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Global Malaria Programme

**Malaria:
Global Fund proposal development
(Round 11)**

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INTRODUCTION

In recent years, visibility and political support for malaria has continued to increase dramatically. This policy brief is a summary of the WHO recommended technical strategies. The purpose is to present in one concise document a summary of WHO Guidance in order to assist countries in developing Global Fund proposals, and in appropriately selecting and budgeting for intervention areas necessary to ensure universal coverage and sustainability. The key intervention areas include: malaria case management – (malaria diagnosis and treatment); malaria prevention in special groups (during pregnancy and infancy); malaria vector control; and surveillance, monitoring and evaluation. It highlights technical areas and implementation activities that countries should ensure are included in the proposal with appropriate funding to ensure effective implementation. This policy briefing is not intended as a substitute for the published WHO documents on which it is based; it is intended to be used together with the reference WHO publications which is provided in a separate document (*Malaria: Global Fund proposal development: Compilation of WHO reference documents, July 2011*).

WHO recommends that everyone at risk of malaria should be protected by effective vector control. This will reduce the vectorial capacity of the malaria-carrying mosquito, and thus reduce transmission, and thereby the mortality and morbidity from malaria. This document focuses on the two main operational interventions for malaria vector control: long-lasting insecticidal nets (LLINs)¹, and indoor residual spraying of insecticide (IRS). In some context-specific situations, where the vector breeding sites meet certain conditions², these core interventions can be locally complemented by other methods (e.g. larval control or environmental management) in the context of Integrated Vector Management (IVM). Effective and sustained implementation of malaria vector control interventions (IRS and/or LLINs) requires clear political commitment and engagement from national authorities as well as long-term support by funding partners.

Access to prompt diagnostic testing and effective treatment of malaria shortens the duration of illness, prevents the progression to severe illness and the majority of deaths from malaria. Access to malaria diagnostic testing and treatment should therefore be seen not only as a component of malaria control but a fundamental right of all populations at risk. As such, it must be an essential part of health system development and a key component of reducing morbidity and deaths due to malaria.

It is the responsibility of all national health programmes to develop a treatment policy for malaria consistent with WHO Guidelines and recommendations. It is recognized that antimalarial treatment policies will vary between countries depending on the epidemiology of the disease, transmission, patterns of drug resistance and political and economic contexts. Nevertheless, the overall objectives of any antimalarial treatment policy are to:

- Detect every case of malaria through parasitological confirmation of diagnosis (diagnostic testing);
- Ensure rapid and long-lasting radical cure of confirmed malaria infections;
- Reduce morbidity and mortality, including malaria-related anaemia;
- Prevent the progression of uncomplicated malaria to severe and potentially fatal disease;
- Reduce the impact of placental malaria infection and maternal malaria-related anaemia on both the mother and the newborn;
- Decrease malaria transmission, by reducing the malaria parasite reservoir.

¹ Because WHO advises that the nets procured and distributed by malaria programmes should all be WHOPES-recommended LLINs, and because WHOPES-recommended long-lasting insecticide net-treatment kits are now available for application to untreated nets found in the field, this document refers to all insecticide treated nets as LLINs.

² These conditions are specified at www.who.int/malaria

Whether the final programme goal is to control and/or eventually eliminate malaria, all main operational interventions – case management and vector control (IRS or /and LLINs) are essential and strategic priorities. These are complemented as appropriate to the contextual setting with IPTp, IPTi and other forms of chemoprevention. However, no matter what interventions are deployed and scaled up, it is essential to measure progress, evaluate setbacks and reorient the programme in order to achieve set national and/or global targets.

This document provides an overview of the currently recommended tools which can and should be incorporated into Global Fund proposals to ensure that reporting requirements against set indicators, including data management of all interventions - in particular performance management, are met in a timely fashion.

Costing is rarely mentioned in this document as figures vary tremendously among programmes (and among countries) and over time. Local information on operational costs which are critical to reach intervention targets (e.g. transportation and distribution costs, supervision, quality assurance, monitoring, community sensitization, and salaries/incentives for the health workers who will be carrying out the interventions) should be included in addition to the cost of commodities in the total budget.



1. CASE MANAGEMENT (MALARIA DIAGNOSIS AND TREATMENT)

1.1 Malaria treatment guidelines³

Malaria case management (encompassing prompt diagnostic testing and treatment with an effective antimalarial) is one of the key strategies in the control of malaria.

Malaria diagnosis

Prompt and accurate diagnosis of malaria is fundamental to effective disease management and essential to improving the overall management of febrile illnesses. WHO currently recommends:

- prompt parasitological confirmation by microscopy or RDTs in all patients suspected of malaria before treatment is started; and
- treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible.

This recommendation is leading to a progressive shift from presumptive treatment to parasitological confirmation prior to treatment, a major paradigm change -- particularly in areas of high malaria transmission for children under five years of age. This has led to an increase in the procurement and use of rapid diagnostic tests and a continued need for strengthening of laboratory and microscopy services.

In line with the above, estimation of the requirements and costs (direct and indirect) of malaria diagnostic tests should be factored into the cost of case management, including training of health workers, consumer education, supervision, and quality assurance.

Malaria treatment

a) Uncomplicated *P. falciparum* malaria

Artemisinin-based combination therapies (ACTs) are the treatment recommended for all cases of uncomplicated falciparum malaria including:

- infants,
- people living with HIV/AIDS,
- for community case management of malaria,
- pregnant women in the 2nd and 3rd trimesters (exception: use in the 1st trimester only if there are no alternative effective antimalarials).

The following five ACTs are presently recommended:

- artemether + lumefantrine
- artesunate + amodiaquine
- artesunate + mefloquine
- artesunate + sulfadoxine-pyrimethamine
- dihydroartemisinin + piperaquine

Second-line treatment:

An alternative effective ACT (because the efficacy of ACTs partially depends on the efficacy of the partner medicine, it is possible to use 2 different ACTs as 1st and 2nd-line options)

It should be noted that fixed-dose combination (FDC) formulations are strongly preferred and recommended over blistered co-packaged or loose tablets combinations to promote adherence to treatment and to reduce the potential selective use of the medicines as monotherapy. Fixed-dose combination formulations are now available for all recommended ACTs, except artesunate plus SP.

³ *Guidelines for the treatment of malaria* 2nd Edition, Geneva: World Health Organization, 2010, http://whqlibdoc.who.int/publications/2010/9789241547925_eng.pdf

Oral artemisinin-based monotherapy medicines

In order to contain the risk of development of resistance to artemisinin-based combination therapies (ACTs), WHO urges Member States to urgently cease the marketing and use of oral artemisinin-based monotherapy medicines, in both the public and private sectors, and to promote the use of ACTs instead. As part of malaria Resolution WHA60.18, (http://apps.who.int/gb/ebwha/pdf_files/WHA60/A60_R18-en.pdf), these recommendations have been endorsed by all WHO Member States at the 60th World Health Assembly in May 2007 and WHO requests international organizations and financing bodies to cease to fund the provision and distribution of **oral** artemisinin-based monotherapies. More information on this can be obtained on the GMP web page: http://www.who.int/malaria/marketing_of_oral_artemisinin_monotherapies/en/index.html.

Antigametocyte medicine:

The addition of a single dose **primaquine** (0.75 mg/kg) to ACT treatment for uncomplicated falciparum malaria as an antigametocyte medicine, particularly as a component of pre-elimination or an elimination programme, is recommended. The safety of use of primaquine in G6PD deficient individual must always be considered.

b) Pregnancy

The following options are recommended for the treatment of uncomplicated malaria in pregnancy:

- 1st trimester⁴:
quinine + clindamycin
- 2nd and 3rd trimesters:
any of the recommended ACTs as listed above
artesunate + clindamycin
quinine + clindamycin

c) Severe falciparum malaria

Initial treatment:

Parenteral artesunate (IV or IM) is the medicine of choice for severe malaria in all age groups. Artesunate should be used in preference to quinine, as it significantly reduces the risk of death, and lowers the risk of treatment-associated hypoglycaemia.

