GOVERNMENT OF SIERRA LEONE

**MINISTRY OF HEALTH AND SANITATION**

**NATIONAL MALARIA CONTROL PROGRAM**

# INSECTICIDE RESISTANCE MONITORING AND MANAGEMENT PLAN (IRMMP)



AUGUST 2016

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## ACKNOWLEDGEMENT

The National Malaria Control Programme (NMCP) of the Ministry of Health and Sanitation (MOHS) extends its gratitude to all those who participated in the development of this plan. The development of this plan would not have been possible without the leadership of the Ministry of Health and Sanitation and the World Health Organization (WHO). Sincere gratitude goes to the Directorate Environmental Health and Sanitation, the Pharmacy Board, the Health Education Division and Neglected Tropical Diseases programme for their valuable contributions.

## LIST OF ACRONYMS AND ABBREVIATIONS

| | |
|---|---|
| ANVR | African Network on Vector Resistance |
| DDT | Dichlorodiphenyltrichloroethane |
| DVS | Dominant vector system |
| GPIRM | Global Plan for Insecticide Resistance Management in malaria vectors |
| IRM | Insecticide resistance management |
| IRMM | Insecticide Resistance Monitoring and Management |
| IRMMP | Insecticide Resistance Monitoring and Management Plan |
| IRS | Indoor residual spraying |
| ITN | Insecticide-treated net |
| IVM | Integrated Vector Management |
| *Kdr* | knock-down resistance gene |
| LLIN | long-lasting insecticidal net |
| LSM | Larval Source Management |
| NMCP | National Malaria Control Programme |
| SOP | Standard Operating Procedure |
| WHO | World Health Organization |
| WHOPES | World Health Organization Pesticide Evaluation Scheme |

## EXECUTIVE SUMMARY

Malaria remains one of the most critical public health challenges in Africa despite intense national and international efforts. Indoor Residual Spraying (IRS) and Long Lasting Insecticide treated Nets (LLINs) are the primary tools for malaria vector control, which have contributed massively in curbing malaria incidence. However, emergence and spread of insecticide resistance in major mosquito vector species could jeopardize the success of malaria control programs. Insecticide resistance in malaria vectors have also been reported in Sierra Leone.

As response to this threat WHO provided a generic guideline for managing insecticide resistance where it occurs in its Global Plan for Insecticide Resistance Management in Malaria Vectors (GPIRM) in 2012. The GPIRM urged endemic countries to develop strategies for preventing and managing insecticide resistance so as to ensure the limited number of insecticides available for vector control are protected. The comprehensive strategies will help to prevent and/or delay resistance development to insecticides, or regain susceptibility in malaria vector populations in areas where resistance has already arisen. Sierra Leone has developed this Insecticide Resistance Monitoring and Management Plan (IRMMP) to respond to this global. The developed plan is for four years (2017-2020) and is in line with the current 2016-2020 malaria strategic plan.

This plan is intended to guide all malaria control programme, vector control stakeholders, policy makers, research institutions and partners on insecticide resistance monitoring and management in the country. The overall objective of IRMMP is to maintain the effectiveness of existing insecticidal vector control interventions, despite the threat of resistance. Specifically, the strategic objectives of this IRMMP are:

- To provide framework for Insecticide resistance monitoring (including detection of resistance mechanisms); data collection and sharing; and implementation of insecticide resistance management.
- To strengthen the capacity of personnel involved in the insecticide resistance monitoring and management.
- To provide forum and strategic framework for IVC among partners to ensure coordinated and harmonized implementation of the vector elimination interventions.

The NMCP will coordinate the implementation of this plan using its existing multisectoral structure. NMCP will form a TECHNICAL WORKING GROUP to oversee and advice NMCP on all issues related to the implementation of IRMMP. The implementation of the IRMMP is estimated to cost **LE 3,423,996,508 (US$ 517,776)** annually. For the period of four years (2017 – 2020), the plan is projected to cost **LE 13,386,880,000 (US$ 2,059,520).**

# 1 BACKGROUND INFORMATION

## *1.1 Introduction*

Vector control is the cornerstone of malaria control initiatives. The use of insecticide-based vector control interventions in malaria endemic countries including Africa are expanding with the rapid scale-up of insecticide treated nets and/or long-lasting insecticide treated nets (LLINs) and indoor residual spraying (IRS) (WHO, 2015). However, the effectiveness of such interventions depends entirely on the high level of susceptibility of malaria vectors to the insecticides. Unfortunately these malaria vector control interventions are dependent on a limited number of insecticides from four chemical classes, namely, the organochlorines, organophosphates, carbamates and pyrethroids (http://www.who.int/whopes/en). By far the pyrethroid is the only class of insecticides currently recommended by the World Health Organization (WHO) for use in LLINs (Ranson et al., 2011; WHO, 2015).

The success of these vector control interventions has contributed towards a dramatic reduction in malaria associated morbidity and mortality in Africa (WHO, 2015). However the emergence and rapid spread of insecticide resistance to malaria vectors presents a great challenge to the gains so far made in malaria control for the insecticide-based tools (WHO, 2015). Therefore to sustain and build further on these gains, and enable further progress, there is a need to effectively manage malaria vector resistance to insecticides.

To respond to these challenges, the WHO developed the Global Plan for Insecticide Resistance Management in malaria vectors (GPIRM). The GPIRM is a call for coordinated actions from all stakeholders to manage this insecticide resistance threat and henceforth maintaining the effectiveness of the malaria vector control interventions. It outlined a comprehensive plan for global, regional and national action. To implement actions against insecticide resistance, the NMCP has developed this insecticide resistance monitoring and management plan as an integral part of the vector control; and surveillance, monitoring and evaluation components of the 2016-2020 national malaria strategic document. Therefore, IRMMP is not a stand-alone document; it adheres to the existing malaria strategic plan and links with other specific implementation documents of the NMCP and the MOHS. An illustration on how the IRMM plan links with the existing national malaria strategic plan is shown in figure 1 below. This plan is intended to guide the malaria control programme, vector control stakeholders, policy makers and partners on insecticide resistance monitoring and management in the country. Malaria control funding agencies, International Organizations as well as academic and research institutions should also utilise this plan to help mobilize resources, which will contribute in the monitoring and management of insecticide resistance.


**Figure 1:** A simple schematic representation of how the IRMM plan feeds into the national malaria strategic (Source: WHO, 2014)

## *1.2 Objectives of the Insecticide resistance monitoring and management plan*

### *1.2.1 General objective*

The overall objective of IRMMP is to maintain the effectiveness of existing insecticidal vector control interventions, despite the threat of resistance.

### *1.2.2 Specific strategic objectives*

- To provide framework for Insecticide resistance monitoring (including detection of resistance mechanisms); data collection and sharing; and implementation of insecticide resistance management.
- To strengthen the capacity of personnel involved in the insecticide resistance monitoring and management.
- To provide forum and strategic framework for IVC among partners to ensure coordinated and harmonized implementation of the vector control interventions.

### *1.2.3 Expected outputs*

- There will be rational and judicious use of insecticides in public health and agriculture to minimize insecticide selection pressure
- The effectiveness of existing insecticidal vector control interventions are maintained
- Malaria vector susceptibility to insecticides are sustained and/or regained.

# 2 SITUATION ANALYSIS

## *2.1 Epidemiological stratification of malaria in Sierra Leone*

Malaria is endemic in Sierra Leone with stable and perennial transmission in all parts of the country. The peak malaria transmission occurs at the beginning and end of the rainy season (April & October). It is still a major public health problem and also an important cause of morbidity, mortality, disability and poverty. The country has two distinct malaria epidemiological strata. In two-thirds of the districts, malaria is characterized by seasonal peaks of transmission and in the remaining one-third of the districts malaria transmission is more stable all year round (NMCP 2015). The estimated malaria prevalence distribution in the country by district among children less than five years in February/March 2013 is shown in figure 2.

*Plasmodium falciparum* is the dominant parasite mainly responsible for all severe cases and over 95% of uncomplicated cases. *Plasmodium malariae* and *Plasmodium ovale* are also implicated to cause clinical malaria in the country (British Medical Research Council, 1998). Mosquitoes from the *Anopheles gambiae* complex and the *An. funestus* group are the vectors responsible for most of malaria transmission.

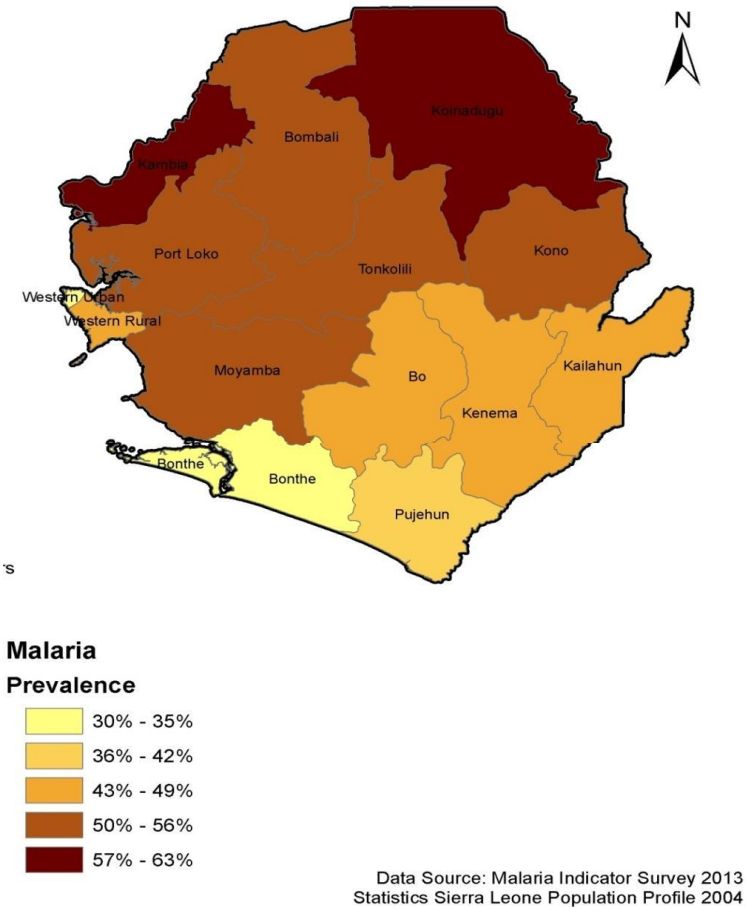


**Figure 2:** Geographical distribution of malaria of malaria transmission in Sierra Leone

## *2.2 Malaria vector species and their distribution*

Africa is a home to the most effective and efficient vectors of human malaria: *Anopheles gambiae s.s*. This *An. gambiae s.s.* form part of the *An. gambiae* complex together with other important vectors such as *An. coluzzii* (Coetzee et al., 2013), *An. arabiensis* and salt water tolerant, coastal species *An. melas* and *An. merus* (Sinka et al., 2012). In Freetown, Sierra Leone, *Anopheles gambiae* (formally known *An. coastalis*) was first incriminated as a vector of malaria by Sir Ronald Ross in 1899. Other members of the *An. gambiae* complex are not regarded as dominant vectors because they are restricted in distribution and they cannot, by themselves, sustain malaria transmission in an area. These include *An. bwambae*, *An. quadriannulatus* and *An. amharicus* (Coetzee et al., 2013).

In addition to the *An. gambiae* complex, large parts of Africa are also home to other important dominant vector system (DVS) including the *An. funestus*, *An. nili* and *An. moucheti*. Others such as *An. rivulorum*, *An. coustani*, *An. pharoensis*, *Anopheles aruni, Anopheles confusus, An. parensis, An. vaneedeni, An. brucei, An. fuscivenosus, An. paludis, An. mascarensis* and *An. hancocki* although not considered DVS in Africa appear to play a significant minor role as weaker, but nevertheless important vectors, in some selected areas (Sinka et al., 2012).

Like in all other parts of sub-Saharan Africa, the most important malaria vectors recorded in Sierra Leone are *An. gambiae s.s*., *An. coluzzii, An. melas* and *An. funestus*. Other dominant but less important malaria vectors in Sierra Leone are An*. nili* group, *An. moucheti* group and *An. hancocki.* Sierra Leone is also rich in other anopheline mosquitoes which are either non-vectors or considered incidental vectors of malaria such as; *An. barberellus, An. cinctus, An. coustani, An. domicolus, An. freetownensis, An. hargreavesi, An. marshalli, An. mauritianus, An. obscurus, An. paludis, An. quadriannulatus*, *An. rhodesiensis, An. rufipes, An. smithii, An. squamosus, An. tenebrosus, An. theilleri* and *An. ziemanni*.

*Anopheles gambiae* complex is ubiquitous across the county. The predominant members of *An. gambiae* complex, are *An. gambiae* s.s., *An. colluzzi* and *An. melas.* There are no reports of *An. Arabiensis* in Sierra Leone. The furthest inland *An. melas* has been reported is along the Rokel river. Members of the *An. funestus* group have also been recorded across the country except in southwest and Port Loko district in the north. The distribution of dominant vector system (DVS) in Sierra Leone is shown in figure 3 and table 1.

