# The work of the African Network on Vector Resistance to insecticides 2000 – 2004

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**CONTENTS**

**Abbreviations/Acronyms**

| | |
|---|---|
| WHO | World Health organization |
| AFRO | Africa Regional Office |
| WHO/AFRO | World Health Organization Regional Offie for Africa |
| RBM | Roll Back Malaria |
| GFATM | Global Fun Fund for HIVAIDs, Tuberculosis and Malaria |
| DDT | Dichloro diphenyl trichloroethane |
| ITNs | Insecticide Treat Nets |
| ANVR | African Network on Vector Resistance |
| WHO/HQ | World Health Organization Head Quarters |
| SAIMR | South African Instituted for Medical Research |
| OCEAC | l'Organisation de Coordination pour la lutte contre les Endemies en Afrique Centrale |
| NMCPs | National Malaria Control Programs |
| VERMAS | Vecror Resistance Management System |

## EXECUTIVE SUMMARY

Malaria vector control in Africa relies principally on the use of insecticides that can be applied as an indoor residual deposit or can be used to treat materials such as mosquito nets and curtains. Resistance in malaria vectors carries the potential to adversely affect the current efforts that rely mostly on the use of insecticides to reduce malaria transmission.

The RBM initiative proposed in 1998 to establish technical support networks designed to support the implementation of malaria control activities at country level. This initiative coupled with lack of capacity for vector control in general and for insecticide resistance maintaining in particular in most vector born disease control programs in Africa gave rise to the establishment in 2000 of the African Network for Vector Resistance to insecticides (ANVR) under the auspices of WHO/AFRO. ANVR is divided into four sub-networks: West Africa, Central Africa, East Africa and southern Africa. The network is based on institutional membership including national vector borne diseases control programs and research institutes in the region.

The establishment of the ANVR has created a platform for effective networking and capacity building which has led to increasing partnerships between research institutions, national vector control programs and the private sector. Since its inception, the network significantly contributed to capacity development of national programs particularly for monitoring and management of malaria vector resistance to insecticides. Sixty-three staff of national program were trained in vector susceptibility tests and related techniques; preliminary data on status of malaria vector susceptibility to insecticides was collected from 24 countries; malaria vector characterization was updated in 9 countries; and standard protocols, guidelines and guiding documents in relations to planning implementation and monitoring of vector resistance were prepared and made available to countries.

Based on outcomes of the various studies on insecticide susceptibility and characterization of malaria vectors conducted by the national vector borne disease control programs with the support of the sub-networks in different parts of the continent, ANVR has established a centralized database for use by members of the network. Roll Back Malaria through the WHO/AFRO funded these activities of the network with additional support from the private sector. However, sustainability of effective vector resistance monitoring and management in Africa will depend on increased commitment and operationalization of the activity by national malaria control programs. ANVR will continue providing technical support and facilitation of partnership and inter-country collaboration, among other activities.

# 1. INTRODUCTION

## 1.1. The malaria problem

Malaria is endemic in 42 out of the 46 nations in the WHO African Region. An estimated more than a million African children die every year due to malaria and related causes. The disease hampers significantly economic development of the region with a lose of about 1.3% growth per annum (DDC/AFRO, 2004).

After the relative silence in the years following the transformation of the global malaria eradication to a control program, malaria control has received a remarkable attention both globally and nationally in recent years. The African Initiative for Malaria control, the Roll Back Malaria (RBM) initiate and recently the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) are the growing commitments for malaria control and reduction of its burden particularly in Sub-Sahara Africa.

## 1.2. Vector control in malaria control

Malaria prevention using anti-vector measures is among the most important components of control strategies of the above malaria control initiatives. Application of chemical methods including indoor residual house spraying and treating mosquito nets and other materials is one of the main strategic elements of RBM to achieve its targets of halving malaria burden by the year 2010.

However, any long-term vector control programme based on repeated applications of insecticides may be faced, sooner or later, with problems of insecticide resistance. Cases of DDT and dieldrin resistance in malaria vectors had occurred in the past and were reported as one of the causes of the failure of malaria eradication programmes. To date, the appearance of vector resistance to insecticides, particularly to pyrethroids, sets a great challenge to the process of taking to scale the use of ITNs in the Region and for the implementation of residual house spraying of insecticides in Southern and Eastern Africa.