Quinine or artemether are acceptable alternatives if artesunate is not available

Follow-on treatment:

Once the patient recovers and can tolerate oral treatment, or after at least 24 hours of parenteral treatment, one of the following options should be used to complete treatment:

Full course of an ACT, or where not available

Quinine + clindamycin or doxycycline

d) Uncomplicated P. vivax malaria

Chloroquine combined with primaquine is the treatment of choice for chloroquine-sensitive infections.

In areas with chloroquine resistant *P. vivax*, artemisinin-based combination therapies (except AS+SP) are recommended.

At least a 14-day course of primaquine is required for the radical treatment of *P. vivax*

⁴ ACT should be used if it is the only effective antimalarial treatment available

In mild to moderate G6PD deficiency, primaquine 0.75 mg base/kg BW may be given once a week for 8 weeks. In severe G6PD deficiency, primaquine is contraindicated and should not be used.

Where ACT (exception AS+SP) has been adopted as the first-line treatment for *P. falciparum* malaria, it may also be used for *P. vivax* malaria in combination with primaquine for radical cure.

Malaria treatment policy

Antimalarial treatment policy is a set of recommendations and regulations regarding the availability, and the rational use of antimalarial medicines in a country. It provides guidelines for early diagnostic testing and prompt and effective treatment to be adapted as appropriate to the local context, for all levels of the health care systems.

The process of policy change

Changing antimalarial treatment policy in countries requires concerted action among all stakeholders and continuous stewardship by the Ministry of Health.

The key evidence of the need for treatment policy change is the therapeutic efficacy of the antimalarial drugs being used as assessed according to standard WHO protocols⁵. WHO's current recommendation is to change a treatment policy when the:

Treatment failure is >10% (as assessed through monitoring of therapeutic efficacy at 28 days).

Similarly, an antimalarial medicine should only be selected as a new treatment policy option only when the medicine has an average cure rate of >95% as assessed in therapeutic efficacy studies.

The process of implementing a new treatment policy

To date, almost all falciparum endemic countries have already revised their antimalarial treatment to include ACTs as first-line treatment. However, in several of these countries ACTs have not been fully scaled up and are particularly dependant on external funding, especially from the Global Fund, to ensure universal coverage.

Below are critical areas and activities required for an effective implementation of a revised and/or expanding policy, which have budgetary implications and should thus be taken into account in the preparation of any proposal intending to support the implementation of an ACT based treatment policy:

- 1) Provision for preliminary activities for planning and development of a framework for implementation or scale-up, such as forecasting, training, and supervision, as applicable
- 2) Provision for procurement and distribution of supplies
 - Estimation of needs (medicines and rapid diagnostic tests)⁶
 - Procurement costs for antimalarials and diagnostic tests should also include costs of insurance, transportation, delivery, and stock management within the country, etc.
 - Drug storage and distribution systems should also be budgeted.
 - Resources for purchase of microscopes and malaria rapid diagnostic tests.
- 3) Provision for orientation and training of all health workers in public and/or private sector
 - Development and production of training materials for all health workers
 - A budget for orientation and training of health workers
 - Costs for periodic supervision of health workers
 - Production of patient cards, data collection tools for monitoring case management.
- 4) Provision for behaviour change communication strategy
 - Production and pre-testing of IEC, BCC and advocacy materials,

⁵ See section on Therapeutic efficacy monitoring for details on protocols

⁶ See section on supply chain management for details on quantification and procurements

- Conduction of education, information, behaviour change communication and advocacy activities targeting various groups (communities, health workers, leaders at different levels and partners)
 - Activities towards enhancing compliance to treatment with ACTs
- 5) Quality assurance
- A system for quality assurance and/or control of medicines and diagnostics
 - Setting up a quality assurance laboratory system linked to sub-national or national central laboratories
- 6) Monitoring and evaluation
- Setting up a system for data collection and reporting on distribution and stock-outs of antimalarial medicines
 - Routine therapeutic efficacy of first and second line antimalarial combinations in representative sites every other year should be conducted as an essential part of a malaria control programme (See Chapter 6 for complete information)
- 7) Pharmacovigilance
- Development and production of data collection forms
 - Cascade training of health workers (public and private sector)
 - Costs for investigation of reported cases
 - Data processing equipment, data management and communication.

Challenges⁷

Estimating quantities of required antimalarial medicines and rapid diagnostic tests - especially in countries lacking a reliable supply information system - is a challenging task. If reliable stock management records are available, needs can be estimated using the consumption method. If past consumption would not serve as a guide to the future (e.g. in case previous budgets were too low, prescribing patterns changed substantially, new treatments are being introduced, successful malaria control interventions have decreased or are decreasing drug consumption over time), the standard morbidity method should be applied. The estimations of needs so obtained should be adjusted to programme delivery capacity, also taking into consideration stock in hand, stock on order, anticipated losses, lead-time and needs for buffer stocks. To translate the forecast into actual orders, the estimated needs should be matched against available funds.

⁷ *Malaria case management: operations manual*, Geneva: World health Organization, 2009.
http://whqlibdoc.who.int/publications/2009/9789241598088_eng.pdf

2. SUPPLY MANAGEMENT FOR MALARIA DIAGNOSTIC TESTING AND TREATMENT

2.1 Malaria diagnostic testing

2.1.1. Background

Demonstration of the presence of malaria parasites prior to treatment with antimalarial drugs is fundamental, as clinical diagnosis has poor accuracy and leads to over-diagnosis of malaria with resultant poor management of non-malarial febrile illness and wastage of antimalarial drugs. WHO recommends parasitological confirmation of malaria through quality-assured diagnostic testing in all settings before treatment is started. Prompt diagnostic confirmation of malaria can be achieved through good quality microscopy. Since this is not feasible in all situations, quality-assured RDTs represent suitable alternatives for the diagnosis of malaria.

2.1.2. Microscopy

While microscopy remains the mainstay of parasite-based diagnosis in most large health clinics and hospitals, the quality of microscopy-based diagnosis is frequently inadequate for ensuring good health outcomes and optimal use of resources.

An acceptable microscopy service is one that is cost-effective, provides results that are consistently accurate and timely enough to have a direct impact on treatment. This requires a comprehensive and active quality assurance (QA) programme. The primary aim of malaria microscopy QA programmes is to ensure that microscopy services are manned by competent and motivated staff, supported by effective training and supervision that maintains a high level of staff competency and performance and by a logistics system that provides and maintains an adequate supply of reagents and equipment. QA programmes must be sustainable, compatible with the needs of each country, and able to fit into the structure of existing laboratory services. A QA programme should appropriately recognize and accredit good performance, identify laboratories and microscopists with serious problems which result in poor performance, establish regional or national benchmarks for quality of diagnostic testing and central reporting of indicators including accuracy, equipment and reagent performance, stock control and workload. Without an efficient QA programme, resources spent on diagnostic services are likely to be wasted and clinicians will have no confidence in the results.

At a minimum, a malaria microscopy QA programme should include the following:

- A central coordinator(s) to oversee QA.
- A reference (core) group of microscopists at the head of a hierarchical structure, supported by an external QA programme and with demonstrable expertise in overseeing programme training and validation standards.
- Good initial training with competency standards that must be met by trainees prior to operating in a clinical setting
- Regular retraining and assessment/grading of competency, supported by a well validated reference slide set (slide bank).
- A sustainable cross-checking (validation) system that detects gross inadequacies without overwhelming validators higher up the structure, with good feed-back of results and a system to address inadequate performance.
- Good supervision at all levels.
- Good logistical management, including supply of consumables and maintenance of microscopes.
- Clear standard operating procedures (SOPs) at all levels of the system.
- An adequate budget is required as an essential part of funding for malaria case management.

2.1.3. Rapid diagnostic tests (RDTs)

It is the responsibility of each national malaria control programme to select well performing RDTs adequate for the setting of intended use. To select malaria RDTs, experts convened at the WHO Technical Consultation on parasitological confirmation of malaria diagnosis, held in October 2009 in Geneva, provided the following advice:

1.1 For detecting *Plasmodium falciparum*:

1.1.1 Low⁸ and moderate⁹ transmission areas:

Select RDTs that achieve well above 50% panel detection score (PDS) at 200 parasites/μl (e.g. >75%).

1.1.2 High¹⁰ transmission areas:

Panel detection score should be at least 50% at 200 parasites/μl. Since the extent of such areas is likely to decrease with effective malaria control, detection rates well above this level should become the basis for product selection in the future years.