*Anopheles gambiae s.s.* and *An. colluzzi* larvae typically inhabit sunlit, shallow, temporary bodies of fresh water such as round depressions, puddles, pools and hoof prints. *An. gambiae* s.s. has been reported from habitats containing floating and submerged algae, emergent grass, rice, or 'short plants' in roadside ditches and from sites devoid of any vegetation. It is considered to be highly anthropophilic, with many studies finding a marked preference for human hosts, typically feeds late at night and is often described as an endophagic and endophilic species, i.e. biting and resting mostly indoors.

*Anopheles funestus* is another major malaria vector in the country, which is found throughout the country, often in the same locations as *An. gambiae* complex. *An. funestus* is considerably more resilient against climatic variations. A typical *An. funestus* larval habitat is a large, permanent or semi-permanent body of fresh water with emergent vegetation, such as swamps, large ponds and lake edges. *An. funestus* is considered to be highly anthropophilic with a late-night-biting pattern,

often peaking indoors after 22.00 hours (Huho *et al*., 2013). Indoor resting behaviour is also commonly reported, and these characteristics are responsible for rapid disappearance of this vector following expanded indoor residual spraying and insecticide-treated nets. Compared to other dominant vector species in Africa, *An. funestus* shows fairly consistent behaviour (generally anthropophilic and endophilic) throughout its range. In the absence of insecticide use, the endophilic behaviour of *An. funestus* combined with a relatively high longevity makes it as good a vector, or better in some areas, as *An. gambiae s.s*.

Other dominant but less important malaria vectors in Sierra Leone are *An. nili, An. moucheti* , *An. melus* and *An. hancocki. Anopheles melus* is confined to the costal areas of western region and furthest inland along the Rokel River. The biting behaviour of *An. melus* is generally opportunistic in host selection with a tendency to bite and rest outdoors.

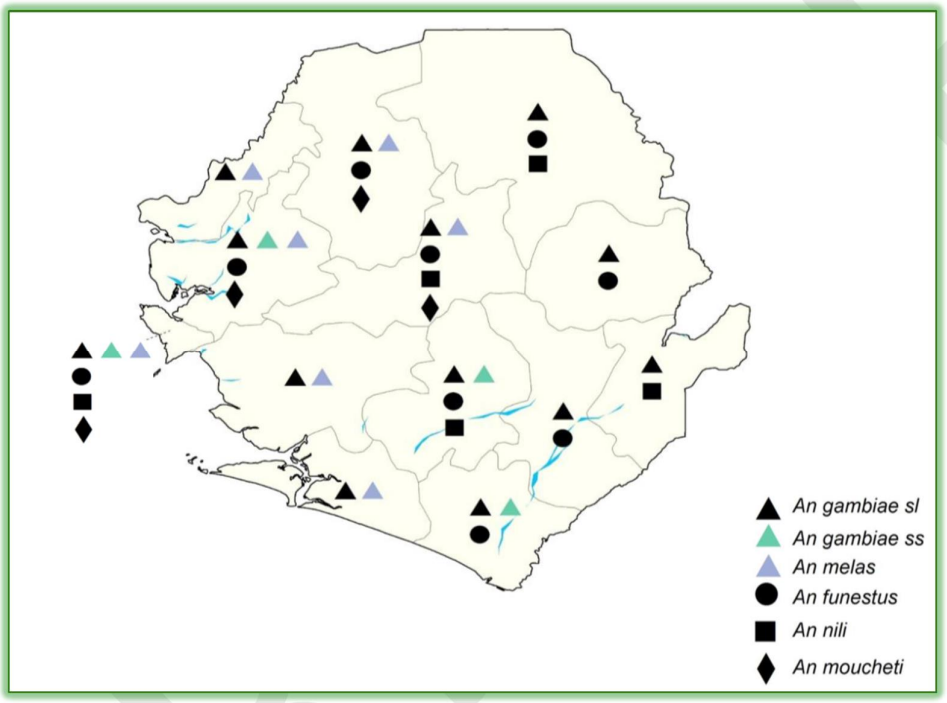


**Figure 3:** The distribution of dominant malaria vector species in Sierra Leone (Source: NMCP, 2015

**Table 1:** Current and historical species of malaria vector mosquitoes and their geographic distribution in Sierra Leone

| Species | Presence confirmed? (Y/N) | Description of geographic distribution |
|---|---|---|
| *Anopheles gambiae s.l.* | | |
| *Anopheles gambiae s.s.* | Y | All over the country |
| *Anopheles arabiensis* | N | |
| *An. coluzzii* | Y | All over the country |
| *Anopheles melas* | Y | Costal belt and along the Rokel river. |
| *Anopheles merus* | N | |
| *Anopheles amharicus* | N | |
| *Anopheles quadriannulatus* | Y | ?? |
| *Anopheles bwambae* | N | |
| *Anopheles funestus s.l.* | | |
| *Anopheles funestus s.s.* | Y | All over the country |
| *Anopheles leesoni* | N | |
| *Anopheles parensis* | N | |
| *Anopheles rivulorum* | N | |
| Anopheles vaneedeni | N | |
| *An. moucheti* | Y | Mostly western and Northern regions |
| *Anopheles nili s.l.* | Y | All over the country |

## *2.3 Malaria vector control interventions in Sierra Leone*

Historically, malaria vector control in Sierra Leone started way back in the 1899 after the visit of Sir Ronald Ross. This mainly involved mosquito larval control and segregation. In 1930s, larval source management (LSM) continued with environmental management and drainage in Freetown and surrounding areas. In 1940, pyrethrum spraying was carried out in Western Freetown to control adult mosquitoes. This was then followed by introduction IRS in 1946 in Freetown and Marampa. DDT was introduced for IRS and larviciding in 1947 and used up to 1960s in Freetown. During this time, BHC was also used for IRS in Freetown (NMCP, 2015).

The use of Insecticide Treated Nets (ITN) started in 2002 mainly targeting pregnant women and children under the age of 5 years. These were distributed routinely through antenatal and EPI clinics. The first free mass distribution of ITN was carried out in 2006 with MSF in Bo and Pujehun districts. This was followed by another countrywide free mass LLIN distribution for children under one year alongside measles vaccine campaigns in the same year. Mass distribution of LLINs continued in 2010 and 2014. These mass distribution campaigns, continued to raise the proportion of children sleeping under ITNs from 5% in 2005 to 72% in 2011 (NMCP, 2015). The brands of LLINs used in the country include Olyset Net, DuraNet and PermaNet. These LLINs are impregnated with Permethrin, Alphacypermethrin and Deltamethrin respectively.

In 2011 and 2012, IRS was introduced in few selected chiefdoms of Bo, Bombali, Kono and Western Area Rural districts. The selected Chiefdoms in each IRS district were: Bo (Badjia, Gbo,

Bagbwa); Kono (Nyawa Lenga, Selenga, Fiama, Gbaneh, Nimikoro, Kamara, Gorama); Bombali (Safroko Limba; M/ Ndohahun, Makari Gbanti, Paki Masabong); Western Area Rural (Malambay, Lumpa, Macdonald, Crossing, Masorie, Newton, Kent, York, John Thorpe, Songo, Waterloo, Kissy town). Lambacyhalothrin was used for IRS and achieved 97% household coverage (NMCP, 2015). IRS coverage by administrative Chiefdoms is shown in figures **4.**

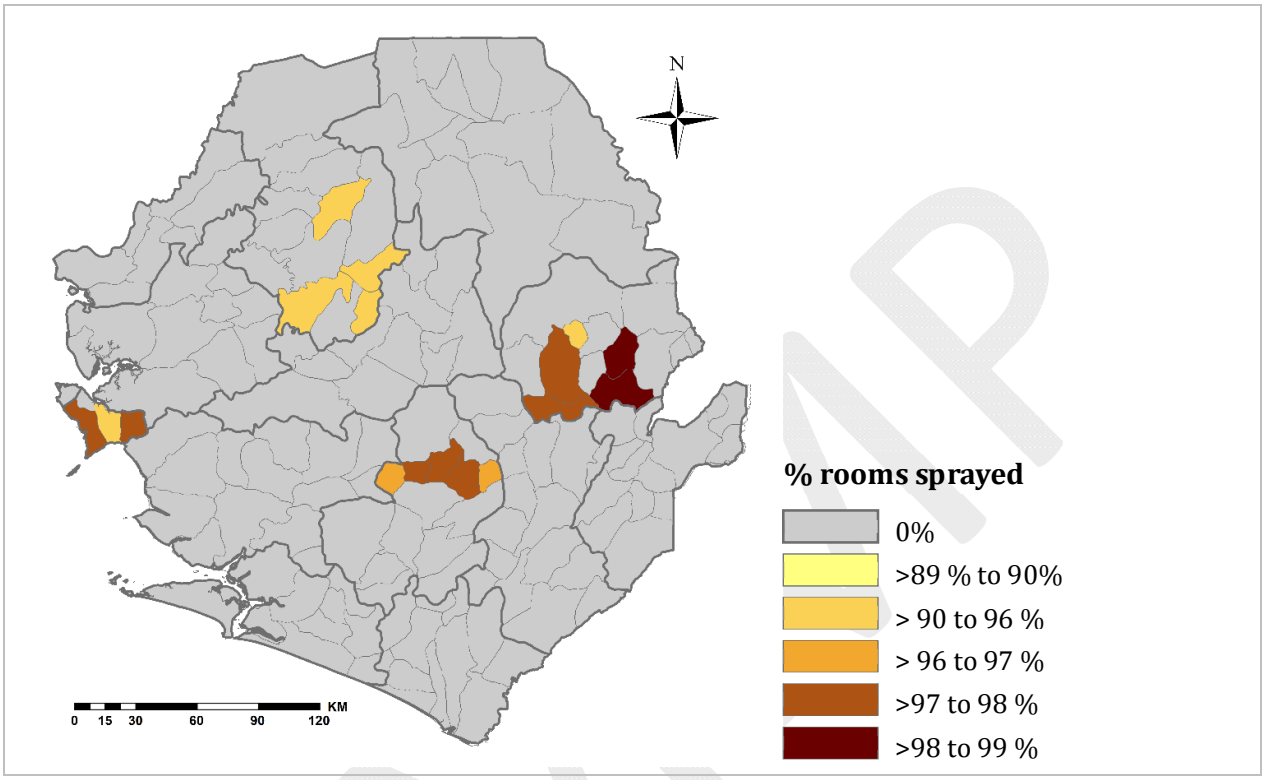


**Figure 4:** IRS coverage by Chiefdoms in 2012 (Source: NMCP, 2015)

## *2.4 Insecticides registered for public health use*

The Pharmacy Board of Sierra Leone registers insecticide products for use in public health. Any new introduced insecticides for public health use must have been dully recommended by WHOPES before being registered in the country. The list of insecticides and insecticide products registered for use in the country todate are indicated in annex 2

## *2.5 Status of vector susceptibility to insecticides in Sierra Leone and neighboring countries*

In Africa, DDT (dichlorodiphenyltrichloroethane) and dieldrin resistance was first found in *An. gambiae* in the West of the continent in the 1950s and 1960s (Brown, 1958, Hamon *et al.,* 1968). Similarly Pyrethroid resistance in *Anopheles gambiae* was first detected in these West African malaria vectors in 1993 (Elissa *et al*., 1993). Since the first occurrence of pyrethroids resistance among these malaria vectors, there have been an increasing number of reports of its spread in west, central, east and southern African countries (Chandre *et al*., 1999, Munhenga *et al*., 2008, Protopopoff *et al*., 2008, Stump *et al*., 2004, Chanda *et al*., 2011, Hunt *et al*., 2010, Ndjemai *et al*., 2009). Pyrethroid resistance extended to another malaria vector, *Anopheles funestus* in different parts of Africa (Chanda *et al*., 2011, Hargreaves *et al*., 2000, Okoye *et al*., 2008). Carbamate and organophosphate resistant populations of *An. gambiae* have also been reported in West Africa (Corbel *et al*., 2007). Increased level of carbamate and organophosphate resistance in African

mosquito populations is worrying for malaria control because these chemicals are increasingly used in replacement to pyrethroids for IRS. The current distribution of resistance to these four classes of insecticide in *An. gambiae s.l.* in West African countries are shown in figures 7 to 10

The first susceptibility testing carried out in Sierra Leone after the implementation of IRS in 2010 indicated that malaria vectors were fully susceptible to pyrethroids (Permethrin, lambdacyhalothrin and deltamethrin), carbamate (bendiocarb) and organophosphate (Malathion). However malaria vectors showed reduced susceptibility to DDT. The follow-up survey carried out in 2016 indicated malaria vectors were resistant to pyrethroids (permethrin, lambdacyhalothrin, cyfluthrin and deltamethrin) and DDT. They however maintained their susceptibility to carbamate (bendiocarb) and organophosphate. The trend of susceptibility status of malaria vectors to insecticides in Sierra Leone in 2010 and 2016 is shown in annex 3 while the current status is shown in figures 5 and 6. This rapid decrease in susceptibility status across sentinel sites in Sierra Leone has occurred after the scale-up of LLINs in the country and IRS six years ago. The current situation might be contributed by the cumulative effects created by the use of ITNs, which have been on-going since the 2002 with relative increases in 2006. Similarly, the introduction of IRS in 2011, might have contributed to the current situation. The occurrence of insecticide resistance to malaria vectors after scaling-up of IRS has already been documented in Uganda (Protopopoff *et al.*, 2013). Indoor residual spraying is commonly associated with the selection of pyrethroid resistance (Sharp *et al.*, 2007). Studies in Senegal and Liberia have also demonstrated increased frequencies of pyrethroid resistance after high LLIN usage (Ndiath *et al.*, 2012, Temu *et al.*, 2013). Use of insecticides in agriculture might have also contributed to the observed emergence of resistance (Diabate *et al.*, 2002). The co-occurrence of pyrethroids and DDT resistance in *An. gambiae* mosquitoes, may indicate the involvement of knockdown resistance mechanism (L1014F) that has already been documented in the country (De Seuza et al., 2013).

