews, Imperial College, London, recalled that the global malaria eradication campaign launched in 1955 had been based on a programme of IRS in which all internal wall surfaces of dwellings were to be sprayed with DDT at a dose of 2 g of active ingredient per m^2, to control mosquitoes and reduce transmission of malaria. A number of problems were soon identified with the equipment for IRS. The compression sprayers used in agriculture invariably had a pump integral with a small opening of the tank, and this had to be removed each time the sprayer was filled with insecticide suspension; and when the pump was re-inserted, soil or other material introduced into the tank caused nozzle blockages. Other problems were found in the field, such as nozzle erosion. Therefore, WHO convened a meeting, which subsequently led to the publication of specifications.

The specifications for compression sprayers, first published in 1964, required that the sprayer have a pump with a T-shaped handle separate from the tank lid, a means for posing the lance when not in use, a foot rest and a hardened stainless-steel

8002 fan nozzle to minimize the effect of abrasive particles in the spray liquid. The performance of the sprayers, in particular the durability of the tank, which was subject to frequent pressurization to 4 bar and depressurization during field operations, was evaluated on a specially designed rig in the USA and also in the United Kingdom.

Similarly, the performance of the trigger valve without leakage was evaluated, initially with a suspension of DDT wettable powder but later with one of the inert silica powder formulants. Hardened stainless-steel nozzles were chosen to mitigate erosion of the nozzle orifice. As deposits on wall surfaces were reported to vary, efforts were made to overcome the variation in spray output due to the decrease in tank pressure while spraying. A brass valve was used, but it could be adjusted by the user and was reported to be easily blocked, due in part to its design but also due to inefficient cleaning at the end of each spray session. Tests were then carried out with a simple rubber disc that constricted the flow of spray at higher pressures, but it absorbed water and therefore the output was not constant. Much later, a new control flow valve, developed for knapsack sprayers, was evaluated, which did maintain constant pressure and output at the nozzle, until the tank pressure was too low to open the valve. Use of the valve was recommended in 2006.

A specific droplet spectrum is needed for space sprays, in order for airborne droplets to be collected by flying insects. Developments in laser measuring systems have enabled more accurate and rapid measurement of droplet spectra, which has led to more accurate evaluation of the performance of commercially available cold and thermal fogging equipment. Use of a hot wire instrument to measure the droplet size of cold fogs was comparable with laser systems, and use of portable equipment allows users to check their equipment regularly. Specific equipment has been designed for molluscicide application and for dispensing larvicides from aircraft to control *Simulium* spp.

Although there have been improvements in sprayer and nozzle design, there has been little research on the performance of alternative equipment in operational programmes.

Specifications are essential to ensure the reliability of equipment and the accuracy of application, to protect the operator from exposure to pesticides, to minimize the requirement for protective clothing by incorporation of engineering controls and to avoid environmental pollution. Hence, concerns have been raised about nozzle design and the cleaning and maintenance of equipment. Nevertheless, a balance must be found in the text of the specifications between precise design and performance criteria. The future should include consideration of use of different nozzles and different types of sprayers and the role of electrostatic spraying and strategies within integrated vector management.

8. IMPROVEMENTS TO LONG-LASTING INSECTICIDAL NETS

8.1 New approaches to the sustained efficacy of long-lasting insecticidal mosquito nets

Dr Helen Pates, Vestergaard Frandsen, Switzerland, reviewed the current situation of LLINs, of which eight are recommended for malaria control. Impregnation involves coating polyester fibre with a resin containing the insecticide or incorporation of the insecticide into the polyethylene filament itself. Only pyrethroid insecticides are used for net impregnation and practically only permethrin, deltamethrin, λ-cyhalothrin and α-cypermethrin.

In spite of the success achieved with the use of LLINs, the spread of pyrethroid resistance calls for new techniques in order to sustain the efficacy of this much-needed tool in areas of high levels of pyrethroid resistance. As active ingredients cannot be rotated in LLINs, only four basic approaches are available: combining several active ingredients in the yarn; knitting together separate yarns with different active ingredients, using different ingredients for the roof panel and the sides and using new active ingredients for treatment of nets.