1.2. For detecting *Plasmodium vivax*:

Selection criteria for *P. vivax*-detecting RDTs should be at least equivalent to those for *P. falciparum*-detecting RDTs, i. e. at least a panel detection score of 50%.

In addition to the above criteria, national health authorities should take the following factors into consideration when selecting appropriate malaria RDTs for procurement:

2. The invalid rate should be less than 5%
3. The false positive rate should be less than 10%.
4. Stability requirements at temperatures of intended storage, transport and use.
5. Ease of use and training requirements by the health workers.

Once all these factors have been considered, other parameters should also be evaluated, such as completeness of the kits (e.g. inclusion of lancets and alcohol swabs) and price. It must be stressed that price alone should not be the determining factor for the procurement of RDTs.

Further guidance can be obtained from the WHO *Information note on recommended selection criteria for procurement of malaria rapid diagnostic tests (RDTs)*

(http://www.who.int/malaria/diagnosis_treatment/diagnosis/RDT_selection_criteria.pdf) and the WHO manual on *Good practices for selecting and procuring rapid diagnostic tests for malaria* (<http://www.who.int/malaria/publications/atoz/9789241501125/en/index.html>).

To guide the selection and procurement of malaria RDTs, a WHO/FIND RDT performance testing system was established in 2008. Results of the second round of product testing were published in April 2010; a third round of testing is currently ongoing and results of Round 3 are expected to be available in August 2011. The currently available Round 2 results (<http://www.who.int/malaria/publications/atoz/9789241599467/en/index.html>) provide comparative data on the performance of all RDTs tested in Round 1 (2008) and in Round 2 (2009). Based on these results, the Foundation for Innovative New Diagnostics (FIND) has developed a web-based interactive guide to inform

⁸ “Low transmission” areas are hypo-endemic areas in which the prevalence rate of malaria is 10% or less during most time of the year among children from 2 to 9 years old. Here, a person may attain adolescence before malaria infection is acquired and may escape acquiring a malaria infection altogether.

⁹ “Moderate transmission” areas are meso-endemic areas in which the prevalence rate of malaria is 11–50% during most time of the year among children from 2 to 9 years old. Here, the maximum prevalence of malaria infection occurs in childhood and adolescence, though still not unusual for adult life to be attained before acquiring infection.

¹⁰ “High transmission” areas are hyperendemic and holo-endemic areas in which the prevalence rate of malaria is over 50% during most time of the year among children from 2 to 9 years old. In these areas by late infancy or early childhood practically all individuals are infected.

RDT selection on the basis of target malaria species, minimum panel detection score¹¹ for both *P. falciparum* and *P. vivax*, invalid rate¹², false positive rate, and test format. The guide is available at: (http://www.finddiagnostics.org/programs/malaria/find_activities/product_testing/malaria-rdt-product-testing#).

Programmes that currently are not undertaking wide-scale use and/or are planning the introduction of a new or different RDTs should consider selecting those tests with the highest performance for temperatures and conditions. In countries with heterogeneous levels of transmission, programmes should consider selecting those RDTs with higher detection levels to cover all areas, including those with low-to-moderate transmission.

Programmes that are already procuring RDTs which detect *P. vivax* with a panel detection score in the range of 25–50% on a large scale should proceed with pre- or post-shipment lot testing (see RDT lot testing programme below) and consider moving to an RDT with a higher Panel Detection Score in the future.

Subsequent plans to replace RDTs should be made with consideration of all corresponding training and programmatic requirements. In addition, production capacity and expected delivery time for orders of the new RDTs should be assessed as part of the decision-making process.

2.1.4. RDT lot testing programme

The performance of individual products is likely to vary between lots over time. It is therefore strongly recommended that all production lots of procured products be checked for quality through lot-testing prior to large-scale deployment in the field and that a process of monitoring RDT performance in the field¹³ should be put in place. This should be applied to all RDTs. Full information on WHO procedures for RDT lot testing is available at: (http://www.wpro.who.int/sites/rdt/who_rdt_evaluation/lot_testing.htm).

2.2 Artemisinin-based antimalarial medicines

Quality is one of the most important considerations in the manufacture and procurement of medicines. The quality of artemisinin-based antimalarial medicines is particularly important, as these medicines are chemically fragile (i.e. they have a relatively short shelf life of 2 to 3 years).

WHO provides guidance on how to select and procure safe and effective quality medicines with the manual on Good procurement practices for artemisinin-based antimalarial medicines¹⁴, which is based on new stringent internationally agreed quality assurance criteria.

2.2.1. Selection of safe, effective and quality antimalarial medicines

The following mechanisms are currently in place to ensure appropriate selection of antimalarial medicines:

Inclusion in the WHO Guidelines for Treatment of Malaria and in the national treatment guidelines, or

Inclusion in the national treatment guidelines, but not in WHO Treatment Guidelines, after review approval by committee of experts in malaria chemotherapy.

In addition, the following quality selection criteria must be applied to the selection of specific products:

Products prequalified by WHO or registered by a Stringent Drug Regulatory Authority (SDRA) are eligible for procurement and have priority selection.

¹¹ Panel detection score (PDS): the percentage of malaria samples in the panel giving a positive result by two RDTs per lot at the lower parasite density, and a single RDT per lot at the higher parasite density. PDS was termed "detection rate" in the report of Round 1 published in April 2009.

¹² Proportion of tests deemed invalid, i.e. without visible control band.

¹³ P.11 <http://www.wpro.who.int/NR/rdonlyres/9F42AF75-AC81-48E5-AAA2-0FB9B630425C/0/RBMGFATMRDTP17Fin2.pdf>

¹⁴ http://whqlibdoc.who.int/publications/2010/9789241598927_eng.pdf

In case there are fewer than two WHO-prequalified or SDRA-registered products, or if the products which meet these standard are unavailable, products complying with partial quality criteria can be selected .

Fixed-dose combination (FDC) formulations are strongly preferred and recommended over blistered co-packaged or loose tablets combinations to promote adherence to treatment and to reduce the potential selective use of the medicines as monotherapy. Fixed-dose combination formulations are now available for all recommended ACTs, except artesunate plus SP.

Partial quality criteria: (i.) GMP compliance certified after inspection by WHO or by a SDRA for the dosage form concerned; (ii.) Submission of the product dossier to the WHO PQ Programme or to a SDRA and acceptance of the corresponding organization to review the dossier; and (iii.) Acceptance of the product after technical review by an “Expert Review Panel (ERP)” convened by WHO.

2.2.2. Procurement of quality medicines

Detailed information on each step of the procurement cycle (from estimation of requirements, over tender-related procedures and pre-/post-shipment quality control to monitoring and evaluation) of antimalarial medicines can be derived from the 16 steps comprising procurement checklist in the manual on Good procurement practices for artemisinin-based antimalarial medicines.

<http://www.who.int/malaria/publications/atoz/9789241598927/en/index.html>.

2.3 Plan of activities for costing purposes (this list is not exhaustive):

- 1) Completion of preliminary activities – such as quantification and training, and introduction and procurement planning of medicines and/or diagnostics supply.
- 2) Orientation and training of all health workers in public and private sector for medicines and rapid diagnostic tests
 - Development and production of training materials for all health workers
 - A budget for orientation and training of health workers
 - Costs for periodic supervision of health workers
 - Production of patient cards, data collection tools for monitoring case management.
- 3) Elaboration of behaviour change communication strategy
 - Development, field-testing and production of IEC and advocacy materials,
 - Education and communication activities targeting various groups (e.g. communities, health workers)
- 4) Procurement and distribution of supplies:
 - Quantification: Estimation of needs and forecast of demand for medicines and rapid diagnostic tests. (Calculating the quantities of required antimalarial medicines and rapid diagnostic tests - especially in countries lacking a reliable supply information system - is a challenging task. In case reliable stock management records are available, needs can be estimated using the consumption method. If past consumption would, however, give an unrealistic picture (e.g. in case previous budgets were too low, prescribing patterns changed substantially, new treatments are being introduced, successful malaria control interventions decreased drug consumption over time), the standard morbidity method should be applied. The estimations of needs so obtained requires to be adjusted to programme delivery capacity, taking also into consideration stock in hand, stock on order, anticipated losses, lead-time and needs for buffer stocks. To translate the forecast into actual orders, the estimated needs should be matched against available funds.)
 - Costs: Procurement costs for medicines and diagnostic tests should not only consider total goods prices but also costs for freight, insurance, programme support, port clearance and customs procedures, in-country distribution and storage.