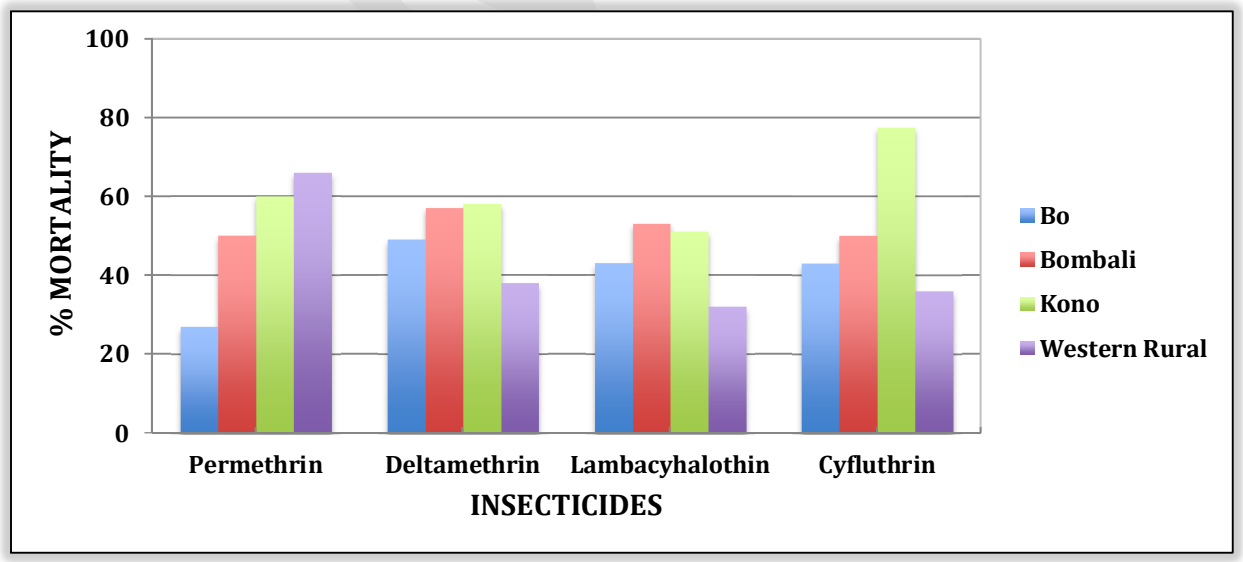


**Figure 5:** The current pyrethroid resistance status in malaria vectors from 4 sentinel districts of Sierra Leone in 2016.

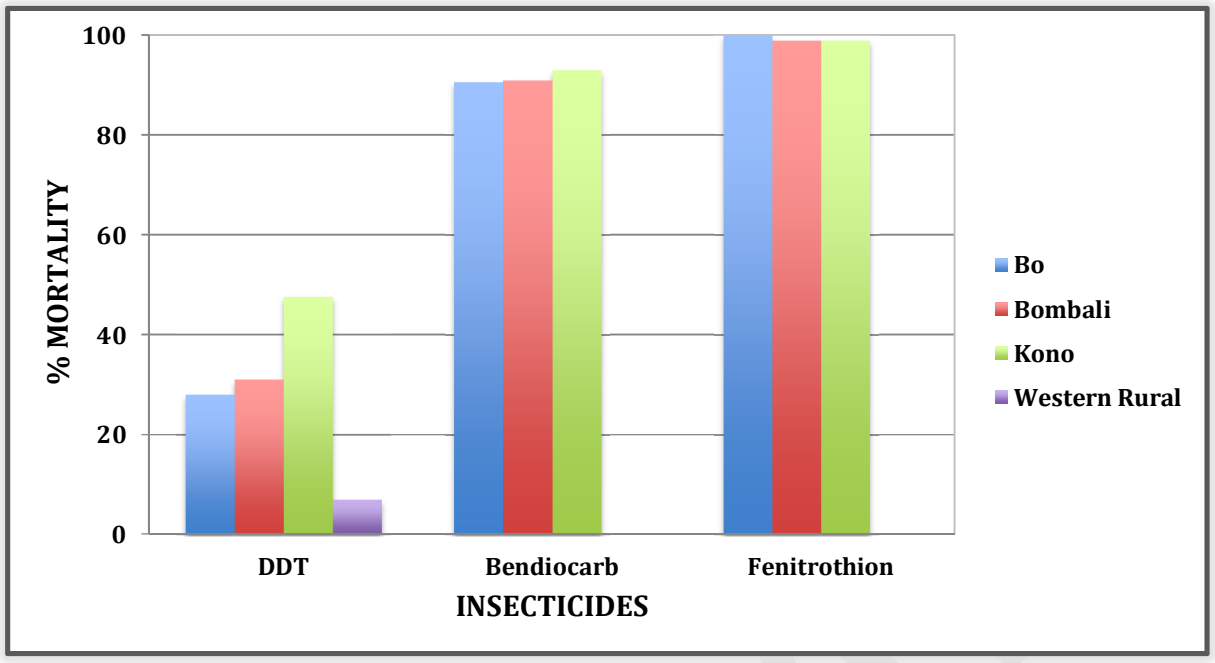


**Figure 6:** The current DDT, Bendiocarb and Fenitrothion resistance status in malaria vectors from 4 sentinel districts of Sierra Leone in 2016.

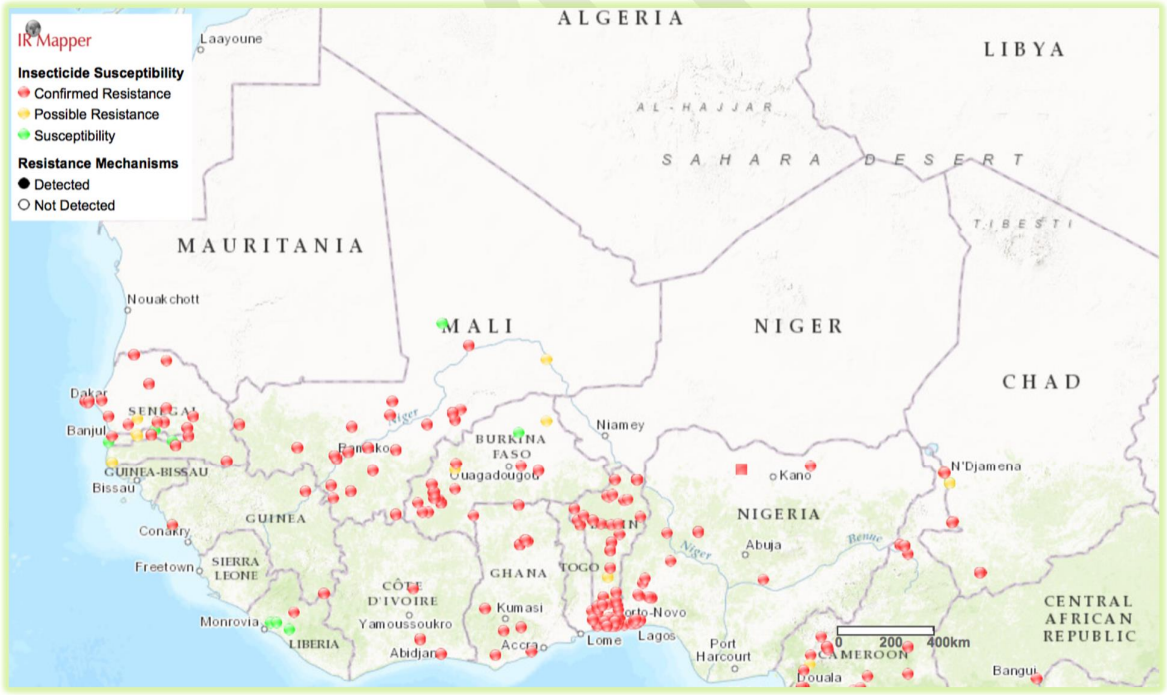


**Figure 7:** Map of West Africa showing the distribution of organochlorines resistance in malaria vectors in 2015 (Source: http://www.irmapper.com)

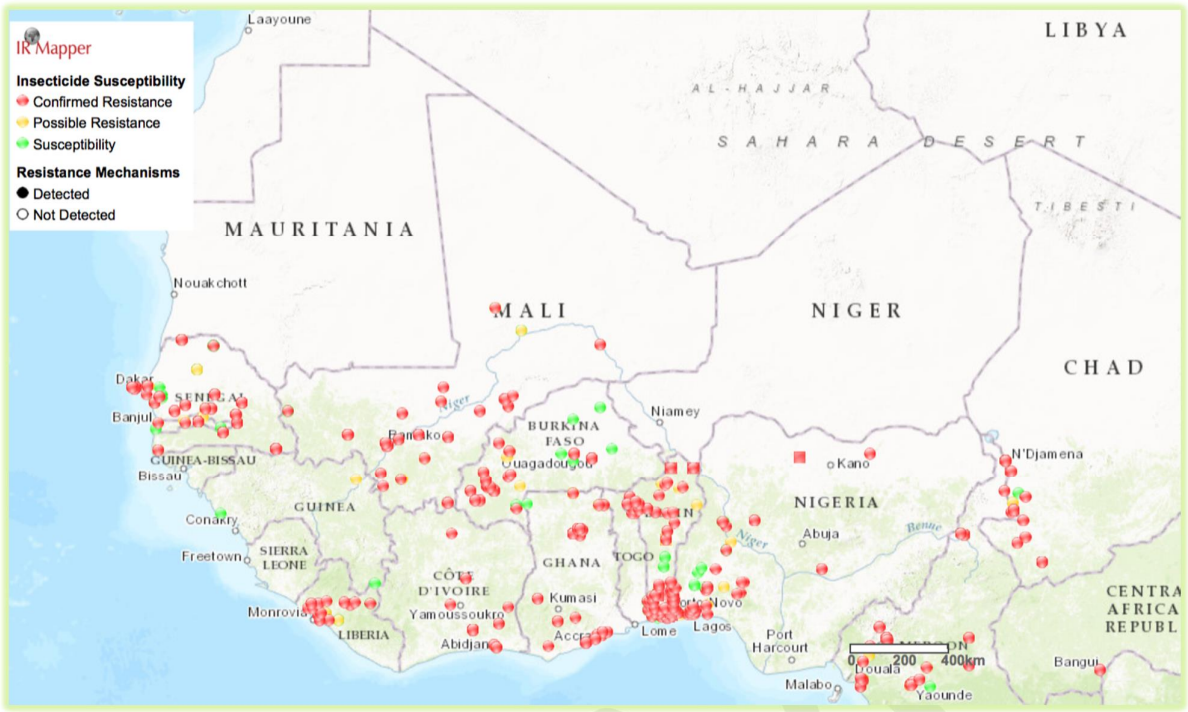


**Figure 8:** Map of West Africa showing the distribution of PYRETHROIDS resistance in malaria vectors in 2015 (Source: http://www.irmapper.com)