## 1.3. The threat of vector resistance to malaria control

Recently, the development of insecticide resistance has been shown to have dramatic effects on the rate of disease transmission in certain areas that historically had achieved significant control through the use of indoor residual spraying. In South Africa, resurgence of malaria during the period 1996 to 2001, was shown to be associated with the emergence of pyrethroid resistance in the major malaria vector *Anopheles funestus* Giles (Hargreaves K at al, 2000). The effect of pyrethroid resistance on the efficacy of ITNs may differ from that of on IRS due to the different mechanisms of protection of the to methods. ITNs provide a chemical and physical barrier against insecticide resistant mosquitoes that may also be repelled by the presence of the insecticide. For instance, in Cote d'Ivoire, resistance that was observed in the major malaria vector *Anopheles gambiae* Giles to pyrethroid and DDT was not associated with a decreased efficacy of pyrethroid treated mosquito nets (Darriet F et al. 1998; Henery MC at al, 1999).

### 1.4. Establishment of the African Network for Vector Resistance to Insecticides

The incidence of insecticide resistance already recorded in different parts of the region coupled with the extremely limited number of insecticide classes and compounds available for use in public health programmes has emphasized the need to find effective ways of circumventing the development and spread of insecticide resistance in the African Region. However, many national vector borne disease control programs lack the required capacity to systematically monitor and manage vector resistance due to scarcity of trained staff and absence of guidelines. In order to build capacity at national level and fill in this critical gap, and also in response to the proposal from the RBM initiative in 1998 to establish technical support networks for supporting the implementation of malaria control activities at country level, the African Network for Vector Resistance to Insecticides (ANVR), was subsequently established in 2000.

The main mandate of the network is to build the capacity in all malaria endemic countries in Africa for monitoring and management of insecticide resistance. The network is managed by its Secretariat, WHO/AFRO and is based on institutional membership including national vector borne disease control programs, research institutions in Africa as well as in Europe. The ANVR is organized into four sub-networks: West Africa, Central Africa, East Africa and Southern Africa. The sub-networks cover countries in the respective WHO/AFRO epidemiological blocks (Annex 1). Most funding for ANVR activities to date has been obtained from Roll Back malaria, through WHO/AFRO.

Since its establishment, the network has significantly contributed to the development of the technical capacity at national level and increased knowledge on the status of malaria vectors in the Region in regards to resistance. This report is, therefore, aimed at sharing information on the achievements and experiences of the network with national disease control programs of member states and partners.

## 2. GENERAL OBJECTIVE AND TERMS OF REFERENCE OF ANVR

General objective of the ANVR is to ensure an effective and judicious use of insecticides in disease vector control in the WHO African region.

The specific terms of reference of the ANVR are:

- To assist WHO/AFRO member states (disease control programs and other vector control organizations) in the testing, monitoring and management of vector resistance to insecticides. This is achieved through building the necessary technical capacity, provision of technical assistance in the supervision of field testing activities, the identification of vector species and resistance mechanisms if they exist, the development and assessment of new monitoring tools and the continuous production of updated vector distribution and resistance maps for each country and for the whole region.
- To provide opportunities for medical entomologists in research institutions and universities and public health workers in vector control programs to collaborate with a view to strengthening operational research and vector control.

- To assist member states in capacity building for vector control and particularly in the training and supervision of nationals in the monitoring and management of insecticide resistance.
- To collaborate with all relevant institutions in order to standardize and harmonize methodologies, protocols and guidelines for analysis of data and interpretation of results.
- To build consensus on approaches to the management of insecticide resistant vector populations and to prepare practical guidelines for the management of vector resistance for use at national level.
- To co-ordinate network activities, facilitate and promote the dissemination and exchange of information on vector resistance to insecticides.

## 3. CURRENT ACHIEVEMENTS OF ANVR

### 3.1. Updating and development of technical documents

Availability of clear and updated protocols for vector resistance monitoring and related activities has been critical in strengthening countries' capacity for vector resistance management. In effect to this, ANVR has updated and/or prepared and made available for countries the required protocols as indicated below.