- Equipment: Required technical equipment (e.g. for distribution and storage, RDT waste management) need to be considered.
 - Staff: Tender related procedures (preparation of tender documents, tender invitation and bid evaluation by sufficient staff with appropriate expertise)
- 5) Budget for implementation and use of a sound quality assurance systems for medicines and diagnostics (pre-/post-shipment quality control systems for medicines and pre-/post-shipment lot testing for RDTs)
- 6) Development and implementation of sound monitoring systems
- To collect and evaluate data on medicines and RDTs concerning in-country distribution and stock-outs (comprising all levels of the health care system).
 - Therapeutic efficacy and resistance monitoring
 - Pharmacovigilance (Development and production of data collection forms, Cascade training of health workers (public and private sector), Costs for investigation of reported cases, Data processing equipment, data management and communication.)

Specific requirements for large scale deployment of RDTs into national programmes are described in Annex 6 of the Malaria Rapid Diagnostic Test performance report Round 2 (see: <http://www.who.int/malaria/publications/atoz/9789241599467/en/index.html>). The summary outline is provided below.

Programme planning and management

- Identify key stakeholders, and secure commitment for introduction of RDTs
- Establish working group and develop terms of reference
- Identify specific focal person(s) responsible for day to day oversight of the implementation plan
- Develop a timeline, scope, and budget for implementation
- Identify human and other resource needs, and a strategy for accessing them
- Review and update, if needed, case-management algorithms for malaria and other causes of febrile illness

Policy and regulatory issues

- Develop appropriate regulatory documents if required
- Register RDT products

Procurement of RDTs

- Develop product specifications and packaging requirements
- Develop product short-list
- Conduct quantification (estimation of needs)
- Procure RDTs
- Procure sharps boxes, gloves etc.

Logistics

- Develop distribution plan
- Train logistics and storage personnel in handling and distribution of RDTs
- Implement a system for data collection and information flows
- Arrange for appropriate transport and storage
- Review and strengthen inventory management, as needed
- Develop a plan for discontinuation and disposal of other diagnostic supplies, if appropriate

Quality assurance

- Develop mechanisms for assessing samples at a national level (lot-testing), and regular (and random) testing at the

- level of use (e.g. microscopy-sentinel sites)
- Implement post-marketing surveillance

Training and communication

- Develop appropriate training and supervision materials
- Train health workers in case management and managing commodities
- Train in RDT use
- Develop and implement a program for community education/ sensitization

Monitoring and evaluation

- Implement effective supervision and monitoring

3. COMMUNITY CASE MANAGEMENT OF MALARIA

3.1. Policy

Malaria imposes its greatest burden in remote rural areas of endemic countries where health services are weakest, thereby denying most people access to diagnostic testing and treatment. WHO therefore recommends that diagnostic testing and effective treatment should be made available at all levels of service delivery up to the community. Once ACTs are adopted by a country as first line treatment, mechanisms to facilitate their access such as making them available at the community level should rapidly be put in place.

WHO recommendation on community case management of malaria (formerly home management of malaria):

The community case management of malaria (CCMm) strategy is based on: diagnosis of fever (WHO strongly recommend the use of RDTs at the community level as part of the CCMm, provided appropriate training and adequate quality assurance measures for RDTs are in place) in children under 5 years of age; medication with the national first-line medicine (ACTs) for uncomplicated malaria; and rectal artesunate as pre-referral treatment for severe malaria.

In areas with a high malaria burden, health service coverage should be extended to areas beyond the easy reach of health facilities by ensuring availability of the following:

- 1) Quality-assured RDTs to confirm/rule out malaria infection in children presenting with fever/history of fever
- 2) First-line oral antimalarials for uncomplicated malaria cases
- 3) Pre-referral treatments (rectal artemisinins) for all children unable to swallow oral medicines and/or other signs of severe disease

These should be provided at the community level along with the following interventions:

- a) identifying and training community treatment providers;
 - b) supplying medicines and diagnostics, to the community workers; and
 - c) implementing a supportive communication strategies (IEC, BCC and advocacy);
- under a rigorous system of supervision of all activities by the health facility level.

2) The provision of malaria diagnostic testing and treatment in the private sector to improve access to quality diagnostics and medicines should be facilitated by training of medicines-sellers and regulated for consistency of health care.

To adequately facilitate access to ACTs at the community level, countries need to recognize CCMm as a service delivery point and incorporate its activities in the overall malaria and child health strategic and implementation plans. At country level therefore, the resources to ensure the following should be in place to facilitate delivery of ACTs, pre-referral rectal artesunate and RDTs at community level:

- Supportive policies allowing the use of these drugs and RDTs at community level;
- A system for procurement, delivery and distribution of drugs and RDTs at all levels to include delivery at the community level
- System for information dissemination through implementation of IEC and BCC activities in communities;
- Identified key community service providers (including private providers);
- Training of all the service providers at community level using training manuals on malaria treatment and necessary job tools.
- Adequate information systems to support implementation, including pharmacovigilance and surveillance systems.

3.2. Implementation requirements

In countries that are already implementing CCMm, the same community delivery structures should be used for the distribution of ACTs by merely sensitizing the community based providers about the new treatment policy. However, a number of countries do not have any experience of community based malaria case management. In these countries, implementation should be undertaken in a phased manner to allow the country to build up experiences and document best practices. Opportunities to learn best practices from neighbouring countries with more experience on CCMm should also be considered.

In order to scale up CCMm, the following key areas outline the implementation steps and should have clear specific budget lines:

- Sensitization of all stakeholders at national, sub-national, district and community levels.
- Development of training materials for the community based providers
- Development of behaviour change communication strategies and materials to improve community participation and mobilization.
- Training of the selected community based providers on malaria case management, diagnostics and medicine handling, and reporting
- Procurement and distribution of the age-based pre-packed treatment dose courses of ACT
- Procurement and distribution of quality-assured RDTs
- Mechanisms for motivation and retention of community based providers
- Record keeping and reporting tools
- Linking communities to health facilities
- Improvement in the quality of care at health facilities for referred cases
- Monitoring and supervision system for community – based interventions and activities for quality assurance

WHO encourages that CCMm be delivered as part of integrated CCM (iCCM), which includes the treatment of pneumonia and diarrheal diseases. While the Global Fund does not currently allow for funding of antibiotics or ORS, the training of Community Health Care workers on iCCM may be conducted under Global Fund Grants.

3.3 Working through the private sector

As much as possible, countries should explore the use of the private sector in the provision of ACTs by using the existing commonly used providers in a public-private- mix. Drug shop owners

could be sensitized to solicit their co-operation in selling the recommended ACT medicines. While recognizing the greater difficulty of incorporating the use of RDTs in the private compared to the public sector, the use of RDTs in order to provide ACTs only to malaria-confirmed cases should nonetheless be strongly encouraged.

Countries should thus develop and explore some innovative models for organizing and engaging the private sector to expand access to subsidized ACTs and RDTs.

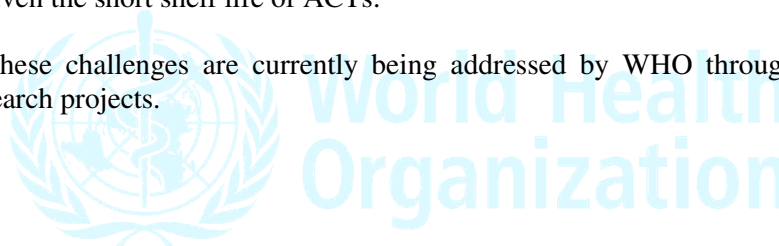
The public sector should provide overall stewardship to private providers including training on drug handling, dispensing, use of RDTs, advice giving and referral of severe cases. In addition, the public sector should then closely monitor private providers to ensure they maintain high standards of performance and record-keeping.