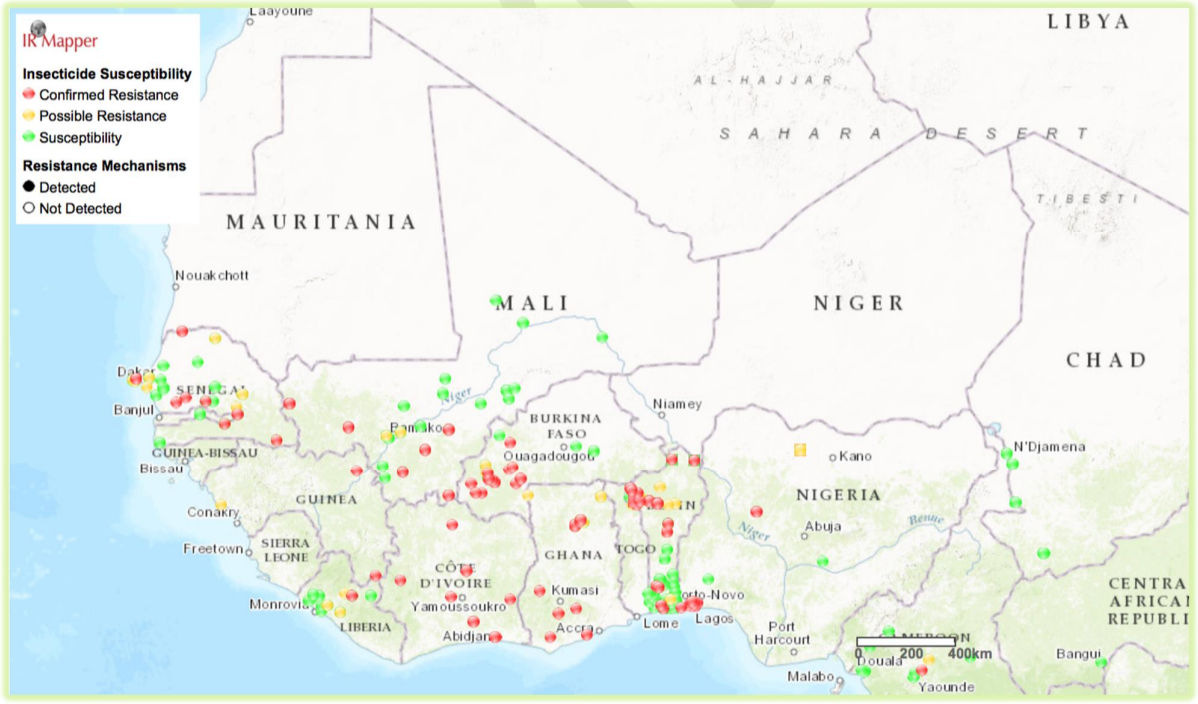


**Figure 9:**Map of West Africa showing the distribution of CARBAMATES resistance in malaria vectors in 2015 (Source: http://www.irmapper.com)

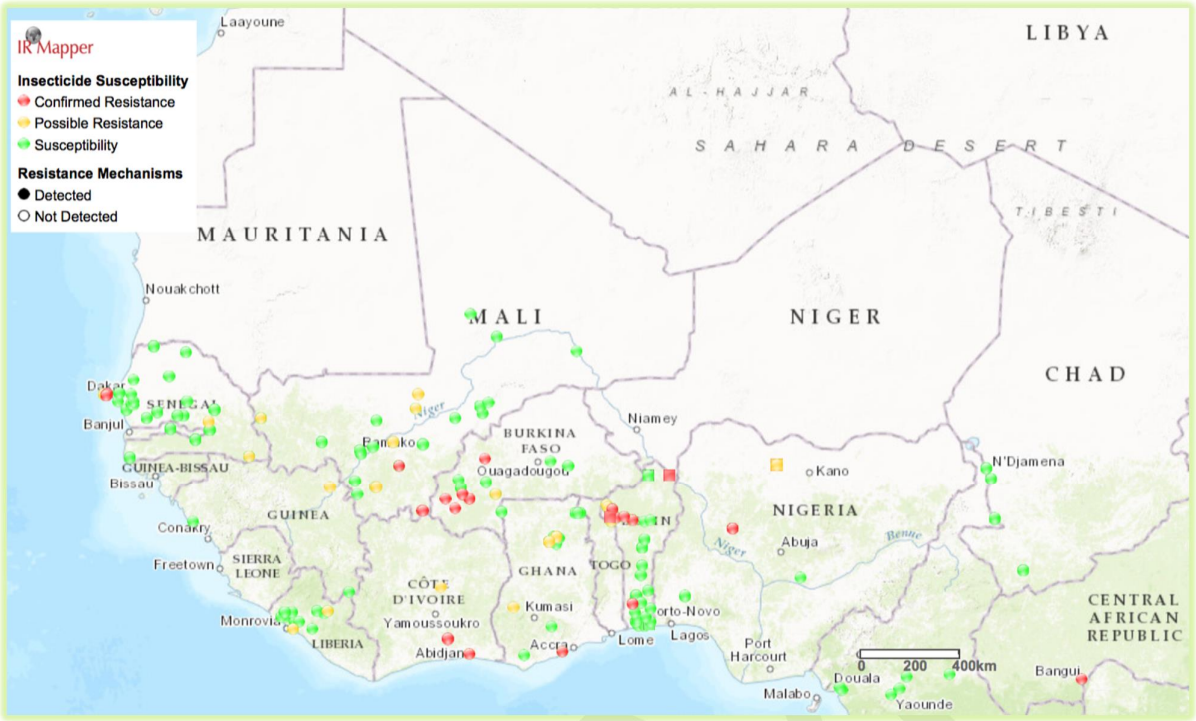


**Figure 10:**Map of West Africa showing the distribution of ORGANOPHOSPHATES resistance in malaria vectors in 2015 (Source: http://www.irmapper.com)

## *2.6 Evidence and knowledge gaps requiring immediate attention*

Current understanding of insecticide resistance is sufficient to justify immediate action to preserve the susceptibility of major malaria vectors to pyrethroids and other insecticide classes. Furthermore, scientific theory and agricultural experience provide enough information on currently available IRM approaches to guide development of IRM strategies for malaria vectors. However the available knowledge is not sufficient enough to guide effective implementation of appropriate malaria vector control interventions taking into account the focus on malaria elimination.

There are gaps in our knowledge about both insecticide resistance and resistance management methods, and additional information is needed to deliver IRM strategies effectively. For example, there is limited understanding of how to measure the impact of resistance on the effectiveness of vector control and on how to assess the relative effectiveness of resistance management strategies in delaying the emergence of resistance and in killing resistant vectors in small-scale trials. Tackling these questions is hampered by a number of factors, including a lack of clear genetic markers for some important oxidase-mediated forms of resistance to pyrethroids. The answers to such questions would facilitate the preparation of better IRM strategies as well as an evidence-based assessment of their success. Briefly the gaps that require immediate attention are:

- **Insecticide resistance mechanisms:** With limited information on resistance mechanisms and resistance genes, it is difficult to track and anticipate the course of resistance, and understand which IRM approaches would be most effective. The evolution of resistance and the possibility of reducing and even reversing resistance

cannot be predicted because of limited information on factors such as baseline frequency (mutation rates), fitness cost, genetic mode of inheritance and the selection pressure due to different uses of insecticides in agriculture and public health. Inability to track resistance genetically makes the consequences of insecticide resistance more difficult to anticipate; it is also difficult to measure the efficacy of IRM approaches. Therefore the genes that confer target site and metabolic resistance must be identified in order to answer several important research questions.

- **Vector Bionomics:** There are no recent studies on the vector bionomics in this country. Little is known on the effect of the vector control intervention the change of vector dynamics. Therefore the country needs to establish entomological surveillance system with state of art to capture all vitally important entomological indices including vector bionomics (such as dynamics, abundance, behaviour, sporozoites rates/biting activity, blood indices, etc.). This is vital in planning and implementing evidence based malaria vector control programs as well as in monitoring the current malaria control interventions
- **Operational impact of insecticide resistance:** Limited evidence is available on the operational impact of resistance. There is a need to conduct **resistance intensity assays, which** may correlate better with control outcomes.
- **Contribution of agriculture on insecticide resistance:** Need to establish the link between resistance and the use of insecticides in agriculture and public health; and how these can co-influence the development of resistance to malaria vectors.

## *2.7 Risks and risk mitigation for effective implementation of IRMMP*

The major existing risk that is likely to constrain the effective implementation of a comprehensive and effective IRMMP is inadequate human and financial resources. Other risks include lack of insectary space and accompanied supplies and consumables. The mitigation plan of the identified risks is outlined below.

| Risk | Mitigation Plan |
|---|---|
| Inadequate human resource | Recruit and train entomological staff at national and district levels including of laboratory technicians |
| Inadequate financial resources | Mobilization of resources for effective implementation of IRMMP |
| Inadequate laboratory and insectary facilities such space for the entomology laboratory, insectary supplies, consumables and reagents | Acquire the laboratory space from the NTD/onchocerciasis in Makeni. Liaise with partners to support with the necessary supplies for the insectary cum Laboratory. |

# 3 MANAGEMENT IMPLEMENTATION FRAMEWORK AND INSECTICIDE RESISTANCE MONITORING

Structures and mechanisms for supporting effective implementation of the IRMMP in Sierra Leone are outlined in this section. This includes the management structure and the IRMM decision-making process in the country. Also this section summarizes in brief the proposed monitoring activities, data collation, reporting and strategies to mitigate the impact of resistance.

## *3.1 Management implementation framework*

### *3.1.1 Insecticide resistance monitoring and management decision-making process*

The National Malaria Control Programme (NMCP) is responsible for overall management of malaria control in the country. The management of the IRMMP will be based entirely on existing NMCP system with some minimal improvements.

In the implementation of the IRMMP, NMCP will form the MALARIA VECTOR CONTROL TECHNICAL WORKING GROUP. Many of the IRMM issues are multisectoral in nature and will therefore require involvement of a wide range of stakeholders such as development partners and other ministry sectors e.g. agriculture, environment in this technical working group. This TECHNICAL WORKING GROUP will be responsible for the coordination of national IRMM activities and ensure appropriate prioritization and use of resources, and to provide a mechanism for decision-making.

Furthermore, THE MALARIA VECTOR CONTROL TECHNICAL WORKING GROUP will be required to:

(i) Advise NMCP on establishment of a system for monitoring the entomological indicators and resistance of mosquito vector species to the insecticides used for malaria vector control
(ii) Advise NMCP on establishment of a data base for monitoring resistance of mosquito vector species
(iii) Receive insecticide resistance analysed data on regular basis and make recommendations
(iv) Advise NMCP on liaison with stakeholder from agriculture and environmental sector on insecticide resistance management

This IRM decision-making body is scheduled to meet quarterly and will report to the IVM National Steering committee (NSC), which will be meeting twice a year. As stipulated in IVC strategic plan, the IVM National Steering committee (NSC) *inter alia* is responsible for policy formulation, review progress from specific programmes and mobilization of resources for IVM activities.

## *3.2 Insecticide resistance monitoring*

### *3.2.1 Selection of Sentinel Sites for insecticide resistance monitoring*

A total of 14 sentinel districts have been chosen to represent the country in routine insecticide resistance monitoring. All administrative districts in the country are represented. **From each district at least two Chiefdoms will be selected. In each chiefdom, one community will be selected**. Where is logistically and financially possible, more than one chiefdoms may be selected from a district. These sentinel sites for monitoring insecticide resistance are chosen to encompass the WHO recommended selection criteria namely:

a. History of insecticides use by communities in the areas (in agricultural and public health);
b. Malaria endemicity in the area (i.e. include all malaria epidemiological stratifications);
c. Coverage of major malaria vector control interventions (ITNs and/or IRS as well as larviciding); demographic settings (Urban/Rural);
d. Easy accessibility to the site.
e. Represent different eco-climatic settings of the country (e.g. forest savannah, grassland savannah, coastal savannah and highlands) and land use pattern.

**Table 2:** Sentinel districts selected for Insecticide Resistance Monitoring

| # | Province | *District | Year Selected |
|---|---|---|---|
| 1 | Northern | Bombali | 2010 |
| 2 | Northern | Kambia | 2016 |
| 3 | Northern | Port Loko | 2016 |
| 4 | Northern | Koinadugu | 2016 |
| 5 | Northern | Tonkolili | 2016 |
| 6 | Eastern | Kono | 2010 |
| 7 | Eastern | Kailahun | 2016 |
| 8 | Eastern | Kenema | 2016 |
| 9 | Southern | Bo | 2010 |
| 10 | Southern | Moyamba | 2016 |
| 11 | Southern | Bonthe | 2016 |
| 12 | Southern | Pujehun | 2016 |
| 13 | Western | Western Area Urban | 2016 |
| 14 | Western | Western Area Rural | 2010 |

*From each sentinel district at least two Chiefdoms will be selected and in each selected chiefdom, one community will be chosen.

### *3.2.2 Insecticide Susceptibility Testing Methodology*

**Frequency of susceptibility testing:** Insecticide susceptibility testing will be conducted once annually at the peak of the transmission season. This is important, as it will supply information that can be used to inform decisions around the choice of insecticide to be used in the following transmission season. Insecticide susceptibility testing must be repeated at the same established sentinel sites each year (WHO, 2013).

**Sampling mosquitoes for testing:** For insecticide susceptibility testing, the test mosquitoes must be alive, and so only certain collection techniques are suitable. Preferred specimens for testing are 2-5 day old adult females reared from larvae, but if these are not available, then F1 generation adults obtained from wild caught females can be used. As a third option, wild caught females can be tested (WHO, 2013). Mosquitoes which are for biochemical enzyme assays for metabolic resistance should be used fresh, or stored at –80˚C or in liquid nitrogen for later use.