#### 3.1.1. Standardized protocol for testing malaria vector susceptibility to insecticides in the African Region

The protocol for vector susceptibility testing was first developed in 1981 by WHO/VBC, Geneva. This was revised and adopted to the regional level by ANVR in 2000 during a workshop organized by the Network in Cote d'Ivoire. Since then, the protocol has been extensively used to evaluate the susceptibility level of malaria vectors to the various groups of insecticides including pyrethroids in Africa. The current information on the susceptibility status of the malaria vectors in the various countries is gathered using this version of the protocol. Nevertheless, experiences of its intense application revealed that there is a need for more detailed understanding of vector resistance in relation to its impact on vector control interventions beyond determination of its occurrence. Due to this need, since 2000, scientific advances have been made with understandings of the vector populations and resistance mechanisms in relation to their impact on vector control interventions. Based on these, in 2004, ANVR further revised and updated the protocol and made available to member states.

#### 3.1.2. Guide to include resistance management in action plans on malaria vector control and requests for funding

Resistance management should be an integral component of any vector control program in order to ensure sustained vigilance and implementation of management interventions in a way that limit the development of resistance and minimize its impact on the efficacy of control interventions. In many vector borne diseases control programs, vector resistance monitoring is considered as research activity conducted once in a while. As a

result, resistance usually is not detected timely enough to plan and implement management tactics. The response is commonly change of insecticide made in a rush in order to keep the intervention effective. In order to help addressing this problem, ANVR produced and made available guiding document to support countries in the preparation of budgeted resistance monitoring plans as part of program implementation action plans and in any proposal soliciting funding for vector control programs.

### 3.1.3. Guidelines for monitoring and management of insecticide resistance

The WHO/HQ, Geneva, has developed general guidelines for monitoring and management of insecticide resistance. These are now being adapted to local conditions by the WHO/AFRO and will soon be made available to national programs for use. The guidelines propose strategies to prevent/delay development of resistance; approaches to minimize impact of resistance should it appear; and possible alternative strategies in case of resistance reached to a level requiring replacement of the insecticide(s) in use.

## 3.2. Training

National capacity building in this regard included development of training curriculum and training national entomologists in the required techniques.

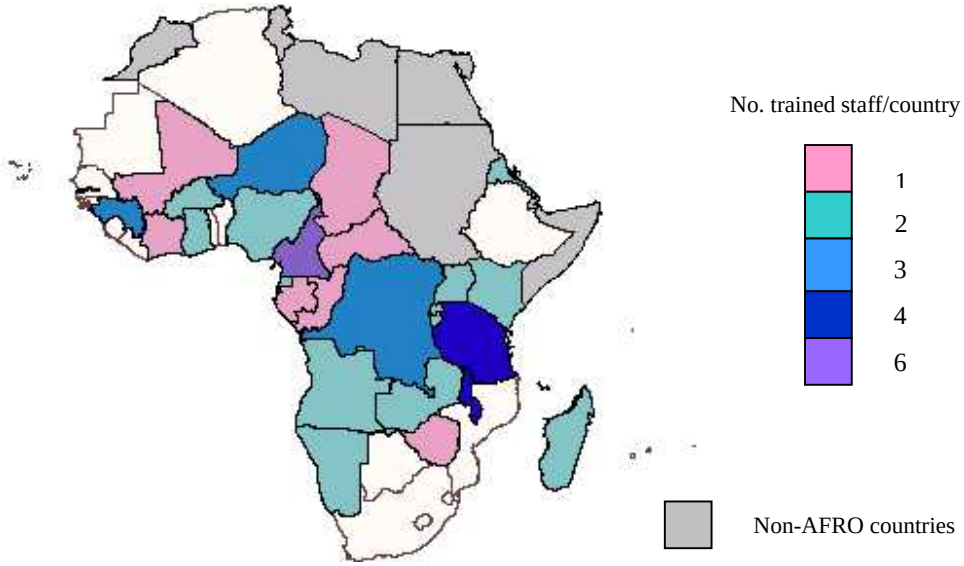
### 3.2.1. Development of training curriculum modules for vector susceptibility testing and resistance management

In order to ensure relevant and quality training, course curriculum and modules were prepared. The curriculum describes topics of the course and how these are going to be delivered and accomplished. The modules focused on methods of collection, handling and preservation of field vector samples; morphological identification of vector species; rearing of mosquito larvae to adult phase in an insectary environment; application of standard WHO insecticide susceptibility assays including data analysis; concept and principles of vector resistance monitoring and management; and skills of writing proposals soliciting grant.