Challenges related to deployment of ACTs and RDTs at community level

While experience implementing ACT-based treatment policies in the public health facilities is rapidly increasing, many countries are in the initial stages of using ACTs and RDTs at the community level. Some of the key challenges include:

- Limited experience of ACTs and RDTs use at the community level
- Current high cost of these medicines and diagnostics
- Challenges in procurement and supply of case management commodities
- Limited penetration into the private sector
- High cost associated with setting up the community based structures and with capacity building at community level
- Lack of robust medicine and diagnostics supply and management systems in countries, especially given the short shelf life of ACTs.

A number of these challenges are currently being addressed by WHO through commissioned operational research projects.



4. MALARIA IN PREGNANCY

National malaria programmes in endemic countries urgently need to ensure that key interventions for malaria control are scaled up towards universal access targets, while at the same time ensuring equity and coverage of the most at risk and vulnerable populations. While WHO guidelines are clear on the need to address women and children as having the greatest burden of malaria, there has been less investment in the linkages between Malaria Programmes and Maternal and Child Health (SRH/MCH) service delivery.

To optimize the use of these resources and accelerate progress towards the MDGs, there is need for increased investment in integrated health system delivery. SRH/MCH service delivery points provide an opportunity not only to scale up disease specific interventions but also improving the health systems that will impact on maternal and child survival.

Pregnant women are also among the most vulnerable and are at high risk for malaria. Around 50 million pregnant women are exposed to malaria each year and up to 10 000 mothers and 200 000 infants die due to malaria infection during pregnancy. Malaria in pregnancy also contributes to high morbidity; 2–15% maternal anaemia 6–14% of low birth weight infants; 8–36% of preterm births; 13–70% of intrauterine growth retardation; 3–8% of infant death and 2–15% of maternal anaemia. In particular, women in their first and second pregnancies are at increased risk. Non-immune pregnant women also risk acute and severe clinical disease. HIV-infected pregnant women are at increased risk.

4.1. Key policy issues

WHO recommends that all endemic countries provide a package of interventions for prevention and management of malaria in pregnancy, consisting of (1) diagnostic testing and treatment for all episodes of clinical disease and anaemia and (2) provision of vector control either through the use of LLINs or protection provided through coverage by an IRS programme. The above strategies should be complemented by (3) intermittent preventive treatment with sulfadoxine–pyrimethamine (SP/IPTp) in countries in sub-Saharan Africa with stable malaria transmission.

Case management: Parasitological diagnosis of suspected clinical malaria cases in pregnancy can be made with microscopy or RDT. Uncomplicated falciparum malaria in pregnancy should be treated according to WHO recommendations. Severe malaria in pregnancy should be treated with full doses of parenteral treatment without delay and follow-up treatment as stipulated in the guidelines.

Personal protection: Insecticide-treated nets (LLINs) are safe for use as personal protection method during pregnancy. Women should start using them as early in pregnancy as possible, and continue to use them throughout pregnancy and in the postpartum period for both mother and child.

Intermittent preventive treatment: All pregnant women at risk of *P. falciparum* infection in countries in sub-Saharan Africa with stable malaria transmission receive at least 2 doses of SP as IPT (3 doses in pregnant women living with HIV/AIDS), given at the first and second scheduled ANC visit (at least one month apart) after "quickening" (the first noted movement of the fetus). IPT-SP should be taken under direct observation (DOT) during the ANC visit.

4.2. Implementation issues

Antenatal clinics provides an excellent entry point for reaching pregnant women with interventions for malaria control. Communication campaigns to increase the use of ANC services (especially early in pregnancy) for malaria control and other interventions for improving pregnancy outcomes are strongly recommended.

Strengthening ANC services for the delivery of effective interventions requires infrastructure development, human resource strengthening and capacity building for reproductive health staff. It also requires commodities and supplies for malaria control and quality service delivery, including well equipped laboratories with diagnostics for basic maternal health tests and procedures such as haemoglobinometers and RDTs. Furthermore, strong partnerships between communities and facilities should be fostered to promote improved access to all reproductive health services and therefore improve maternal health outcomes.

In addition, effective and safe treatment for malaria and anaemia in pregnancy (suitable antimalarials, training on case management) should be made available close to home through peripheral health services.

Routine distribution of LLIN to pregnant women should occur through ANC, supplemented by campaign approaches. The nets should be handed out during the very first ANC visit, combined with clear instructions on their use. This requires budgeting for the delivery, storage and distribution of nets within ANC facilities as well as provision and administrative structures for accountability.

4.3 Exploiting linkages to improve the delivery malaria specific interventions and the health outcomes of all women and children

Integrated delivery of health care entails incorporating malaria diagnostic testing, treatment and referral into the general health services. Where malaria is primarily a childhood illness such as it is in Africa, clinical management of malaria forms an essential part of the Integrated Management of

Childhood Illness (IMCI). Recently, IMCI algorithms were updated to include the use of malaria RDTs.

ANC services already reach more than 90% of pregnant women; therefore strengthening ANC service delivery through increased coverage of interventions like LLINs and IPTp could be an incentive for the use of other services such as delivery with the assistance of a skill birth attendant. Using malaria in pregnancy as an entry point to comprehensive maternal and child health services, will not only reduce the burden of malaria during pregnancy but will also improve MCH outcomes.

4.4. Issues to be considered in the development of Global Fund proposals

Global Fund Malaria proposals often focus only on IPT for addressing malaria in pregnancy, and the allocated budget is often mainly for drugs (SP). Often, no provision is made for the delivery of this intervention through ANC and no provision is made for the delivery of the other effective interventions i.e. training and commodities for case management and the delivery of ITNs through antenatal care, quality improvement and supervision as well as community engagement..

To impact on the burden of malaria during pregnancy, a comprehensive approach is needed, and the full range of logistics to ensure the delivery of these interventions within ANC services is required and must be adequately budgeted for in Global Fund malaria proposals. Support for capacity building of personnel for improving quality of care, with resources, staff training and supervision should be part of the Global Fund proposal. Specific items to be included in the proposal and budget, include:

- Drugs for IPT (sulphadoxine- pyrimethamine): Enough doses to cover the whole pregnant population which is about five percent (5%) of the total population times two or three doses of SP (three tablets per dose) per pregnant woman depending on national policy.
- Antimalarial medicines for treatment of malaria illness in pregnant women according to national guidelines. An accurate estimation should be made based on the national epidemiology and burden of disease.
- Supplies for diagnosis and treatment of anaemia in all pregnant women, including routine iron and folic acid supplementation.
- Supply, management, storage and distribution of LLIN through ANC including training of reproductive health care workers and provision of relevant counselling and communication materials and skills.
- Logistics for distribution of medicines and commodities to facilities and specifically to ANC clinics throughout the country so that they are not kept in ware houses at central level or in stores at facility level to which ANC staff have no access.
- Education and behaviour change communication materials and campaign activities targeting communities and providers to improve the use of ANC services for malaria and other interventions for improving pregnancy outcomes
- Strengthening the capacity of reproductive health workers and supervisors to deliver and support MIP interventions effectively. Such capacity building should not be isolated or vertical but must be included in comprehensive capacity building plans for reproductive health departments, budgeted for and organized jointly with national malaria control programs.
- Strengthening existing health information systems for monitoring and evaluation purposes and modifying ANC registers and cards to include indicators for malaria in pregnancy.
- Operational research to ensure effective programming for MIP and continued monitoring of the efficacy of SP in the light of increasing resistance in countries, as well as pharmacovigilance to monitor the safety of the medicines used for treatment of malaria in pregnancy.

5. INTERMITTENT PREVENTIVE TREATMENT IN INFANCY (IPTi)

Intermittent preventive treatment in infancy (IPTi) is defined as the administration of a full course of an effective antimalarial treatment at specified time points to infants at risk of malaria, regardless of whether or not they are parasitaemic, with the objective of reducing the infant malaria burden.

WHO has now recommended a new intervention against *Plasmodium falciparum* malaria: Intermittent Preventive Treatment for infants (IPTi):

The co-administration of sulphadoxine-pyrimethamine as IPTi with DTP2, DTP3 and measles immunization to infants, through routine EPI in countries in Sub-Saharan Africa, in areas

- with moderate-to-high malaria transmission (annual entomological inoculation rates ≥ 10), and
- where parasite resistance to SP is not high – defined as a prevalence of the Pf dhps 540 mutation of $\leq 50\%$.