**Insecticide susceptibility tests:** The susceptibility tests will be carried out using the standard World Health Organization test protocol for adult female mosquitoes (WHO, 2013). Mosquitoes will be exposed to papers impregnated with the WHO-recommended discriminating concentrations of insecticides prepared at University Sains, Malaysia (WHO, 2013). Malaria vector susceptibility tests will be carried out to all four classes of insecticides approved by WHO. However, the selection of the insecticides for testing will be based on the insecticides being used in the vector control interventions in public health and agriculture in the country. Particular

consideration will be given to insecticides used for bed net treatment the potential candidates to be used for IRS in the respective order as listed below:

1. alphacypermethrin
2. permethrin
3. deltamethrin
4. bendiocarb
5. pirimiphos-methyl
6. New insecticide products e.g. Chlrophenapyr (pyrrole) and Pyriproxyfen (PPF)]
7. DDT

**Target Mosquito species for Insecticide susceptibility testing**

***Malaria vectors*:** All Insecticide susceptibility tests will be done with locally collected, field populations of *An. gambiae s.l.* and *An. funestus s.l*. in all sites in rural and urban settings.

### *3.2.3 Species identification and detection of resistance mechanisms*

WHO susceptibility tested mosquitoes from each sentinel site will be stored in plastic tubes containing silica gel and transported to reference laboratory for species identification by specific PCR method (Scott et al 1993). The tubes must be labelled according to insecticide tested and whether the individual was dead or alive after 24 hours. The target site mutations (i.e. kdr and Ace-1) will also be screen using specific available molecular technique e.g. Taqman assay (Bass et al, 2010). All survivors and at least 20% of the mosquitoes killed in a bioassay test for any given insecticide will be identified to species level as recommended by WHO. The same number of mosquitoes identified to species level will be used in the detection of resistance mechanisms. Biochemical enzyme assays (biochemical resistance mechanisms) will be carried out in mosquitoes which were frozen fresh from field and kept at -80˚C or in liquid nitrogen.

### *3.2.4 Testing the strength of insecticide resistance*

Resistance intensity assays have been found to provide useful information on the strength of resistance (WHO, 2015) and therefore guiding the deployment of management strategy. Intensity assays will be used to evaluate strategies for managing insecticide resistance by monitoring shift in $LD_{50}$ over time. This will be carried out using the rapid kit with different levels of diagnostic concentration (e.g. X1, X2, X5, X10 and X20) in areas where insecticide resistance have been recorded (CDC, 2006). To determine the level of resistance ($LD_{50}$ and $LD_{95}$) and changes in the level of resistance to pyrethroids, mosquitoes will be exposed to different concentrations in CDC bottle bioassays. Alternatively, the $LT_{50}$ and $LT_{95}$ of the mosquito populations to various insecticides can be obtained by fixing concentration and varying the exposure times in WHO test papers.

### *3.2.5 Institution responsible for insecticide resistance monitoring*

The NMCP will be will be responsible for coordinating periodic monitoring of susceptibility status of malaria vectors to insecticides. Other partners such as research and academic institutions may also be involved in insecticide resistance monitoring under the coordination of NMCP for harmonization.

### *3.2.6 Data recording and reporting*

Data should be recorded on standardized WHO susceptibility test forms, and entered into a national database. The database will be developed and stored by NMCP. The nation insecticide resistance database will then be linked with existing malaria epidemiological data. The

epidemiological data will be mapped and overlaid with resistance surveillance data to show the correlation. These should also be linked with the management functions and tools of Health Management Information System such as District Health Information software 2 (DHIS2). Insecticide susceptibility data collected each year will be disseminated to the malaria vector control stakeholders and also presented to the decision-making body at the earliest opportunity. This way will allow any new data to be used to inform the decision-making process regarding any changes that may need to be made to the insecticide resistance-monitoring plan, or to the vector control interventions being applied. Insecticide resistance data must be shared annually with the WHO regional offices, WHO Global Malaria Program, ANVR (African Network for Vector Resistance) and other key partners.

## *3.3 Insecticide resistance management*

### *3.3.1 Interpretation of Test Results and Policy Implications*

Where resistance is suspected or confirmed, the relevant national decision-making body (in consultation with regional and global institutions, including WHO regional offices, WHO Global Malaria Program, ANVR and other key partners) will review the current vector control programme and make the appropriate adjustments, e.g. changing the insecticide used for IRS, 'rotating' insecticides, introducing a 'mosaic' system of application of insecticides for IRS, or other methods. The national decision-making body is supposed to discuss the insecticide resistance monitoring at least once every year. The decision tree based on guidance contained in the GPIRM, which can potentially be used to guide decisions regarding any necessary adjustments to the national vector control programme following suspicion or confirmation of resistance are shown in tables 3 & 4.

### *3.3.2 Approaches for managing resistance*

The overall aim of the IRM strategies is to maintain the effectiveness of vector control, despite the threat of resistance. Several approaches are proposed for managing resistance to insecticides for vector control. These include:

i) Rotations of insecticides (i.e. two or more insecticides with different modes of action rotated from one year to the next) ,

ii) Combination of interventions (i.e. two or more insecticide- based vector control interventions are used in a house e.g. IRS & LLINs),

iii) Mosaic spraying (i.e. one compound is used in one geographic area and a different compound in neighboring areas, the two being in different insecticide classes) and use of mixtures (i.e. two or more compounds of different insecticide classes are mixed to make a single product or formulation).

iv) Integrated vector management, by reducing reliance on chemical control, can also be considered a means of IRM. In certain settings, non-insecticidal tools, such as non-insecticide-based larviciding and environmental management, can also be used to reduce the overall mosquito population and limit the number and size of breeding sites without selecting for resistance.

### *3.3.3 Resistance mitigation plan in areas where IRS is used in malaria vector control*

In Sierra Leone, IRS was piloted in areas where the endemicity of malaria is high. These areas are also having high LLINs coverage.

The pyrethroids are the only class approved for use on LLINs (http://www.who.int/whopes/en/) therefore, insecticides of different classes should be used for IRS and continue to monitor for resistance, at least once a year. In addition, if malaria vectors are still susceptible to insecticides, pre-emptive actions must be taken so as to preclude the emergence of resistance. In such situations (where pre-emptive actions are being taken or resistance have been identified) insecticides of different classes should be sprayed in rotation, ideally in **annual cycle.**

While the insecticides are being rotated, susceptibility tests should be carried out routinely to identify any return to full vector susceptibility. If resistance has reversed, you may think of reintroducing the original insecticide into this rotations scheme. If this kind of reversion is not seen, the rotations scheme should not include the original insecticide. In this case define resistance mechanisms by using biochemical and genetic methods that will help to refine options available for insecticide resistance management. The detailed recommendations for each scenario are shown in table 4.

### *3.3.4 Resistance mitigation plan in areas where LLINs are used in malaria vector control*

This is applied every-where in Sierra Leone since the ownership of LLINs in the country is more than 84%. Therefore the insecticide resistance management in most of our settings in which LLINs are the main form of vector control should be aligned with the perceived level of threat from resistance, which depends on:

1) The nature and strength of the resistance mechanism/s and the frequency of the mechanism/s in the vector population; and
2) Whether the number of confirmed malaria cases has increased.

Several potential resistance scenarios with recommendations for action are summarized in Table 5.

**Different scenarios on resistance mitigation plan in areas where LLINs are used**

**Scenario 1:** In any case whether resistance is confirmed or not**,**
**Recommendation for scenario 1:** continue to scale-up or maintain coverage with LLINs both because they act as a physical barrier and because the sub-lethal irritant effects of the pyrethroids may still contribute to malaria control. It is assumed that the irritant effect of pyrethroids persists, at least to some extent, even when there are resistant vectors in the Anopheles population. As continued use of LLINs is likely to contribute to selection pressure, resistance and any associated operational impact must be monitored closely. Thus, resistance must be tested annually.

**Scenario 2: I**n all areas in which operationally significant metabolic resistance has been identified, and all areas in which there is kdr resistance and an increase in the number of malaria cases (with no other clear cause),
**Recommendation for scenario 2:** Introduce focal IRS with a non-pyrethroid active ingredient. It may be financially and logistically difficult to introduce IRS in all areas with reported resistance. However, it may be possible to identify the foci where the frequency of resistance is highest or where the threat of control failure is greatest. In such areas, it is essential to target those areas for IRS. In places where resistance have already spread across a wide geographical area, spraying should focus on those areas in which the epidemiological risk of malaria is greatest. If budget

constraints from adding IRS in all the areas where there is resistance, and in the event of a sustained outbreak of malaria, the final option, is to prepare an emergency response plan with IRS.

**GENERAL NOTE:** It is incorrect to assume that resistance to pyrethroids will require a general change to IRS from LLINs. Both LLINs and IRS are expected to continue to be core elements of vector control in the short, medium and longer term. A general switch would probably be counter-productive.

- Firstly some forms of pyrethroid resistance may have no impact on the effectiveness of LLINs.
- Secondly, annual spraying is still not feasible in many places, for logistical reasons, and LLINs are the only practical form of effective vector control. Hence, the goal of universal coverage cannot be achieved and sustained with IRS alone but also requires the use of LLINs.

### *3.3.5 Choosing alternative insecticides*

When introducing additional insecticides in an IRS rotation (which may or may not include the current insecticide, depending on the resistance status), or non-pyrethoid-based IRS in areas with high coverage with LLINs, or when changing from an insecticide to which there is resistance, it is important to consider factors related to cross-resistance, efficacy and costs in choosing the insecticides.

1) **Cross-resistance to other insecticides**: Information about the mode of action of the insecticides and therefore this will guide on which insecticides may confer cross-resistance. This can be obtained either by identifying the resistance mechanism and examining the known cross-resistance patterns or by conducting susceptibility tests for each of the other insecticides.
2) **Efficacy of the insecticides**: Testing should be conducted to all four classes of insecticides so as to determine which ones are resistance and avoid using these insecticides in IRM if necessary. In the event of resistance to all four classes of insecticide, vector control programmes should rotate annually through as many classes as possible and should start rotations with the insecticides to which there is the lowest frequency of resistance.
3) **Costs of insecticides**: The less expensive insecticide should be opted for the mitigation plan. Where vectors are still susceptible to DDT, the programme should, in line with WHO guidelines, consider using it as an alternative insecticide for IRS in the absence of other "locally safe, effective and affordable alternatives" (GPIRM, 2012). As DDT is less expensive than organophosphates and carbamates, the cost implications are potentially significant.
4) **Duration of the efficacy of each insecticide** used in a rotation should also be considered, together with the length of the transmission season, as this will have implications for the number of spray rounds required, and will therefore have a potential effect on total cost.

### *3.3.6 Other vector control intervention to mitigate insecticide resistance*

Non-insecticidal tools, such as non-insecticide-based larviciding and environmental management should be used in selected settings. These interventions could provide an additional, urgently needed, degree of vector protection without selecting for resistance.

**Table 3**: Recommendations for areas in in which IRS is used in the vector control intervention (Adapted from GPIRM, 2012)

| Status | Scenarios and responses |
|---|---|

| | |
|---|---|
| **Susceptibility** | **Scenario:** no foci of possible resistance identified, according to WHO test procedures<br><br>**Interpretation:** resistance is not an immediate threat, vector control is still effective.<br>**Monitoring action:**<br>• conduct frequent monitoring of vector susceptibility through susceptibility tests to confirm that there is no resistance emerging<br>**Vector control action:**<br>• implement pre-emptive rotations, preferably on annual basis. While full susceptibility is consistently confirmed, rotations can include the insecticide which is currently being used |
| **Resistance** | **Scenario:** resistance has been confirmed based on bioassays according to WHO test procedures, or genotypic data show rapid increase in resistance<br>**Interpretation:** resistance is an immediate threat and action should be taken<br>**Monitoring action:**<br>Å conduct frequent susceptibility tests in a range of locations to monitor any increase in resistance or return to full susceptibility<br>Å investigate resistance mechanisms using bio-chemical and molecular testing methods<br>Å check and if necessary reinforce epidemiological surveillance<br>Å reinforce entomological surveillance<br>**Vector control action:**<br>Å in geographic areas with confirmed resistance, switch away from the current insecticide that is being used as quickly as practicable; the aim is that by promptly removing the selection pressure, the spread of resistance to the initial insecticide will be reduced or even reversed; in some cases, such reversal may allow for future reintroduction of the initial insecticide<br>Å use new insecticide in annual rotation |