### 3.2.2. Implementation of training courses

A series of six training courses on testing of vector susceptibility to insecticides, and resistance management were given annually from 2000 to 2003 with collaboration of WHO/AFRO and three ANVR member institutions, namely: South African Institute for Medical Research of South Africa (SAIMR); Centre Muraz of Burkina Faso and l'Organisation de Coordination pour la lutte contre les Endemies en Afrique Centrale (OCEAC) of Cameroon. The courses strictly followed the curriculum and used the modules developed. A total of 163 national entomologists and/or vector control specialists from 30 countries were trained. Annex 2 summarizes the number of trained staff per country through the training programs that were organized in collaboration with the three institutions.

**Figure 1**. Number of national staff trained in vector resistance testing and related techniques, 2000-2003.




The courses were specifically designed to give national entomologists/vector control specialists practical skills in the detection and evaluation of insecticide resistance in malaria vector species and ensure understanding of resistance management strategies. Each training course focused on field collection, laboratory analysis and handling of vector mosquito samples, morphological identification of species, rearing of larvae to adult stages in an insectary/ laboratory environment. Trainees conducted the WHO standard insecticide susceptibility assays and data analysis. Theoretical background relevant to all the above practical sessions were presented and discussed thoroughly. Concept and principles of vector resistance monitoring and management, and building skills for the development/writing of proposals for soliciting grant were emphasized during the courses. The later was intended to obtain financial support for the initiation of vector susceptibility tests by each trainee in each participated country. Figure 1 shows number of trained national entomologist/vector control specialist from each participating country.

At the end of each course students were guided in the development of proposals detailing their plans and financial requirements that would enable them to conduct initial surveys of vector susceptibility to insecticides in their respective countries. The proposals were submitted to WHO/AFRO and most of them were funded.

### 3.3. Financial, material and technical support for vector susceptibility studies

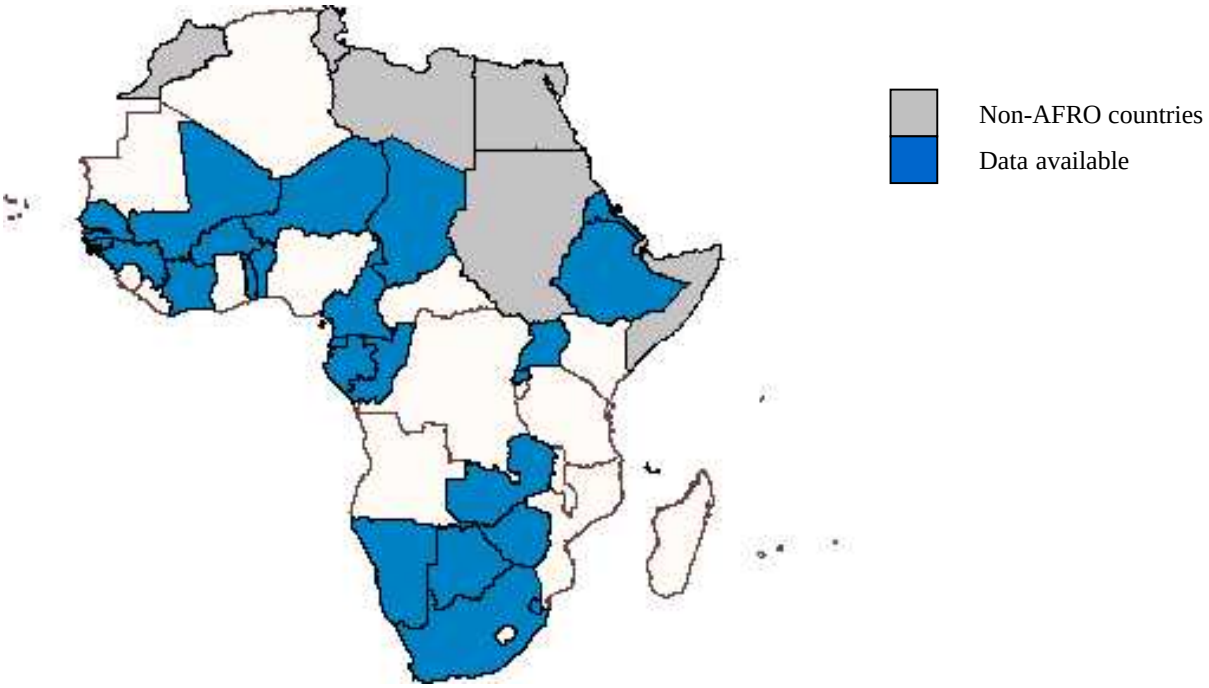
Based on the proposals submitted by each country at the end of the training, the ANVR (WHO/AFRO) provided financial and logistical (susceptibility test kits and insecticide impregnated papers) support to 24 countries. Also, vector control experts from ANVR member institution were deployed in each country during initiation of the surveys to

ensure appropriate and quality implementation. Countries were provided with a total of about US$200,000 to collect preliminary database on the status of malaria vector susceptibility level. This does not include the cost of test kits and supplies they were provided with.