5.1 Considerations and caveats for implementation

- In situations where a National-scale implementation may not be feasible due to varying levels of the Pf dhps 540 mutation, IPTi may be implemented at a Provincial or District scale, targeting areas with Pf dhps 540 mutation prevalence $\leq 50\%$.
- Programmes implementing the SP-IPTi strategy should regularly monitor and evaluate the impact on immunization services and performance.
- Pharmacovigilance systems to monitor potentially serious adverse reactions to SP should be strengthened.
- Surveillance of parasite resistance to SP should accompany the implementation of SP-IPTi as a surrogate measure of its efficacy

5.2 Contra-indications

SP-IPTi should not be given to infants receiving a sulfa-based medication for treatment or prophylaxis, including co-trimoxazole (trimethoprim-sulfamethoxazole) which is widely used as prophylaxis against opportunistic infections in HIV-infected infants.

5.3 Issues to be considered in the development of Global Fund proposals

Similar to the issues discussed above with respect to implementation of IPTp, Global Fund Malaria proposals should not focus only on allocation of funds mainly for drugs (SP), which is a fairly inexpensive commodity. Provision should be made for the delivery of this intervention through EPI programme. Support for capacity building of personnel for improving quality of care, with resources, staff training and supervision should be part of the Global Fund proposal. Specific items to be included in the proposal and budget, include:

- Medicines for IPT (sulphadoxine pyrimethamine)
- Logistics for distribution of medicines to facilities and specifically to EPI clinics throughout the country.
- Education and communication materials and campaign activities to improve the use of EPI services and acceptance of IPTi
- Strengthening the capacity of health workers to deliver IPTi through appropriate training and supervision.

- Strengthening existing health information systems for monitoring and evaluation purposes and modifying EPI and other health registers and cards to include indicators for malaria in infancy.
- Operational research to ensure continued monitoring of the efficacy of SP in the light of increasing resistance in countries, as well as pharmacovigilance to monitor the safety of SP use in IPTi.

6. MONITORING ANTIMALARIAL DRUG EFFICACY

Antimalarial drug resistance is a major public health problem, which hinders the control of malaria. A summary of worldwide data on antimalarial drug efficacy and drug resistance is available in the Global Report on Antimalarial Drug Efficacy and Drug Resistance 2000-2010 (WHO, 2010). *P. falciparum* resistance to artemisinins was reported on the Cambodia-Thailand border in 2008. Because of this threat, WHO, together with Roll Back Malaria partners, developed the *Global Plan for Artemisinin Resistance Containment* (WHO 2011). In that document, the need to monitor antimalarial drug efficacy is one of the 4 pillars of the response to this public health threat.

6.1 Guidelines for surveillance

In 1996, WHO developed a protocol for assessing antimalarial drug resistance for high transmission areas. This protocol was updated in 2009 including methodology for high transmission areas and for low to moderate transmission areas as well as for monitoring efficacy of antimalarial medicines against vivax malaria.

These protocols are designed to provide essential information for monitoring the therapeutic efficacy of a range of antimalarial drugs against uncomplicated *falciparum* malaria and to ensure a sufficient evidence base from which Ministries of Health can develop informed treatment policies and guidelines. The use of a standardized protocol allows for the comparison of the results in country and among countries in the same region.

6.2 Organization and survey outline

6.2.1 Implementation and management of the surveillance programme

National Coordination team

At the initial stage, a national core group of experts (national malaria control programme, ministry of health, universities, institutes of research, national reference laboratory) should be established to coordinate all activities. The coordinating team requires strong official backing by the authority in charge of health services. The coordination team is responsible for the preparation of the survey, development and implementation of the protocol, supervision and quality assurance during the survey and the final collection, analysis and reporting of results to the National Authorities responsible for drug policy.

6.2.2 Epidemiology

Sentinel site surveillance system

Malaria control programmes should establish sentinel site surveillance to monitor antimalarial drug efficacy. A system of a limited number of well-selected sentinel sites will enable the collection of consistent longitudinal data and documentation of trends. The minimal requirements for establishing a sentinel site are the availability of trained and motivated clinical personnel and microscopist, with a laboratory for blood film examination. This can be at the periphery (community-based), or based at a health facility at district level. Patients attending hospitals in

urban settings may have more complex clinical presentations, are more likely to have been referred because of previous drug failures and may be more difficult to follow up. Thus, whenever possible, monitoring should be done at the periphery.

Although no definitive scientific advice can be given regarding the number of sites needed, experience suggests that **between four and eight sites** achieve a balance between representativeness and practicality. Programmes should increase or decrease this number as needed to account for geographic size, population distribution and density, differing malaria epidemiology or ecology and other factors deemed important to the programme. When making such decisions, emphasis must be placed on the need for a “manageable” number of sites to ensure proper monitoring and supervision.

Again, based on experience rather than definitive science, it is recommended that assessments of **the efficacy of first and second line drug be conducted at least once every 24 months in all the sites**. For comparability, assessments should be conducted during the same time of year. Most programmes conducting sentinel site surveillance of therapeutic efficacy find it easiest to alternate test sites (e.g. four sites tested per year with each site being assessed every other year).

The following characteristics should be considered in the selection of sentinel sites:

- population density;
 - accessibility to and feasibility of supervision;
 - epidemiology of malaria, especially intensity and seasonality of transmission;
 - population mobility and migration (especially in border areas);
 - distribution of malaria treatment failures reported by health information system.
- The sentinel sites should be selected to be representative of each major epidemiological strata into which the country can be divided.

Sample size and sampling strategies

The use of classical statistical methods are recommended for determining sample size, based on an expected proportion of treatment failures, desired confidence level (95%) and precision (5% or 10%). In the case of an expected failure rate lower than 15% and in order to be representative, a minimum of 50 patients should be included.

6.2.3 Protocols for surveillance of therapeutic efficacy of antimalarial drugs

Inclusion criteria

- Age: between 6 and 59 months, i.e. less than 5 years in areas of intense transmission and all patient over 6 months in for low transmission area;
- Absence of severe malnutrition;
- Parasitaemia: limits of parasite count for inclusion are 2 000–200 000/μl in areas of intense transmission, and 1 000–100 000/μl for low-moderate transmission area;
- Absence of general danger signs or signs of severe and complicated falciparum malaria according to definition given by WHO [Severe falciparum malaria. Transactions of the Royal Society of Tropical Medicine and Hygiene, 2000, 94; supplement 1];
- Presence of auxiliary temperature $\geq 37.5^{\circ}\text{C}$, or history of fever for low to moderate transmission areas;
- Absence of febrile conditions caused by diseases other than malaria;
- Ability to comply with the stipulated follow-up visits, and easy access to health facility
- Informed consent of parent or guardian;
-

The recommended length of follow-up for assessments is 28 days but can be longer according to the half life of the drug for both intense and low-moderate transmission area. **Studies must be accompanied by molecular assessment (e.g. PCR) to assist in distinguishing recrudescence from re-infection.** The minimum duration of follow-up for chloroquine, amodiaquine, sulfadoxine-pyrimethamine, mefloquine and lumefantrine should be 28, 28, 28, 42 and 28 days, respectively.

Drugs to be tested

Each national malaria control programme should monitor the first- and second-line drugs according to their national treatment guidelines. In addition, combination therapies should be monitored in order to obtain background information of new treatments.

Data analysis

Survival analysis is the preferred method for analyzing data derived from these assessments of therapeutic efficacy. This method allows for inclusion of data from patients who are withdrawn or lost to follow-up without requiring that assumptions be made about ultimately unknown outcomes.

Computer-based applications have been developed by WHO to provide assistance in all aspects of data management and analysis.

Data interpretation and policy considerations

After validation of the data, the national coordination team should forward recommendations to the drug policy-makers for action. It is likely that results will differ between sites; some sites may identify a substantial deterioration in treatment efficacy while others continue to record an acceptable response to the same drug. The programme should consider how to respond to this eventuality: can specific treatment guidelines be targeted to affected areas without changing national policy or guidelines? How many sites need to show unacceptable treatment failures before national policy or treatment guidelines are altered?