The choices for combinations of active ingredients are pyrethroids with synergists, non-pyrethroids with pyrethroids and non-pyrethroids only. Some common pesticide synergists are piperonyl butoxide, propyl isome, sesamex and sulfoxide. The effectiveness of synergists depends on the resistance mechanism affecting the vector species in the area concerned. The resistance mechanisms that have been identified are:

- enhanced metabolism due to enzymes such as esterases, oxidases, glutathione *S*-transferases, peroxidises, ATP-binding cassette (ABC) transporters and efflux pumps;
- altered site of action by changes in DNA, such as *kdr*, insensitive acetylcholinesterase (*MACE*, *Ace1*), *rdl* gene, γ-aminobutyric acid (GABA) receptor; and
- reduced penetration, e.g. by altered cuticle or stomach lining.

The most commonly used synergist, piperonyl butoxide, is a known inhibitor of detoxifying enzymes, such as mixed-function oxidases (cytochrome P450s) and esterases; it also accelerates insecticide penetration, thus acting against reduced penetration resistance. *S*,*S*,*S*-tributyl phosphorothionate (DEF) mainly inhibits esterases, but it has also been reported to inhibit some P450s in some *Diptera* species. It is nevertheless not well understood how the chemical structure of the synergist interacts with complex molecules like enzymes, such as the exact binding site of piperonyl butoxide on esterases or P450s. Even if the amino acid sequence is known, the folding of the molecule is still unknown, leaving much to chance.

The options are therefore limited to nets treated only with a non-pyrethroid or nets treated with a pyrethroid plus a non-pyrethroid, either all over the net or with the non-pyrethroid on the roof and the pyrethroid on the sides. The non-pyrethroid might be either an organophosphates or a carbamate, a repellent, a re-purposed agricultural insecticide or a new active ingredient developed exclusively for public health,

Thus, new tools are needed with sustained efficacy, which are reliable and easily used, particularly in the move from ‘control’ to ‘pre-elimination’ and ‘elimination’. The development of new products will require better knowledge of the problem, including the extent of resistance, the mechanisms of resistance and clear guidelines for assessing the efficacy of new tools. Implementation will require WHO and FAO recommendation of non-pyrethroids for use in public health or use on nets and a clear pathway for evidence-based decision-making on use of the most appropriate tools, including monitoring and reporting of insecticide resistance, clarity for donors and incentive for industry to keep innovating.

8.2 Determination of retention and release of active substances in long-lasting insecticidal mosquito nets: a real challenge

Dr Olivier Pigeon, Walloon Agricultural Research Centre, Agriculture and Natural Environment Department, Plant Protection Products and Biocides Physico-chemistry and Residue Unit (WHO Collaborating Centre for Quality Control of Pesticides), Belgium, outlined the role of ITNs in the control of malaria. Nets treated with insecticide are currently manufactured by mixing the insecticide (generally a pyrethrinoid active substance) with polyethylene fibre before weaving, either by coating the multifilament polyester fibre with a polymer containing the insecticide (all the active ingredient is on the surface) or by bonding an insecticide formulation to the fibre (part of the active ingredient is on the surface but most is uniformly incorporated into the yarn). The term 'long-lasting insecticidal net' reflects the longer time and greater number of washings for which biological efficacy is maintained, in comparison with conventional nets treated by soaking in an insecticide preparation at the point of use.

LLINs can be considered as slow-release formulations that combine a physical barrier with chemical protection. Acceptable performance of LLINs is defined by WHO as retention of biological activity through 20 standard washes and 3 years of recommended use under field conditions. WHO has published guidelines for laboratory and field testing of LLINs and has incorporating specifications for LLINs in the WHO/FAO Pesticide Specifications.