### 3.3.1. Vector susceptibility survey in individual countries

With the help of the financial, supplies and technical support from the sub-networks, the 24 countries (Fig.2) conducted 473 tests in 196 sites and produced initial information on the status of vector susceptibility to insecticides. The information has been forwarded to the WHO/AFRO where a regional preliminary database has been created (section 3.4). Of note, in addition to wide spread DDT and pyrethroid cross-resistance in West Africa, are indications of resistance to DDT and pyrethroids in *An. gambiae* sl in Cameroon. Surveys in Sao Tome and Principe indicated DDT resistance in *An. gambiae*. There are also indications of DDT resistance in *An. gambiae* in Congo and Bioko Island off Equatorial Guinea. Early indications of pyrethroid resistance in *An. gambiae* were observed in Uganda, among other results. Detailed outcomes of the studies are presented in a separate report of the network (DDC/AFRO, 2005)

**Fig 2**. Countries with information on malaria vector susceptibility level to insecticides in ANVR database




### 3.3.2. Multi-centre studies on vector susceptibility

Two multi-centric studies, one in west and another in southern Africa were carried out for characterization of malaria vector populations including distribution and resistance status Nine out of the 24 countries (Fig. 3), 5 in southern and four in western Africa sub-regions

were involved in the study. Center Muraz of Burkina Faso, Malaria Research and Training Center of Mali, Centre de Recherches Entomologiques of Benin and National Institute for Communicable Diseases of South Africa, in collaboration with the respective NMCPs, conducted the tests in the respective sub regions. The studies were fully financed by the RBM through WHO/AFRO.

Some notable outcomes were observed from the study. Significant levels of resistance to DDT and pyrethroids were recorded in *Anopheles gambiae* sl in Togo. The study in Burkina Faso established the spatio-temporal vector species composition as well as the extent of DDT/pyrethroid resistance in *An. Gambiae* S form and its early appearance in the M form. In southern African pyrethroid resistance in *An. funestus* and DDT resistance in *An. arabiensis* were detected in Kwazulu/Natal, South Africa. There were also indications of insecticide resistance in malaria vectors in Zambia (*An. gambiae*) and Zimbabwe (*An. arabiensis*). Surveys conducted in Namibia, Botswana and Swaziland revealed full susceptibility to all insecticide classes tested.

### 3.4. Development of database

#### 3.4.1. Vector Susceptibility level to insecticides

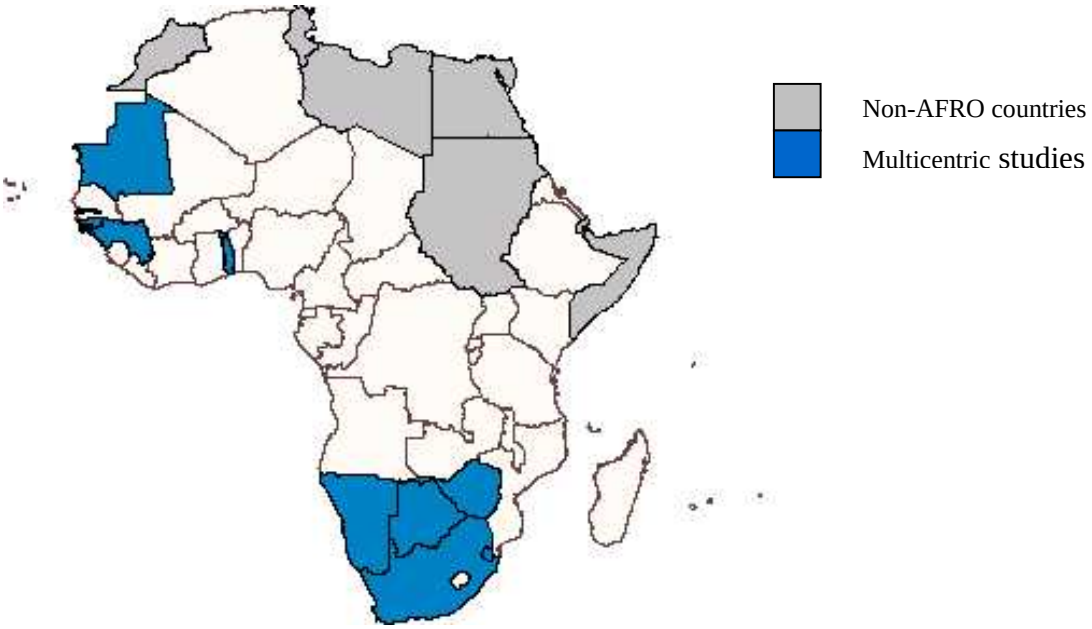
Based on the outputs from the above studies, the WHO/AFRO has developed a database input screen called VERMAS to computerize all information on the vector resistance status collected from the countries. The database is composed of different attribute tables (Characteristics of the survey area, insecticides used, vector species tested, vector susceptibility status, knock down time) linked to each other and to the geographical locations (latitude and longitude) of the survey sites. This was presented during the 3$^{rd}$ annual meeting of ANVR and discussed by experts representing member institutions. Although the input screens still have to be further refined, it is however usable by the WHO/AFRO. The screen will soon be finalized, produced and distributed to the national programs for the establishment of national databases. This is intended to serve as a decision-making tool and ensure effective management of vector resistance throughout the region. National entomologists or vector control responsible individuals would be trained on the use of the database at national level.