**Table 4:** Recommendations for areas in in which LLINs is the primary vector control intervention (Adapted from GPIRM, 2012)

| Status | No increase in confirmed malaria cases | Increase in confirmed malaria cases |
|---|---|---|
| **Susceptibility** | **Scenario:** no foci of possible resistance identified, according to WHO test procedures<br>**Interpretation:** resistance is not an immediate threat; vector control is still effective<br>**Monitoring action:**<br>Å conduct vector susceptibility tests to determine that there is no resistance emerging<br>**Vector control action:**<br>Å No change | **Scenario:** no reports of resistance but evidence o an increase in the number of malaria cases and no other clear cause<br>**Interpretation:** insecticide resistance is not an immediate threat and is probably not the cause of the increase in the number of cases<br>**Monitoring action:**<br>Å Conductvectorsusceptibilityteststoconfirmthatthereis noresistanceemerging<br>Å monitor the quality and coverage of vector control interventions, which could be responsible for the increase in malaria cases<br>**Vector control action:**<br>Å ensure system for timely replacement of worn-out nets and assure the quality and extent of LLIN coverage |
| **Resistance but unknown mechanism/s** | **Scenario:** resistance has been confirmed according to WHO test procedures but mechanism/s have not been tested for or identified<br>**Interpretation:** resistance is an immediate threat and could at some point bring about an increase in malaria cases<br>**Monitoring action:**<br>Å investigate resistance mechanisms<br>Å conduct vector susceptibility tests to monitor any increase in resistance<br>Å reinforce epidemiological surveillance<br>**Vector control action:**<br>Å continue to promote the use of LLINs<br>Å Introduce, in addition, focal IRS with a non pyrethroid insecticide, preferably on annual rotations. Best practice is to do this in all areas of resistance<br>Å Review and revise IRM strategy once | **Situation:** resistance has been confirmed according to WHO test procedures but mechanism/s are unknown; also evidence of an increase in malaria cases and no other clear causality<br>**Interpretation:** resistance is an immediate threat and could already be contributing to the increase in malaria making it a serious and current public health problem<br>**Monitoring action:**<br>Å investigate resistance mechanisms<br>Å conduct vector susceptibility tests to monitor any increase in resistance<br>Å reinforce entomological surveillance<br>**Vector control action:**<br>Å continue to promote the use of LLINs<br>Å introduce, in addition, focal IRS with a non-pyrethroid insecticide, preferably on annual rotations. Best practice is to do this in all areas of resistance<br>Å Review and revise IRM strategy once resistance mechanism/s are known |

<table>
<tr>
<td>Kdr resistance only</td>
<td>Scenario: kdr resistance reported but no evidence of increase in malaria cases<br>Interpretation: vector control working well despite kdr- based resistance<br>Monitoring action:<br>• conduct extensive susceptibility tests to monitor any increase and spread in resistance<br>Å check for metabolic resistance using bio- chemical and molecular testing methods<br>Å reinforce epidemiological surveillance<br>Å reinforce entomological surveillance<br>Vector control action:<br>• continue to promote the use of LLINs<br>• ensure system for timely replacement of worn- out nets and assure the quality and extent of LLIN coverage</td>
<td>Scenario: resistance has been confirmed base on bioassays according to WHO test procedures, or genotypic data show rapid increase in resistance, with confirmation of kdr only; also evidence of an increase in the number of malaria cases and no other clear cause.<br>Interpretation: resistance is an immediate threat and might already be contributing to the increase in malaria cases making it a serious and current public health problem<br>Monitoring action:<br>Å conduct frequent and extensive susceptibility tests to monitor any increase in resistance<br>Å check whether metabolic resistance is present using bio-chemical and molecular testing methods<br>Å reinforce entomological surveillance<br>Vector control action:<br>Å continue to promote the use of LLINs<br>Å Introduce, in addition, focal IRS with a non-pyrethroid insecticide, preferably on annual rotations. Best practice is to do this in all areas of resistance.</td>
</tr>
<tr>
<td>Metabolic resistance<br>(with or without kdr in the same vector species)</td>
<td colspan="2">Scenario: resistance has been confirmed according to WHO test procedures and metabolic resistance is known to be present<br>Interpretation: resistance is an immediate threat; I f there is also evidence of an increase in malaria cases and no other clear causality, resistance could already be contributing to an increase in transmission making it a serious and current public health problem<br>Monitoring action:<br>• conduct frequent monitoring of vector mortality rates through susceptibility tests to monitor any increase in resistance<br>ÅMonitor for any increase in operationally significant metabolic resistance<br>ÅCheck for the possible appearance or increase in the frequency of kdr genes<br>Å Check and if necessary reinforce epidemiological and entomological surveillance<br>Vector control action:<br>• continue to promote the use of LLINs<br>ÅIntroduce, in addition, focal IRS with a non-pyrethroid insecticide, preferably on annual rotations. Best practice is to do this in all areas of resistance.</td>
</tr>
</table>

# 4 CAPACITY STRETHENING AND HUMAN RESOURCES REQUIREMENT

The country has a limited entomologist staff. However, NMCP will map all entomologists, environmental health officers and other stakeholders involved in insecticide resistance and share the strategic framework for insecticide resistance management. All partners involved in the insecticide resistance monitoring and management will be required to train their staff regularly, preferably annually (as stipulated in specific SOP e.g. IRS SOPs). These include IRS and LLINs implementing partners. Staff involved in insecticide resistance monitoring from NMCP will also receive refresher training annually.

The human resource available, gaps and the description of how the capacity will be strengthened at the national level is shown in table 6.

**Table 5:** Human Resource requirements and gaps at National and district level

| Personnel required | Number required | Number available | Gap | Job description and training/recruitment need |
|---|---|---|---|---|
| Senior Entomologist | 4 | 0 | 4 | To oversee all activities pertaining to insecticide resistance monitoring including coordination of stakeholders meetings, data analysis, compilation of reports, etc. |
| Data entry clerk | 2 | 0 | 2 | Data entrant to be recruited and trained. |
| Malaria entomology technicians | 4 | 2 | 2 | Carrying out field insecticide monitoring and laboratory activities. |
| Epidemiologist | 2 | 1 | 1 | To work in collaboration with Entomologist, Statistician to design studies, analyse and interpret data and preparation of reports. Also, to work closely with data management unit. This will be hired from M&E /surveillance unit of the NMCP |
| Statistician | 2 | 0 | 2 | Data analysis-Hired from surveillance unit |
| IT specialist | 2 | 1 | 1 | To create and maintain soft/hardware-To be hired or recruited |
| Procurement officer | 1 | 0 | 1 | To provide procurement services when required. The available PO at the NMCP will be used |
| *Entomology technician at district level | 14 | 6 | 8 | Carrying out field insecticide monitoring and laboratory activities in the districts. |

** Requirement at district level*

Other capacity strengthening plans include:

- Re-orient existing laboratory entomologists on new technologies at different levels (from district to national level). This need to be done at least once every year.
- Strengthen the capacity of appropriate district environmental officers on malaria entomology and insecticide resistance monitoring.
- Advocacy on IRMMP to decision makers including community and policy makers annually.

The NMCP will liaise with other vector control stakeholders including WHO, research/academic institutions, ANVR and other development partners to facilitate the capacity strengthening of its entomological laboratory and staff involved in specific activities stipulated in this IRMMP.

# 5 REGULATORY REQUIREMENTS AND QUALITY CONTROL FOR INSECTICIDES AND SUPPLIES

The regulatory body for registration and quality control of insecticides for public health use in the country is the Pharmacy Board of Sierra Leone. Any new introduced insecticides for public health use must have been dully recommended by WHOPES before being registered in the country. Outlined below are the steps to be taken to register insecticide products in the country:

- Application for the registration of products from the manufacturer to the Pharmacy Board
- Submission of dossier and sample for quality test from the manufacturer to the Pharmacy Board
- Evaluation of dossier and Quality Control Test (QCT) by the Pharmacy Board
- Approval of applications by the Pharmacy Board
- Application for import permits by the manufacturer to the Pharmacy Board
- Post market surveillance on samples in circulation by the Pharmacy Board

## *5.1 Quality control and bio-efficacy tests of vector control products*

Once an insecticide product for public health use is registered the quality checks of the imports are conducted according to the guidelines for submission of samples for QCT available on www.pharmacyboard.gov.sl with reference to the WHOPES guidelines. Similarly the bio efficacy of these vector control products in the field are checked in the routine post market surveillance on samples in circulation by the Pharmacy Board.

# 6 WORK-PLAN FOR IRMMP IMPLEMENTATION

The work plan and budget for monitoring and management of insecticide resistance are outlined below.

## *6.1 Insecticide Susceptibility Monitoring*

### *6.1.1 Frequency of Testing and Insecticides to be tested*

Insecticide susceptibility testing should be conducted at least once annually. In order to supply information that can be used to inform decisions around the choice of insecticide to be used in the following transmission season in sites where resistance has been detected (and if this is logistically and financially appropriate) susceptibility testing can be carried out twice per annum; at the beginning of the transmission season and repeated towards the end of the season. Insecticide susceptibility testing will continue to be performed at sentinel sites (at least one per eco-epidemiological zone or one million population protected or along transects through ecological zones (Table 4). The frequency of testing is shown in table 7

Susceptibility testing will be carried-out against all four-insecticide classes approved by WHO. Emphasis will be given to insecticides that are currently used for malaria vector control in the country as indicated in the priority order under section 3.2.2 above. These will include:

i) Pyrethroids (e.g. permethrin, deltamethrin, alphacypermethrin)
ii) Carbamates (e.g. Bendiocarb)
iii) Organophosphates (e.g. pirimiphos-methyl)
iv) Other good insecticide candidates that are in pipeline [e.g. Chlrophenapyr (pyrrole) and Pyriproxyfen (PPF)].

v) Organochlorine (e.g. DDT)
vi) Synergist bioassay tests

### *6.1.2 Mosquitoes to be tested*

Three to five day old adult female *Anopheles gambiae s.l.* and *Anopheles funestus* mosquitoes will betested as recommended by WHO. The mosquitoes for testing will either be F1 generation adults obtained from wild caught females or reared from larvae. In some cases, wild caught females will be tested (WHO, 2013). Prior to testing mosquitoes must be identified to their complex groups based on morphological features. The species of malaria vectors will be identified by genotyping using standard known PCR techniques. PCR is normally conducted on specimens after susceptibility testing has been conducted. Prior to identification by PCR, individual mosquito specimens should be appropriately labelled and stored on silica gel in Eppendorf tubes. All survivors and at least 20% of the mosquitoes killed in a susceptibility test for any given insecticide should be identified to species level.

### *6.1.3 Identification of Resistance Mechanisms*

Samples of mosquitoes from each site will be screened for resistance mechanisms (target site and biochemical mechanisms). The target site mutations (i.e. kdr and Ace-1) will be screened using specific available molecular technique e.g. Taqman assays (Bass et al., 2010). Biochemical resistance mechanisms will be conducted using specific biochemical assays. NMCP will coordinate the implementation of monitoring of insecticide resistance and detection of resistance mechanisms.

**Table 6:** Frequency and location of susceptibility testing

| Sentinel District | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bombali | | | | | | | | | | | | |
| Kambia | | | | | | | | | | | | |
| Port Loko | | | | | | | | | | | | |
| Koinadugu Tonkolili | | | | | | | | | | | | |
| Kono Kailahun | | | | | | | | | | | | |
| Kenema Bo | | | | | | | | | | | | |
| Moyamba | | | | | | | | | | | | |
| Bonthe | | | | | | | | | | | | |
| Pujehun | | | | | | | | | | | | |
| Western Area Urban | | | | | | | | | | | | |
| Western Area Rural | | | | | | | | | | | | |
| | =Susceptibility testing season | | | | | | | | | | | |

### *6.1.4 Testing for the strength of insecticide resistance*

To determine the level of resistance ($LD_{50}$ and $LD_{95}$) and changes in the level of resistance to pyrethroids, mosquitoes will be exposed to different concentrations in CDC bottle bioassays (CDC, 2006).

## *6.2 Insecticide Resistance Management*

The national decision-making body, which is proposed to take charge of the monitoring and management of insecticide resistance and provide technical advice to the MOHS for policy decision, need to be established. This national decision-making body will hold its meetings once for every quarter. This body will receive and review the insecticide resistance monitoring report from NMCP once every year. As indicated in section 3.1 above, this body will be responsible for overseeing the implementation of IRMMP and advice the IVM committee on the decision making process e.g. switching the insecticide for IRS, LLINs replacement, etc. The guidelines for which action to take and at what situation are provided in section 3.3 above.

# 7 TIMELINE / GANTT CHART

This section provides action points and detailed annual timeline of implementation in each specific strategic objective (table 7). It also shows implementation timeline for the period of 4 years (2017-2020) in table 9.

# 8 IMPLEMENTATION BUDGET

This section provides specific activity for each of the action point and an estimated annual budget. It also gives the projection of the budget for the following three years of IRMMP implementation. The implementation of the IRMMP is estimated to cost **LE 3,423,996,508 (US$ 517,776)** annually. For the period of four years (2017 to 2020) the plan is projected to cost **LE 13,386,880,000 (US$ 2,059,520).** The detailed annual budget is shown in table 8 while the budget for the 4 years is in table 10.