Budgeting for antimalarial efficacy monitoring

In order to ensure that the country has sufficient resources for adequate programme monitoring of the antimalarial treatment policy, the following are key areas that should be budgeted for:

- Equipment (microscopy, centrifuge)
- Supplies and medicines
- Per diem and staff
- Travel and transportation
- Patient costs
- Genotyping- subcontract laboratory
- Training and data validation

In most cases the total budget will vary according to the number of sites and local costs, but a total of \$US 50 000 to 75 000 per year is reasonable. In addition, provision should be made for the necessary training, data validation, and data analysis which is usually done by a consultant and lasts 2 to 3 weeks, and for PCR to distinguish between recrudescence and reinfection. It is recommended that funds for these monitoring activities be included in the proposal. For proposals where this is not the case, there should be a clear explanation as to the source of funds for these activities.

7. MALARIA VECTOR CONTROL INCLUDING INSECTICIDE RESISTANCE

WHO recommends Universal Coverage of the population at risk of malaria with effective vector control. In most cases, this means full coverage LLINs and/or IRS. In selected countries, other interventions may have a role in specific situations or settings.

- **LLINs** should whenever possible be provided in sufficient numbers to cover everyone exposed to transmission in target communities (see note on quantification below). Normally, a combination of campaign (catch-up) and routine (keep-up) systems of distribution will be needed to sustain this coverage. When supplies are constrained, however, LLINs can still be used to provide personal protection to risk groups, especially young children and pregnant women in high transmission areas. LLINs may be distributed through specialized delivery channels or through integrated strategies, e.g. with ante-natal care and with vaccination. WHOPES-approved LLINs should be used. The insecticide on an LLIN should last for 3 years, but recent data shows that the physical lifespan of an LLIN is extremely variable (see section on LLIN durability); hence the need for continuous distribution.
- **IRS**, when implemented properly, is a highly effective intervention providing protection to communities through a rapid mass effect on vector populations, reducing densities and longevity of vectors and their “vectorial capacity” to transmit malaria parasites. The effectiveness of IRS is highly dependent on the quality of the spraying operation: at least 80% of premises in target communities must be properly sprayed. IRS is *effective for months*: usually 3 to 6 months, but occasionally up to 9 months, depending on the insecticide-used, the type of surface sprayed, and the seasonality of transmission.

7.1. Conditions for implementation of LLINs

- In most contexts, LLINs tend to be less logistically demanding than other forms of malaria vector control. However, as mosquito nets being bulky, special attention must be given to storage and transport to peripheral target communities. When planning LLIN campaigns, due attention should be given to the time required for procurement, storage and transport so that LLINs can be made available when and where needed in sufficient numbers.
- Implementation of LLINs relies on availability of effective procurement and distribution systems through public and/or the private sectors.
- LLINs should be free or highly subsidized and available in the immediate proximity of target communities, without any gap in the supply chain.
- Implementation of LLINs relies mainly on sociological and demographic information.

7.2. Conditions for implementation of IRS

- IRS implementation relies on availability of operational national vector control services with adequate human, financial and logistical resources (including skilled spray teams, storage and transport facilities, spraying equipment, etc.). As several years of consecutive rounds of IRS are usually required to achieve and sustain the full potential of this intervention, adoption of IRS requires medium to long-term political and financial commitment by national programmes, local authorities, and funding partners.
- IRS should not be planned unless full capacity for implementation, monitoring and evaluation is in place at national, provincial and district levels.
- IRS planning must be based on accurate entomological and epidemiological information: identification and bio-ecology of vectors with special reference to their feeding and resting behaviour, dynamics of transmission (rhythm and intensity), incidence and prevalence of malaria (morbidity and overall mortality).

- Data on insecticide resistance must be collected in the target area, before and after the spraying operation. In any vector control operation using insecticides, the responsibility for ensuring the adequacy and quality of this data remains with the main implementation agency responsible for the intervention.
- Insecticide choice for IRS should follow the national policy on insecticide resistance management (see section 7.4 for WHO recommendations on resistance management).
- The procurement decision must take into account all relevant data on insecticide resistance, within and near to the target area. The decision should be consistent with and checked against national resistance management policies. The process of assembling the data and choosing an insecticide must be done early in the planning process, since that procurement delays are a common operational problem in many vector control programmes.
- The number, nature and location of premises to be sprayed as well as access must be determined through geographical reconnaissance prior to decision-making and planning.

7.3. Target areas for malaria vector control

Both IRS and LLINs can be used in a range of epidemiological settings (from low to high endemicity). The choice between them should be guided by the objectives of the malaria control programme. These two tools form the mainstay of modern vector control. Not only is their deployment associated with decreased malaria burden (cases and deaths), but when deployed correctly on a large scale, both have an impact on decreasing the vector population and therefore malaria transmission intensity.

7.3.1 LLINs are indicated as a long-term intervention in most situations, especially the following:

Epidemiological factors

- In a wide range of transmission conditions where long-term protection is needed;
- In areas with a relatively long season of malaria transmission, or perennial transmission, such that more than one IRS cycle would be required;
- In areas where IRS cannot be used and only personal protection can be achieved (e.g. forest malaria or among nomadic populations).

Socioeconomic factors

- In places where IRS may face problems of acceptability for one reason or another.

Access and programmatic factors

- In areas where routine ITN distribution can easily be integrated into existing health systems such as routine EPI or ANC;
- In areas where the specialised skills and programme infrastructure needed for IRS have not (yet) been developed, an LLIN distribution campaign can rapidly achieve high levels of coverage;
- To protect hard-to-reach populations, where repeated IRS spray-cycles are not feasible (a one-time distribution of LLINs can provide relatively long-term protection, compared to the shorter-duration of protection given by one IRS spray cycle);
- In some urban settings where the number buildings needing to be sprayed is excessive and nuisance from urban mosquitoes is high.

In every country, there is a different range of local situations and eco-epidemiological settings. Therefore, there it will often be justifiable to use IRS in some settings and LLINs in others.

7.3.2 IRS is best indicated as a means of rapidly reducing malaria transmission in the following conditions:

Epidemiological factors

- To contain malaria outbreak or emerging drug resistance;

- To control malaria in complex emergencies (e.g. displaced populations and refugee settings, climatic events, etc.) where the facilities for IRS are available;
- To prevent transmission in epidemic prone areas and in areas with low seasonal transmission (e.g. highlands, fringes). Both IRS and LLINs can be used in epidemic prone areas as preventive measures, but IRS is normally the first line intervention for interrupting an epidemic;
- To cut-off well identified peaks of seasonal transmission;
- To interrupt transmission in residual foci at the end of the elimination programme phase;
- In areas of very intense transmission, in order to bring about a rapid and substantial reduction in the burden of malaria;
- In areas where LLINs would not be effective enough due to pyrethroid resistance.

Socio-economic factors

- In areas of special economic interest where a high protection level is required (e.g. mining, agricultural schemes, dams, tourist resort areas, etc).

Access and programmatic factors

- Access to target communities should be possible, including during the transmission (i.e. rainy) season;
- A pre-requisite for IRS is the programmatic capacity -planning. Logistics and supervision - to ensure an operation of adequate quality.

IRS is contra-indicated when conditions for effective implementation are not met or where there are no structures to spray (e.g. nomadic populations, forest malaria) or where the local vectors are strongly exophagic and exophilic (i.e. tend to bite and rest outdoors, respectively).

7.3.3 When should IRS and LLINs be combined?

IRS and LLINs may be deployed in combination for epidemiological reasons (e.g. to hasten reduction of transmission), and/or as a means of resistance management. The evidence that the combination can be effective for either of these purposes is encouraging but not yet complete. Therefore, the deployment of IRS and LLINs in combination should always be carefully evaluated through operational or implementation research.

Insecticide resistance is the first and most important factor to be considered:

Do not use IRS with pyrethroids in an area with high LLIN coverage, because this is likely to produce excessive selection for pyrethroid resistance; conversely

Do select insecticides other than pyrethroids for IRS if it is to be deployed together with LLINs; this is recommended because it is thought to be one of the more promising of the available resistance management methods.

Because of the urgency of the threat of insecticide resistance, these recommendations should be regarded as applicable to all large-scale spraying programmes.