At the moment, the regional database comprises 473 records (test results) collated from 196 survey sites in 24 countries. To this effect, results of surveys that were conducted by each national vector control program with the support of member institutions were forwarded, through the respective sub-network coordinator, to WHO Regional Office to Africa. Here, each result was validated using test specifications of the WHO standard protocol for testing adult mosquito susceptibility to insecticides. These include physiological condition (unfed, bleed fed etc) of sample mosquitoes; total numbers of tested and control mosquitoes; number of replicates and test conditions (temperature, relative humidity). Only results of tests confer to the standards and conditions stated in the protocol were entered into the database. In all cases feedback was given to the countries. In case of results where test conditions seem not confer to that of the standard protocol, countries where requested to provide more information and/or clarifications on

the gaps. If no more information is obtained to validate, the results were excluded from the database.

The results show that some countries were sampled more than others. The least being countries with one site, which included Congo, Gabon and Chad. Countries with the highest number of sites include Burkina Faso, Cameroon, Mali, Namibia, Uganda and Zimbabwe with more than 10 sites each and the remaining were in between. This information however needs to be updated as more studies are carried out in more sites of these countries and in other countries of the region where the study has not yet been initiated. The results from these tests have led to the production and publication of the first atlas of malaria vector resistance to insecticides in Africa (DDC/AFRO, 2005)

**Figure 3**. Countries of multi-centric studies for vector characterization in west[1] and southern Africa




### 3.4.2. Vector distribution

Thus far, based on the results of the two multi-centric studies, individual country surveys and also some available information from research institutions, a regional perspective of vector distribution is updated and a database created. The information compiled in this regard is still limited. Data collection would continue in order to get a more complete and elaborated map of malaria vector distribution in the region.

[1] The study in Cote d'Ivoire was cancelled due to the security problem prevailed during implemenation

### 3.7. Annual meetings

The ANVR holds annual meetings to review network achievements, identify constraints, agree on standards for vector susceptibility monitoring and management procedures and assess the results of vector composition and insecticide susceptibility studies in the various participating countries. Future priorities and action plans are then formulated accordingly. Annual meetings to date have been held in Yaounde, Cameroun (2000); Bobo Dioulasso, Burkina Faso (2002), Johannesburg, South Africa (2003) and Cotonou, Benin (2004). Apart from assessing implementation of POAs of outgoing years and planning for incoming ones, the following are major outputs of the ANVR annual meetings:

- South Africa in 2003 – Reviewed the VERMAS and recommended modifications
- Benin in 2004 – Agreed upon and prepared draft outline on guideline for vector resistance management, and draft guiding document for establishment of sentinel sites for vector resistance monitoring

### 3.8. Partnerships

ANVR itself being a network of collaborating institutions including the national vector born disease programs in the region, it also established a successful partnership with research institutions, similar networks out of the region and the private sector. These have contributed financially and technically towards the achievements of ANVR. The following are the major partners:

- The International Resistance Action Committee (IRAC)
- The European Network on Insect Resistance (ENMARIA)
- The Liverpool School of Tropical Medicine, Liverpool
- The Public Health Project Team, Croplife International
- Environmental Health Project, USAID
- Insecticide producers and supplies: BAYER, AVIMA, Syngenta, Wefco

## 4. CONCLUSION AND THE WAY FORWARD

The establishment of the ANVR has created a platform for effective networking and capacity building which has led to increasing partnerships between research institutions, national vector control programs and the private sector. Since the inception of the ANVR, large-scale entomological surveys focusing on establishing vector susceptibility to insecticides and updating vector distribution have been conducted throughout the WHO African region.