The bio-efficacy of LLINs depends mainly on the amount of active substance present on the surface of the fibre. The retention or release of active substance is therefore an important parameter for characterizing LLINs. Some retention and some release are both essential to achieve good insecticidal activity. The draft guidelines for LLINs are based on the consideration that the surface concentration must be sufficient for efficacy but not excessive, to avoid unacceptable exposure of users to the active ingredient and unacceptable losses by washing. The surface concentration is an important characteristic of LLINs but is conceptually and practically difficult to define; its measurement cannot therefore be directly included in the guideline specification.

The 11th WHOPES Working Group, in 2007, recommended that the WHO washing procedure be standardized and asked the Collaborative International Pesticides Analytical Council (CIPAC) to develop and adopt the standard, which was submitted in 2010. The protocol permits calculation of a 'retention index' for the active ingredient after four washes from the following equation (free migration stage behaviour):

$$\text{Average active ingredient retention index} = \sqrt[n]{(t_n/t_0)},$$

where t_n is the total content of active ingredient in g/kg after *n* washes and t_0 is the total content of active ingredient in g/kg at wash 0 (before washing). Phase 1 studies of the standard have been carried out with four types of LLIN on three pieces measuring 25 × 25 cm in each washing cycle. The LLINs were either coated with α-cypermethrin (75 denier), had α-cypermethrin incorporated (150 denier) or were coated with deltamethrin at 100 or 75 denier. An accurate average retention index was obtained after four washes. Thus, an average retention index (percentage at each wash) calculated from the equation for free migration stage behaviour after four washes can be proposed as the CIPAC wash method; the wash cycles can be performed within 1 week

Ten washing cycles were carried out to compare Marseilles soap at 2 g/l with three concentrations of IEC-A* reference detergent 60456 without phosphate. In 2010, however, a new washing agent was developed by Sumitomo, for which the following aspects require evaluation:

- the concentration of the agent that replicates washing conditions that are as close as possible to the current WHO method to allow comparison;
- the type of movement during washing and rinsing, including static (no movement of flasks), shaking, as used in the WHO method and experiments at the Walloon Agricultural Research Centre, and rolling, as used for determination of the attrition of granules and the slow-release characteristics of capsule suspension formulations;
- a proposed heating step between washes of incorporated nets, to allow equilibration of the distribution of active ingredient (replenishing active ingredient on the surface after the wash step);
- the appropriate temperature at which the net should be stored for 22 h to ensure equilibration but minimize degradation and evaporation; and
- a temperature for the method that is not product-specific, as it is expected that the temperature depends on the specific product.

9. CONTROLLING VECTOR-BORNE DISEASE AND ADAPTING TO CLIMATE CHANGE WITH RESEARCH ON DISEASE FORECASTING AND NEW VECTOR CONTROL MATERIALS AND TECHNIQUES

Dr Kenneth J. Linthicum, Center for Medical, Agricultural and Veterinary Entomology, Agricultural Research Service, United States Department of Agriculture, said that population growth, agricultural expansion and urbanization transform the landscape and the surrounding ecosystems, affect climate and interactions between animals and humans and significantly influence the transmission and geographical distribution of malaria, dengue and other arboviruses and tick-borne diseases. To detect and control the vector-borne diseases that ravage the world's population, the Center for Medical, Agricultural and

Veterinary Entomology, the first national centre for insect research and the largest entomology laboratory in the world, conducts research and transfers technology to reduce or eliminate the harm caused by insects to crops, stored products, livestock and humans. Means are developed to detect and respond effectively to emerging vector-borne diseases globally.

The Center, in collaboration with numerous international institutions, including FAO and WHO, has studied the global climate and its variability, monitoring the El Niño and southern oscillation phenomena, sea surface temperature, cloudiness and their correlation with rainfall anomalies since 1979. This research is complemented by data from satellites to determine a 'normalized difference vegetation index' and anomalies in 'outgoing long-wave radiation'. Analyses of these variables over time result in new and improved predictive models and allow mapping of the spatial and temporal distribution of increased vector populations and potentially enhanced disease transmission and risk for epidemic outbreaks. The link between climate variation and transmission has been studied not only for malaria and dengue but also for Murray Valley encephalitis, Bluetongue disease, Rift Valley fever, African horse sickness, Ross River virus and chikungunya. Rift Valley fever served as a model for understanding climate variation and how to use it to mitigate disease transmission, resulting in the Emergency Prevention System for Transboundary Animal and Plant Pests and Diseases with FAO.[7]

Another area of research has been vector control for harsh climates or environments, including the effect of pathogens on the efficacy of repellents, the efficacy of barrier applications on mosquitoes in subtropical and desert environments, the efficacy of ultra-low volume and thermal fogging, the efficacy of barrier and ultra-low volume applications on sandflies and translation of research into operations.