**Table 7**: **DETAILED ANNUAL TIMELINE (FOR 2017) / Gantt chart**

| Strategic intervention | Action point | Timeline | | | | | | | | | | | | Responsible institution |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Q1 | | | Q2 | | | Q3 | | | Q4 | | | |
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | |
| To provide framework for IRMM decision making process; Insecticide resistance monitoring; data collection and sharing; and implementation of insecticide resistance management | Select sites for susceptibility testing | ■ | ■ | | | | | | | | | | | MOHS/NMCP |
| | Conduct susceptibility tests in sentinel sites | | | | | | ■ | ■ | ■ | | | | | MOHS/NMCP |
| | Supportive supervision and coordination to insecticide resistance sentinel sites | | | | | | ■ | ■ | ■ | | | | | |
| | Identify resistance mechanisms | | | | | | | | | ■ | ■ | | | MOHS/NMCP |
| | Conduct resistance intensity testing | | | | | | ■ | ■ | ■ | | | | | MOHS/NMCP |
| | Conduct Malaria Vector Control Technical Working Group (MVCTWG) meeting | | | ■ | | | ■ | | | ■ | | ■ | | MOHS/NMCP |
| | Conduct Integrated Vector Control (IVM) National Steering committee Meeting | | | | | | ■ | | | | | | ■ | MOHS/NMCP |
| | Conduct stakeholders meeting to discuss findings | | | | | | | | | | | | ■ | MOHS/NMCP |
| | Establish insecticide resistance database | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | MOHS/NMCP |
| | Annual review of insecticide of IRMMP | | | | | | | | | | | | ■ | MOHS/NMCP |
| To strengthen the capacity personnel's involved in the insecticide resistance monitoring and management so as to effectively implement the plan | Identify and build capacity of the vector control staff at national and in selected districts | ■ | ■ | | | ■ | | | | ■ | ■ | | | MOHS/NMCP |
| | Strengthen capacity of NMCP/Laboratory for vector control & quality control | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | MOHS/NMCP |
| To provide a forum and strategic framework for IVC among partners to ensure coordinated and harmonized implementation of the interventions | Mapping of IR stakeholders in stratified areas | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | MOHS/NMCP |
| | Establish functional decision bodies-Malaria Vector Control Technical Working Group and IVM National Steering committee | ■ | ■ | ■ | | | | | | | | | | MOHS/NMCP |
| | Conduct meetings of the Malaria Vector Control Technical Working Group (as above) | | | ■ | | | ■ | | | ■ | | | ■ | MOHS/NMCP |
| | Conduct Integrated Vector Control (IVM) National Steering committee Meeting (as above) | | | | | ■ | | | | | | | ■ | MOHS/NMCP |
| | Conduct quality control of malaria vector control tool pre and post community consumption | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | MOHS/NMCP |
| | Work with regulatory bodies responsible for registration of insecticides | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | NMCP |

## Table 8: DETAILED ANNUAL BUDGET (FOR 2017)

| No. | Action point | Specific Activity | Estimated cost Le | Estimated cost in US$ |
|---|---|---|---|---|
| 1. | Select sites for susceptibility testing from each district | Selection of chiefdoms and communities for monitoring in collaboration with DHMT | 39,303,750 | 6,047 |
| 2 | Conduct susceptibility tests in sentinel sites and identify resistance mechanisms | Insecticide resistance surveillance activities in 14 sentinel districts | 447,300,000 | 68,815 |
| | | Equipment and Supplies | 45,940,570 | 7,068 |
| | | Shipping and custom clearance cost | 65,000,000 | 10,000 |
| | | Data Analysis & Report writing | 16,775,000 | 2,581 |
| 3 | Conduct resistance intensity tests | Field sampling and transportation, laboratory testing | 447,300,000 | 68,815 |
| 4 | Supportive supervision to insecticide resistance sentinel sites | DSA and transportation | 131,117,188 | 20,170 |
| 5 | Identify resistance mechanisms | 300 mosquitoes x 14 sites X 8U$ | 281,400,000 | 33,600 |
| 6 | Conduct Malaria Vector Control Technical Working Group meeting | 4 meeting annually | 37,800,000 | 5,815 |
| 7 | Conduct Integrated Vector Control IVM National Steering committee Meeting | 2 meetings annually | 20,650,000 | 3,177 |
| 8 | Conduct stakeholders meeting to discuss IR findings | 1 Meeting | 14,790,000 | 2,275 |
| 9 | Establish Insecticide resistance database | Consultant hiring cost | 29,250,000 | 4,500 |
| | | 2 technical staff to work with a consultant for 15 days | 9,000,000 | 1,385 |
| | | Computer, software and accessories | 6,500,000 | 1,000 |
| | | Resistance database maintenance cost | 64,250,000 | 9,885 |
| 10 | Annual review of IRMM work plan | Three days stakeholders review meeting | 156,510,000 | 24,780 |
| 11 | Identify and build capacity of the vector control staff at national and in selected districts | Training of national and district staff on basic field entomology and insecticide resistance testing | 218,810,000 | 33,663 |
| | | Training of 2 national staff on malaria entomology abroad-fee, upkeep and transport | 117,000,000 | 18,000 |
| | | Recruitment of 2 senior malaria entomologists to oversee the IRMMP –annual salary | 520,000,000 | 80,000 |
| 12 | Strengthen capacity of NMCP Laboratory for vector control & quality control | Laboratory and insectary supplies for the NMCP. | NEEDS assessment needed | |
| 13 | Mapping of IR stakeholders in stratified areas | Communication and meetings (2 meetings) | 22,650,000 | 3,485 |
| 14 | Establish functional decision bodies- Malaria Vector Control Technical Working Group and IVM committee | Communication, internal consultative meeting and other logistics | 10,000,000 | 1,538 |
| 15 | Conduct quality control of malaria vector control tool pre and post community consumption | Conduct bioassay test on LLINs in the field | 702,000,000 | 108,000 |
| 16 | Work with regulatory bodies responsible for registration of insecticides | Consultative meetings 2 per year | 20,650,000 | 3,177 |
| | **Grand total** | | **3,423,996,508** | **517,776** |

**Table 9: A FOUR-YEAR TIMELINE**

| Strategic intervention | Action point | Timeline | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 2017 | | | | 2018 | | | | 2019 | | | | 2020 | | | |
| | | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |
| To provide framework for IRMM decision making process; Insecticide resistance monitoring; data collection and sharing; and implementation of insecticide resistance management | Select sites for susceptibility testing | | | | | | | | | | | | | | | | |
| | Conduct susceptibility tests in sentinel sites | | | | | | | | | | | | | | | | |
| | Supportive supervision and coordination to insecticide resistance sentinel sites | | | | | | | | | | | | | | | | |
| | Identify resistance mechanisms | | | | | | | | | | | | | | | | |
| | Conduct resistance intensity testing | | | | | | | | | | | | | | | | |
| | Conduct Malaria Vector Control Technical Working Group (MVCTWG) meeting | | | | | | | | | | | | | | | | |
| | Conduct Integrated Vector Control (IVM) National Steering committee Meeting | | | | | | | | | | | | | | | | |
| | Conduct stakeholders meeting to discuss findings | | | | | | | | | | | | | | | | |
| | Establish insecticide resistance database | | | | | | | | | | | | | | | | |
| | Annual review of insecticide of IRMMP | | | | | | | | | | | | | | | | |
| To strengthen the capacity personnel's involved in the insecticide resistance monitoring and management so as to effectively implement the plan | Identify and build capacity of the vector control staff at national and in selected districts | | | | | | | | | | | | | | | | |
| | Strengthen capacity of NMCP/Laboratory for vector control & quality control | | | | | | | | | | | | | | | | |
| To provide a forum and strategic framework for IVC among partners to ensure coordinated and harmonized implementation of the interventions | Mapping of IR stakeholders in stratified areas | | | | | | | | | | | | | | | | |
| | Establish functional decision bodies-Malaria Vector Control Technical Working Group and IVM National Steering committee | | | | | | | | | | | | | | | | |
| | Conduct meetings of the Malaria Vector Control Technical Working Group (as above) | | | | | | | | | | | | | | | | |
| | Conduct Integrated Vector Control (IVM) National Steering committee Meeting (as above) | | | | | | | | | | | | | | | | |
| | Conduct quality control of malaria vector control tool pre and post community consumption | | | | | | | | | | | | | | | | |
| | Work with regulatory bodies responsible for registration of insecticides | | | | | | | | | | | | | | | | |

## Table 10: A FOUR-YEAR BUDGET

| No. | Action point | Specific Activity | Estimated cost in US$ | | | |
|---|---|---|---|---|---|---|
| | | | 2017 | 2018 | 2019 | 2020 |
| 1. | Select sites for susceptibility testing from each district | Selection of chiefdoms and communities for monitoring in collaboration with DHMT | 6,047 | 6,047 | 6,047 | 6,047 |
| 2 | Conduct susceptibility tests in sentinel sites and identify resistance mechanisms | Insecticide resistance surveillance activities in 14 sentinel districts | 68,815 | 68,815 | 68,815 | 68,815 |
| | | Equipment and Supplies | 7,068 | 7,068 | 7,068 | 7,068 |
| | | Shipping and custom clearance cost | 10,000 | 10,000 | 10,000 | 10,000 |
| | | Data Analysis & Report writing | 2,581 | 2,581 | 2,581 | 2,581 |
| 3 | Conduct resistance intensity tests | Field sampling and transportation, laboratory testing | 68,815 | 68,815 | 68,815 | 68,815 |
| 4 | Supportive supervision to insecticide resistance sentinel sites | DSA and transportation | 20,170 | 20,170 | 20,170 | 20,170 |
| 5 | Identify resistance mechanisms | 300 mosquitoes x 14 sites X 8U$ | 33,600 | 33,600 | 33,600 | 33,600 |
| 6 | Conduct Malaria Vector Control Technical Working Group meeting | 4 meeting annually | 5,815 | 5,815 | 5,815 | 5,815 |
| 7 | Conduct Integrated Vector Control IVM National Steering committee Meeting | 2 meetings annually | 3,177 | 3,177 | 3,177 | 3,177 |
| 8 | Conduct stakeholders meeting to discuss IR findings | 1 Meeting | 2,275 | 2,275 | 2,275 | 2,275 |
| 9 | Establish Insecticide resistance database | Consultant hiring cost | 4,500 | 4,500 | 4,500 | 4,500 |
| | | 2 technical staff to work with a consultant for 15 days | 1,385 | 1,385 | 1,385 | 1,385 |
| | | Computer, software and accessories | 1,000 | 1,000 | 1,000 | 1,000 |
| | | Resistance database maintenance cost | 9,885 | 9,885 | 9,885 | 9,885 |
| 10 | Annual review of IRMM work plan | Three days stakeholders review meeting | 24,780 | 24,780 | 24,780 | 24,780 |
| 11 | Identify and build capacity of the vector control staff at national and in selected districts | Training of national and district staff on basic field entomology and insecticide resistance testing | 33,663 | 33,663 | 33,663 | 33,663 |
| | | Training of 2 national staff on malaria entomology abroad-fee, upkeep and transport | 18,000 | 18,000 | 18,000 | 18,000 |
| | | Recruitment of 2 senior malaria entomologists to oversee the IRMMP – annual salary | 80,000 | 80,000 | 80,000 | 80,000 |
| 12 | Strengthen capacity of NMCP Laboratory for vector control & quality control | Laboratory and insectary supplies for the NMCP. | | | | |
| 13 | Mapping of IR stakeholders in stratified areas | Communication and meetings (2 meetings) | 3,485 | 3,485 | | |
| 14 | Establish functional decision bodies-Malaria Vector Control Technical Working Group and IVM committee | Communication, internal consultative meeting and other logistics | 1,538 | | | |
| 15 | Conduct quality control of malaria vector control tool pre and post community consumption | Conduct bioassay test on LLINs in the field | 108,000 | 108,000 | 108,000 | 108,000 |
| 16 | Work with regulatory bodies responsible for registration of insecticides | Consultative meetings 2 per year | 3,177 | 3,177 | 3,177 | 3,177 |
| | **TOTAL** | | **517,776** | **516,238** | **512,753** | **512,753** |

# 9 BIBLIOGRAPHY


BROWN, A. W. (1958) The insecticide-resistance problem: a review of developments in 1956 and 1957. *Bull World Health Organ,* 18**,** 309-21.

CHANDA, E., HEMINGWAY, J., KLEINSCHMIDT, I., REHMAN, A. M., RAMDEEN, V., PHIRI, F. N., COETZER, S., MTHEMBU, D., SHINONDO, C. J., CHIZEMA-KAWESHA, E., KAMULIWO, M., MUKONKA, V., BABOO, K. S. & COLEMAN, M. (2011) Insecticide resistance and the future of malaria control in Zambia. *PLoS One,* 6**,** e24336.

CHANDRE, F., DARRIER, F., MANGA, L., AKOGBETO, M., FAYE, O., MOUCHET, J. & GUILLET, P. (1999) Status of pyrethroid resistance in *Anopheles gambiae sensu lato*. *Bull World Health Organ,* 77**,** 230-4.