These surveys have highlighted the widespread incidence of insecticide resistance in target vector populations and have established the need for generating sound, evidence-based management interventions where resistance already occurs as well as initiating programs designed to prevent the spread of resistance to areas currently unaffected. The information gathered through the multi-centre studies has contributed significantly to the

process of filling the gap in the knowledge of malaria vector distribution and bionomics in the region.

African Network on Vector Resistance has built the capacity for vector resistance monitoring and management in most countries of the WHO African region. It has laid the ground for effective data collection, analysis and utilization for evidence-based vector control program implementation. However, sustained monitoring of malaria vector resistance and management in the region relies on increased commitment of national programs.

Vector susceptibility testing should be operationalized and become part of the budgeted national malaria control plan of each country. It also needs to be incorporated in any proposal looking for funding for program implementation. NMCPs are encouraged to use the opportunity provided by the GFATM and other similar initiatives to ensure availability of resources for sustained vector resistance monitoring. African Network on Vector Resistance remains committed to facilitate partnership and inter-country collaboration, providing technical support to NMCPs, compiling and dissemination of information at regional and sub-regional levels.

## ANNEXES

**Annex1.** Countries of the four epidemiological blocks of the WHO/AFRO

**West Africa epidemiological block**:
Algeria, Benin, Burkina Faso, Cot d'Ivoire, The Gambia, Ghana, Guinea Bissau, Guinea, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo

**Central African epidemiological block:**
Cameroon, Cape Verde, Central African Republic, Chad, Congo, Democratic Republic of Congo, Equatorial Guinea, Gabon, Sao Tome and Principe;

**East Africa & Grate lakes epidemiological**
Burundi, Eritrea, Ethiopia, Kenya, Rwanda, Tanzania and Uganda

**Southern African epidemiological block**
Angola, Botswana, Madagascar, Malawi, Mauritius, Mozambique, Namibia, South Africa, Swaziland, Zambia and Zimbabwe.

**Annex 2**. Trainings conducted by 3 ANVR member institutions, 2000 – 2003

| Year | Training Institution | Trainee home country | No. trained staff |
|---|---|---|---|
| 2000 | National Institute for Communicable Diseases, South Africa | Malawi | 2 |
| | | Namibia | 2 |
| | | Uganda | 2 |
| | | Zambia | 2 |
| | | Zimbabwe | 1 |
| | Centre Muraz, Burkina Faso | Burkina Faso | 2 |
| | | Comoros | 2 |
| | | Cote d'Ivoire | 1 |
| | | DRC | 1 |
| | | Guinea Conakry | 1 |
| | | Mali | 1 |
| | | Niger | 1 |
| | | Chad | 1 |
| 2001 | National Institute for Communicable Diseases, South Africa | Eritrea | 2 |
| | | Gambia | 1 |
| | | Nigeria | 2 |
| | | Tanzania | 2 |
| | l'Organisation de Coordination pour la lutte contre les Endemies en Afrique Centrale (O.C.E.A.C), Cameroun | Cameroun | 6 |
| | | Congo | 1 |
| | | CAR | 1 |
| | | Angola | 1 |
| | | Gabon | 1 |
| | | E. Guinea | 2 |
| | | Rwanda | 2 |
| 2003 | National Institute for Communicable Diseases, South Africa | Gambia | 2 |
| | | Kenya | 2 |
| | | Ghana | 2 |
| | | Malawi | 2 |
| | | Zanzibar | 2 |
| | l'Organisation de Coordination pour la lutte contre les Endemies en Afrique Centrale (O.C.E.A.C), Cameroun | Angola | 1 |
| | | Burundi | 2 |
| | | DRC | 2 |
| | | Guinea Conakry | 2 |
| | | Niger | 2 |
| | | Sao Tome & Principe | 2 |
| | | Madagascar | 2 |
| **Total trained** | | | **63** |

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