The evaluation of barrier applications in harsh temperate and desert environments showed the following:

[7] http://www.fao.org/ag/againfo/programmes/en/empres/home.asp

- Camouflage netting treated with bifenthrin at label rates in the USA can be stored, shipped internationally, used in the field and still retain significant bioactivity against sandflies for at least 1 year.
- Camouflage netting treated with bifenthrin can be used to construct enclosures that can reduce the risk for being bitten by *P. duboscqui, P. martini* and *Segentomyia schwetzi* in *Leishmania*-endemic regions in exceptionally dry and hot desert regions of the Old World.
- Ultra-low volume treatment with malathion or Duet (prallethrin, sumithrin and piperonyl butoxide) was effective against caged and field populations of *P. duboscqui* and other sandflies.
- An outdoor screened cage constructed to contain released laboratory-reared sandflies at a field site in Marigat, Kenya, could serve as a model for strategies to protect deployed troops from sandflies and the *Leishmania* parasites they transmit.

Additionally, new insect repellents and pesticide compounds have been identified by artificial neural network modelling in quantitative structure–activity relation approaches. As the key to stopping vector-borne disease transmission is preventing infected vectors from biting humans, some research is focused on examining the behaviour and response to repellents and pesticides of vectors infected with human pathogens. Many of the haemorrhagic and encephalitic human arboviruses were found to alter vector responses to the host and to insect repellents, compoundng the challenge of interrupting disease transmission.

It is essential to understand the impact of climate on the transmission of vector-borne diseases in order to help public health and agricultural authorities to design better containment or exclusion strategies, increase disease surveillance and control, minimize the cost of surveillance over large areas, forecast risk and anticipate globalization of vector-borne disease and reduce human suffering. Better understanding of the impact of climate change on control strategies will permit optimization of vector control, particularly in harsh environments, which might become more prevalent.

10. CONCLUSIONS AND RECOMMENDATIONS

(1) The various partners acknowledge the work of WHOPES and cherish their collaboration, in which WHOPES plays an independent, communicative role. This win–win collaboration is the best way of using limited resources cost-effectively for the control and prevention of vector-borne disease. WHOPES is an essential, paramount platform.

Recommendation:

- WHOPES must be given the appropriate resources to undertake its normative role and to meet the expectations of its partners efficiently and rapidly.

(2) Vector control is important in the control and elimination (where relevant) of disease vectors, including those of malaria and of re-emerging infectious diseases. In view of the cross-cutting nature of vector control and the need for synergy in interventions, it must adhere to good pesticide management practices in the framework of integrated vector management. Resolution 21 of the Sixty-third World Health Assembly (May 2010), calling for a reduction in reliance on the use of insecticides, is the basis for integrated vector management, and WHOPES and its partners are therefore essential for implementing the Resolution.

Recommendations:

- Capacity should be strengthened for the detection and surveillance of vector-borne diseases, in view of the emergence and re-emergence of these diseases seasonally and geographically. Vector control with broad-based insecticides could be a flexible, speedy response.

- Trained field entomologists and vector control experts are needed to gather data and test and apply control strategies for disease vectors. As entomology is not a popular career path, political and financial incentives are needed to encourage and sustain suitable candidates, to ensure that ministries of health provide the necessary leadership.
- The capacity to manage vector control programmes for multiple diseases should be developed and strengthened, with the support of all relevant stakeholders.