COETZEE, M., HUNT, R. H., WILKERSON, R., DELLA TORRE, A., COULIBALY, M. B. & BESANSKY, N. J. (2013) Anopheles coluzzii and Anopheles amharicus, new members of the Anopheles gambiae complex. *Zootaxa* 3619

CORBEL, V., N'GUESSAN, R., BRENGUES, C., CHANDRE, F., DJOGBENOU, L., MARTIN, T., AKOGBETO, M., HOUGARD, J. M. & ROWLAND, M. (2007) Multiple insecticide resistance mechanisms in *Anopheles gambiae* and *Culex quinquefasciatus* from Benin, West Africa. *Acta Trop,* 101**,** 207-16.

DIABATE, A., BALDET, T., CHANDRE, F., AKOOBETO, M., GUIGUEMDE, T. R., DARRIET, F., BRENGUES, C., GUILLET, P., HEMINGWAY, J., SMALL, G. J. & HOUGARD, J. M. (2002) The role of agricultural use of insecticides in resistance to pyrethroids in *Anopheles gambiae s.l*. in Burkina Faso. *Am J Trop Med Hyg,* 67**,** 617-22.

ELISSA, N., MOUCHET, J., RIVIERE, F., MEUNIER, J. Y. & YAO, K. (1993) Resistance of *Anopheles gambiae* s.s. to pyrethroids in Cote d'Ivoire. *Ann Soc Belg Med Trop,* 73**,** 291-4.

HAMON, J., SUBRA, R., SALES, S. & COZ, J. (1968) Presence in the southwestern part of Upper Volta of a population of *Anopheles gambiae* "A" resistant to DDT. *Med Trop (Mars),* 28**,** 521-8.

HARGREAVES, K., KOEKEMOER, L. L., BROOKE, B. D., HUNT, R. H., MTHEMBU, J. & COETZEE, M. (2000) *Anopheles funestus* resistant to pyrethroid insecticides in South Africa. *Med Vet Entomol,* 14**,** 181-9.

HUNT, R., EDWARDES, M. & COETZEE, M. (2010) Pyrethroid resistance in southern African *Anopheles funestus* extends to Likoma Island in Lake Malawi. *Parasit Vectors,* 3**,** 122.

MUNHENGA, G., MASENDU, H. T., BROOKE, B. D., HUNT, R. H. & KOEKEMOER, L. K. (2008) Pyrethroid resistance in the major malaria vector *Anopheles arabiensis* from Gwave, a malaria-endemic area in Zimbabwe. *Malar J,* 7**,** 247.

NDIATH, M. O., SOUGOUFARA, S., GAYE, A., MAZENOT, C., KONATE, L., FAYE, O., SOKHNA, C. & TRAPE, J. F. (2012) Resistance to DDT and pyrethroids and increased kdr mutation frequency in *An. gambiae* after the implementation of permethrin-treated nets in Senegal. *PLoS One,* 7**,** e31943.

NDJEMAI, H. N., PATCHOKE, S., ATANGANA, J., ETANG, J., SIMARD, F., BILONG, C. F., REIMER, L., CORNEL, A., LANZARO, G. C. & FONDJO, E. (2009) The distribution of insecticide resistance in *Anopheles gambiae* s.l. populations from Cameroon: an update. *Trans R Soc Trop Med Hyg,* 103**,** 1127-38.

NMCP, INFORM and LSHTM (2015). Sierra Leone: A Profile of Malaria Control and Epidemiology.

NMCP (2015) Sierra Leone Malaria Control Strategic Plan 2016-2020. Ministry of Health and Sanitation, Republic of Sierra Leone, October 2015

OKOYE, P. N., BROOKE, B. D., KOEKEMOER, L. L., HUNT, R. H. & COETZEE, M. (2008) Characterisation of DDT, pyrethroid and carbamate resistance in *Anopheles funestus* from Obuasi, Ghana. *Trans R Soc Trop Med Hyg,* 102**,** 591-8.

PROTOPOPOFF, N., VAN BORTEL, W., MARCOTTY, T., VAN HERP, M., MAES, P., BAZA, D., D'ALESSANDRO, U. & COOSEMANS, M. (2008) Spatial targeted vector control is able to reduce malaria prevalence in the highlands of Burundi. *Am J Trop Med Hyg,* 79**,** 12-8.

RANSON, H., N'GUESSAN, R., LINES, J., MOIROUX, N., NKUNI, Z. & CORBEL, V. (2011) Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? *Trends Parasitol,* 27**,** 91-8.

SHARP, B. L., RIDL, F. C., GOVENDER, D., KUKLINSKI, J. & KLEINSCHMIDT, I. (2007) Malaria vector control by indoor residual insecticide spraying on the tropical island of Bioko, Equatorial Guinea. Malar J, 6, 52.

SINKA, M. E., BANGS, M. J., MANGUIN, S., RUBIO-PALIS, Y., CHAREONVIRIYAPHAP, T., COETZEE, M., MBOGO, C. M., HEMINGWAY, J., PATIL, A. P., TEMPERLEY, W. H., GETHING, P. W., KABARIA, C. W.,

BURKOT, T. R., HARBACH, R. E. & HAY, S. I. (2012) A global map of dominant malaria vectors. Parasit Vectors, 5, 69.
STUMP, A. D., ATIELI, F. K., VULULE, J. M. & BESANSKY, N. J. (2004) Dynamics of the pyrethroid knockdown resistance allele in western Kenyan populations of Anopheles gambiae in response to insecticide-treated bed net trials. Am J Trop Med Hyg, 70, 591-6.
TEMU, E. A., MAXWELL, C., MUNYEKENYE, G., HOWARD, A. F., MUNGA, S., AVICOR, S. W., POUPARDIN, R., JONES, J. J., ALLAN, R., KLEINSCHMIDT, I. & RANSON, H. (2013) Pyrethroid resistance in Anopheles gambiae, in Bomi County, Liberia, compromises malaria vector control. PLoS One, 7, e44986.
WHO (2010) The technical basis for coordinated action against insecticide resistance: preserving the effectiveness of modern malaria vector control. Technical report. Global Malaria Programme.
WHO (2012) Global Plan for Insecticide Resistance Management in Malaria Vectors (GPIRM). Geneva, Switzerland
WHO (2013) Test procedures for insecticide resistance monitoring in malaria vector mosquitoes. Geneva, Switzerland.
WHO (2014), Framework for Development of National IRM Plans, Geneva, Switzerland.
WHO (2015) World malaria report 2015. Geneva, Switzerland.

# 10 ANNEXES

**Annex 1:** List of Participants in the Stakeholders Meeting to Develop and Validate Insecticide Resistance Monitoring and Management Plan (IRMMP)

| No | NAME | ORGANIZATION |
|---|---|---|
| 1 | Mr Samuel Sesay | Health Education Division/MOHS |
| 2 | Mr Alphan Tejan-Kella | Pharmacy Board Sierra Leone/MOHS |
| 3 | Mr Emmanuel K Margao | Pharmacy Board Sierra Leone/MOHS |
| 4 | Mr Manfred A Moronvia | Neglected Tropical Diseases/MOHS |
| 5 | Mr Paul M. Conteh | Neglected Tropical Diseases/MOHS |
| 6 | Sr. Anitta Kamara | NMCP/MOHS |
| 7 | Dr Samuel J Smith | Programme Manager-NMCP/MOHS |
| 8 | Mr Saffa A Koroma | Health superintendent/Environmental Health |
| 9 | Mr Frederick Yamba | NMCP/MOHS |
| 10 | Mr Sebora Kamara | WHO-Country office |
| 11 | Dr Bilali Kabula | WHO-Consultant and meeting facilitator |
| 12 | Mr Olivier Byicaza | Leadership Management and Governance/NMCP |
| 13 | Mr Musa Sillah-Kanu | NMCP/MOHS |
| 14 | Mr Edward Chaka | MOHS |
| 15 | Mrs Juliana Kamanda | Directorate of Environmental Health and Sanitation /MOHS |
| 16 | Mr Osman B. Gbabai | Directorate of Environmental Health and Sanitation/MOHS |
| 17 | Mr William Pessima | DHMT-Western Area |
| 18 | Mr Mohamed S Turay | Freetown City Council |
| 19 | Dr Ansumana Sillah | Director for Environmental Health and Sanitation/MOHS |
| 20 | Mr Philip Brewah | NMCP/MOHS |
| 21 | Dr A. A. Kamara | NMCP/MOHS |
| 22 | Mr Michael A Gray | NMCP/MOHS |
| | | |

**Annex 2.** Insecticides registered in a country for vector control

| Insecticide Class | Insecticide Type | Product Name | Use (IRS, LLIN, larvicide, agriculture | Formulation | Date of Registration |
|---|---|---|---|---|---|
| Pyrethroid | Permethrin | Olyset net | LLIN | Incorporated polyethyylene | |
| Pyrethroid | Deltamethrin | PermaNet | LLIN | Coated polyester | |
| Pyrethroid | DuraNet | Alphacypermethrin | LLIN | | |
| Pyrethroid | Icon | Lambdacyhalothrin | IRS | WP | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

**Annex 3:** Trend of insecticide resistance in malaria vectors in 2010 and 2016 in Sierra Leone

| INSECTICIDE | DISTRICT | Mean corrected mortality (%) | |
|---|---|---|---|
| | | 2010 | 2016 |
| Pemethrin | Bombali | 100 | 50.4 |
| | Kono | 100 | 60.0 |
| | Bo | 98.3 | 27.0 |
| | Western Rural | 100 | 66.0 |
| Deltamethrin | Bombali | 100 | 57.0 |
| | Kono | 100 | 58.0 |
| | Bo | 100 | 49.0 |
| | Western Rural | 100 | 38.0 |
| Lambdacyhalothrin | Bombali | 100 | 53.0 |
| | Kono | 100 | 51.0 |
| | Bo | 100 | 43.0 |
| | Western Rural | 100 | 32.0 |
| Cyfluthrin | Bombali | - | 50.0 |
| | Kono | - | 77.4 |
| | Bo | - | 43.0 |
| | Western Rural | - | 36.0 |
| DDT | Bombali | 96.7 | 31.0 |
| | Kono | 96.7 | 47.6 |
| | Bo | 93.3 | 28.0 |
| | Western Rural | 96.7 | 7.0 |
| Bendiocarb | Bombali | 100 | 91.0 |
| | Kono | 100 | 93.0 |
| | Bo | 100 | 90.7 |
| | Western Rural | 100 | 91.0 |
| Fenitrothion | Bombali | - | 99.0 |
| | Kono | - | 99.0 |
| | Bo | - | 100.0 |
| | Western Rural | - | 94.7 |
| | Bombali | 100 | - |
| | Kono | 100 | - |
| | Bo | 100 | - |
| | Western Rural | 100 | - |

**Annex 4:** Programme for Stakeholders' Working Meeting to develop Insecticide Resistance Monitoring and Management Plan for Sierra Leone on 06/08/2016

| TIME | ACTIVITY | RESPONSIBLE |
|---|---|---|
| 08:30- 09:00 | Registration | NMCP |
| 09:00-09:10 | Opening remarks | PM- NMCP |
| 09:10 – 09:15 | Meeting objectives and Expected outputs | Mr. Yamba/NMCP |
| 09:15 – 09:30 | Global plan of insecticide resistance management in malaria vectors | Dr Bilali Kabula (consultant) |
| 09:30– 09:45 | Update on Insecticide resistance status in Sierra Leone | Dr. Bilali Kabula (consultant) |
| 09:45- 10:00 | Discussion | ALL |
| 10:00 – 10:15 | Overview of the framework for development of IRMMP | Dr. Bilali Kabula (consultant) |
| 10:15-10:40 | Overview of the draft IRMMP | Dr. Bilali Kabula (consultant) |
| 10:40- 10:50 | Discussion | ALL |
| **10:50 – 11:30** | **TEA BREAK** | **ALL** |
| 11:30 – 11:45 | Groups Formation -4 groups<br>1. Introduction, foreword and Acknowledgement<br>2. Situation Analysis<br>3. IRMMP Implementation Framework<br>4. Work plan & budget | |
| 11:45– 13:00 | Group Works | ALL |
| **13:00 – 14:00** | **LUNCH BREAK** | |
| 14:00 – 16:00 | Group Works | ALL |
| 16:00 – 17:30 | Presentation of group consolidated works and plenary discussion | ALL Groups |
| 17:30 – 18:00 | **CLOSURE** | Director for Environmental Health and Sanitation/MOHS |

**Annex 5:** Programme for Stakeholders' Meeting to review and validate the consolidated Insecticide Resistance Monitoring and Management Plan for Sierra Leone on 12/08/2016

| TIME | ACTIVITY | RESPONSIBLE |
|---|---|---|
| 10:00- 10:15 | Registration | NMCP |
| 10:15-10:20 | Opening remarks | PM- NMCP & DIRECTOR-ENVIRON HEALTH |
| 10:20 – 10:30 | Meeting objectives and Expected outputs | NMCP |
| 10:30 – 12:00 | Overview of consolidated IRMMP | Dr Kabula/Cosultant |
| 12:00– 13:00 | Plenary discussion | ALL |
| 13:00 – 13:30 | Closing remarks | PM- NMCP/DIRECTOR-EH |