(3) Public health pesticides should be managed throughout their life-cycle to ensure judicious use with minimum risk to human health and the environment. As capacity is weak in most countries, measures are needed to strengthen policy, legislation, regulation, enforcement, information sharing and exchange and capacity development (institutional and technical).

Recommendations:

- The tools and guidelines developed by WHO and FAO are valuable; resources are needed to disseminate them and to ensure:
  - sharing of knowledge about the management of public health pesticides at all levels and strengthening collaboration;
  - harmonizing the requirements and criteria for registration of public health pesticides, including work sharing and information exchange; and
  - establishing or strengthening national regulatory frameworks, including human and financial capacity to regulate the availability, sale and use of pesticides and the capacity for safe disposal of wastes.

- Funding for vector control should include provision for pesticide management and capacity strengthening.

(4) New techniques and approaches should be sought for the development of products, with the support and collaboration of partners such as industry and research and development institutions.

Recommendations:

- Improve, diversify and use existing techniques and approaches, and spell out clearly the roles and functions of all partners.
- Coordinate a shared vision of vector control, including the role of industry in the development of new products.
- Support WHOPES in independent, objective testing and evaluation of new products and techniques.
- Request WHOPES to prepare guidelines for testing and evaluation of new products and techniques.
- Request WHOPES to review recommended products and techniques in the light of new knowledge and requirements when fulfilling its normative role.
- Ensure optimum global collaboration for the development of pesticides for public health by sharing information on new products and techniques for timely and appropriate testing and evaluation and to reduce the time taken to bring a new product to the market.

(5) The threat of failure of malaria control due to spread of pyrethroid resistance is a stimulus for new vector control tools and delivery. This will require partnerships between manufacturers, international health and technical authorities, public health research and academic institutions. The resources currently invested in this area are limited.

Recommendations:

- The number of product development partnerships should be increased, and the resources should be equivalent to those for drug or vaccine development.
- Industry should be supported to search its chemical 'library' for active ingredients with public health attributes.

(6) As many years pass between identification of a new active ingredient and the launch of a new public health pesticide product, the immediate successors to pyrethroids are likely to emerge from existing agricultural insecticides ('re-purposed insecticides'). Existing insecticides should be used judiciously in order to expand their useful life.

Recommendations:

- New formulations should be developed to prolong the residual activity of re-purposed insecticides and make them suitable for use on walls and ceilings or on mosquito nets.
- Capacity to ensure judicious use of insecticides and resistance prevention and management strategies should be built by national vector-borne disease control programmes in the context of integrated vector management.

(7) On the basis of experience in the use of combination therapy to preserve drug sensitivity and the efficacy of treatment, research into vector control tools, especially insecticide-treated mosquito nets, based on such principles is urgently needed.

Recommendation:

- Guidelines should be drawn up for testing and evaluating 'combination nets'.

(8) Irritability or repellency induced by DDT has been underrated. Active ingredients with repellent properties that can be used on household surfaces or with an appropriate emanator would result in new categories of products and new approaches to household protection.

Recommendation:

- Draw up guidelines for testing and evaluation of spatial repellents as a priority.

(9) Alternative delivery mechanisms, such as durable wall lining, could extend the residual activity of insecticides of shorter persistence.

Recommendation:

- Draw up guidelines for testing and evaluating durable wall lining as a priority.

ANNEX 1. AGENDA

Thursday, 24 June 2010

09.00–09.15	Message from the WHO Director-General
	Dr Hiroki Nakatani, Assistant-Director General HIV/AIDS, Tuberculosis, Malaria and Neglected Tropical Diseases
	Opening of the meeting
09.15–09.30	WHOPES—50 years of global leadership in standard setting and evaluation of public health pesticides
	Dr Lorenzo Savioli, Director, Department of Control of Neglected Tropical Diseases
09.30–10.30	Presentation of commemorative plaques
11.00–11.05	Appointment of chairperson and rapporteurs
11.05–11.25	Emerging and re-emerging vector-borne diseases
	Dr Ron Rosenberg, Centers for Disease Control and Prevention, USA
11.25–11.45	Malaria elimination and the role of vector control
	Professor Brian Greenwood, London School of Hygiene and Tropical Medicine, United Kingdom
11.45–12.05	Code of conduct on the distribution and use of pesticides—FAO/WHO joint programme on sound management of pesticides
	Dr Mark Davis, FAO
12.05–12.30	Discussion
14.00–14.20	Capacity-strengthening essential to sustainable vector-borne disease control and pesticide management
	Dr Michael Macdonald, United States Agency for International Development, USA

14.20–14.40	Collaboration with other international instruments: Stockholm Convention and Strategic Alliance for International Chemicals Management
	Mrs Agneta Sundén-Byléhn, UNEP Chemicals, Switzerland
14.40–15.00	Partnership and coordination: key to success
	Dr Kate Aultman, Bill and Melinda Gates Foundation, USA
15.00–15.30	Discussion
16.00–16.20	Development of new public health pesticides: challenges and way forward
	Dr Egon Weinmüller, Vector Control Team, CropLife International, Germany
16.20–17.00	Challenges with public health pesticide management: country perspectives
	Dr Qiyong Liu, National Institute for Communicable Disease Control and Prevention, Chinese Centre for Disease Control and Prevention, China
17.00–17.40	Challenges with public health pesticide management: WHO regional perspectives
	Dr Birkinesh Ameneshewa, WHO Regional Office for Africa
	Dr Abraham Mnzava, WHO Regional Office for the Eastern Mediterranean
17.40–18.00	Discussion

Friday, 25 June 2009

	Innovative techniques for vector control
09.00–9.15	Devising novel strategies against vector mosquitoes and houseflies
	Dr Gary Clark, Center for Medical, Agriculture and Veterinary Entomology, United States Department of Agriculture, USA

09.15–09.30	New repellents, insecticides and application systems from the Deployed War-fighter Protection programme Dr Graham White, United States Armed Forces Pest Management Board, USA
09.30–09.45	Update on the product portfolios of the Innovative Vector Control Consortium in insecticides and information systems and tools Dr Robert Sloss, Innovative Vector Control Consortium, United Kingdom
09.45–10.00	The threat of pyrethroid resistance for control of malaria caused by *Anopheles gambiae* and the prospect for sustaining insecticidal control using alternatives as indoor residual spraying and long-lasting insecticidal nets Dr Mark Rowland, London School of Hygiene & Tropical Medicine, United Kingdom
10.00–10.15	Insecticide combinations for controlling insecticide-resistant malaria vectors Dr Vincent Corbel, Institut de Recherche pour le Développement, Benin
10.15–10.30	Discussion
11.00–11.15	Advances in the discovery of novel repellents and application strategies Dr Ulrich Bernier, Center for Medical, Agriculture and Veterinary Entomology, United States Department of Agriculture, USA
11.15–11.30	Shaping vector control policy to include spatial repellents Dr Nicole Achee, Uniformed Services University of the Health Sciences, USA
11.30–11.45	Application of near-infrared spectroscopy to medical entomology: age-grading and species identification Dr Robert Wirtz, United States Centers for Disease Control and Prevention, USA

11.45–12.00	Delivering pesticides on target—the role of good-quality spray equipment Professor Graham Matthews, Imperial College, United Kingdom
12.00–12.30	Discussion
14.00–14.15	New approaches to the sustained efficacy of long-lasting nets Dr Helen Pates Jamet, Vestergaard Frandsen, Switzerland
14.15–14.30	Development of physico-chemical test methods for characterization of long-lasting insecticidal nets Dr Olivier Pigeon, Walloon Agricultural Research Centre, Belgium
14.30–14.45	Controlling vector-borne diseases and adapting to climate change with novel research on disease forecasting to target new vector control materials and technologies Dr Kenneth Linthicum, Center for Medical, Agriculture and Veterinary Entomology, United States Department of Agriculture, USA
14.45–15.30	Discussions
16.00–17.00	Conclusions
17.00	Closure

ANNEX 2. LIST OF PARTICIPANTS

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