Another reason to consider the combination of LLINs plus IRS is to increase epidemiological impact, as part of an overall malaria control strategy. The published evidence indicating that the combination does result in a greater impact is limited but encouraging: it suggests that there can be added protective benefit from such a combination, with the two interventions acting independently and additively. On the other hand, there are still large gaps in the evidence, and in particular the cost-effectiveness of the additional benefit has not yet been measured. Thus:

The available evidence does justify pilot implementation, which may be on the large-scale if this is necessary for proper evaluation.

Conversely, in order to fill the gaps in the evidence, any such pilot operation should be accompanied by careful operational or implementation research. This research should assess not only the epidemiological benefits, but also costs, with particular attention to the effects on insecticide resistance.

The combination of IRS and LLINs is primarily a tool for maximising the intensity of vector control. It may be employed as a special transitional and/or local measure, as part of a longer-term plan. For example, the intention may be to use the combination to bring about an immediate and large reduction in the intensity of transmission (e.g. from high to low, from moderate to near-zero), and subsequently to sustain this suppression using LLINs alone as the main long-term measure.

The combination of IRS and LLINs also has implications for coverage:

The benefits are likely to be greater when the combination extends coverage, that is, when one intervention reaches people not covered by the other.

The use of a combination should never be considered as a remedy for poor implementation of a programme normally based on one of the two interventions.

According to the principle of universal coverage, it will normally be appropriate to ensure that the entire risk population is adequately protected with one or other of the two interventions (i.e. to ensure that coverage gaps are filled) before the benefit of both interventions is given to a subset of the risk population.

7.4. Resistance management

All malaria vector control programmes must have an insecticide resistance management strategy. Resistance management activities and policies must be introduced from the outset, and cannot be delayed until resistance has appeared.

- For IRS, the minimum resistance management policy is to alternate between insecticide classes in rotation system; this means rotating between insecticides with different modes of action (changing from one pyrethroid to another is not considered a rotation).
- A pyrethroid may be used as one element of the rotation, except where there is high LLIN coverage.
- As already noted, pyrethroids should not be used for IRS in areas with high LLIN coverage; conversely, the combination of LLINs with non-pyrethroid-IRS is a recommended resistance management strategy.
- In the process of approving insecticide procurement requests, funding agencies should check that recent and relevant data on insecticide resistance in and near the target area was available and taken into account in the decision to choose a particular insecticide.
- Resistance monitoring must be conducted at least once a year from several locations that are targeted with vector control activities. Wherever possible, resistance should be tracked not only with conventional bioassays but also molecular genotyping methods. It is recommended that funds for these activities be included in the proposal. For proposals where this is not the case, there should be a clear explanation as to the source of funds for these monitoring activities.
- WHO recommendations on resistance testing methods, and on the collation and interpretation of such data, are currently being updated, and are available on request from the WHO Global Malaria Programme. Round 11 proposals that include an element of IRS should make provision for flexibility in insecticide choice.
- The impact of resistance on the effectiveness of vector control is also a key question: where possible, monitoring schemes should attempt to assess whether vector control operations tend to have less impact in areas with relatively high levels of resistance.

See <http://www.who.int/malaria/publications/atoz/9789241501095/en/index.html> for further recommendations.

7.5. Net usage

- Continuous net usage is essential for the success of LLIN interventions: nets are effective when people use and maintain them properly. Regular information and advocacy

campaigns are therefore needed to ensure effective use of LLINs. Some LLIN distribution campaigns have successfully used follow-up field operations to support "hang-up" and promote use of nets after a campaign. There is some evidence to suggest that the promotion of net repair activities (sewing in order to close holes) may also be useful.

- WHO is preparing interim recommendations on the end-of-life management of LLINs, including opportunities for recycling and requirements for safe disposal. So far, no clear justification has been established for systematic collection of old nets. In practice, users often convert the fabric from old nets to other purposes that may be beneficial. Research is underway to establish whether this kind of re-use might be hazardous, but so far no clear reason to discourage such re-uses has emerged.

7.6. Timing and sustaining coverage

7.6.1 Timing in IRS operations is essential.

Because of the generally short duration of efficacy of most insecticides when sprayed on walls, IRS campaigns must be completed just before the onset of the transmission season. In addition, insecticide efficacy must be maintained throughout the whole transmission season. Depending on the duration of this season, insecticide used and surfaces sprayed, one or two spray cycles per year may be required. Large-scale implementation requiring more than 2 spray cycles per year, (e.g. in perennial transmission areas) is very difficult to achieve in most situations, because of factors such as logistics, cost and social acceptability.

Generally, IRS should not be implemented continuously for very long periods of time (feasibility, cost, insecticide resistance, community fatigue). It is very effective at reducing malaria parasite prevalence and incidence, but once these goals have been achieved, IRS can be supplemented and progressively replaced by other interventions (including LLINs) in the context of integrated vector management. In epidemic prone areas, IRS should be considered an intermittent intervention, and spray cycles should be planned on the basis of accurate entomological, epidemiological and climate surveillance systems involving specialized vector control services.

7.6.2 "Keep-up" strategies are needed to avoid gaps in LLIN coverage

WHO has long recommended both "catch-up" and "keep-up" systems to sustain high levels of coverage. In practice, however, some countries have tended to rely mainly or solely on the implementation of repeated campaigns, as a means of sustaining coverage. The problem with this approach is that net lifespan is variable: the loss of nets through wear and tear does not happen all at once after three years; rather it is a gradual process that starts soon after distribution and continues for years. Indeed, some countries have observed serious gaps in coverage less than three years after the last campaign.

In order to correct this tendency to implement catch-up campaigns but not continuous "keep-up" distribution through routine ante-natal care (ANC) and immunization (EPI) systems, WHO has adjusted its guidance on this issue: the recommendation now is that LLIN distribution through these "routine" channels should be given as much priority, in national plans, as campaigns. Delivery through ante-natal care (ANC) as well as through immunization (EPI) channels is especially valuable because (a) it gives a continuous flow of nets into the population, partially balancing the continuous loss of nets through wear and tear, and (b) it ensures sustained protection for the most vulnerable groups, even if there are gaps in the coverage of the population as a whole. More generally, experience suggests that countries with a combination of distribution systems, including campaigns, routine provision through EPI and/or ANC channels, and with supplementary availability through private sector channels, may be more successful in sustaining high coverage.

7.7. Budget considerations

The following key factors, at minimum, should be budgeted for in the proposal:

7.7.1 ITNs

- In planning procurement quantities, the aim should be to distribute enough LLINs to achieve a full 100% coverage, with 1 net for 2 people. There must be a clear plan as to how this is to be achieved at household level, and a good way to do this is to give nets to household at the rate of 1 net for every 2 household members, rounding up in households with odd numbers of members. The procurement ratio must be adjusted to allow for this rounding up, and this implies a procurement ratio of 550 LLINs for 1000 population, or 1 net for 1.8 people, in a population with a mean household size of five. Note that these figures have been adjusted in the light of practical experience following previous GF rounds.
- Logistics and funds for the supply, management, storage and distribution of LLINs such that they are not kept in warehouses at central level or are inaccessible to target populations. Adequate and efficient planning of distribution methods (e.g. decisions to distribute through ANC clinics, integrated with immunization campaigns, etc.) are key to ensuring that feasible targets are set and achieved. It is recommended that funds for these activities be included in the proposal. For proposals where this is not the case, there should be a clear explanation as to the source of funds for these activities.
- There may be opportunities to give a greater role to manufacturers and/or procurement agents to deliver LLINs up to final destination, e.g. district level.
- Education, communication materials and campaign activities to improve the use and proper maintenance of LLINs, particularly where a culture of net-use does not exist.
- Funds must be made available for insecticide resistance monitoring and for proper monitoring of effective biological activity and physical durability of LLINs.
- This brief focuses on the distribution and use of LLINs, as the most cost-effective way to provide large-scale treated-net coverage in most situations. However, there are some areas where a large proportion of people habitually use untreated nets bought from local commercial sources, and in this specific situation, re-treatment of these nets using a WHOPES-recommended long-lasting treatment kit, as a supplement to LLIN distribution to those without nets, may represent a cost-effective opportunity. Funds and logistics for such re-treatment should then be considered a justifiable option, as long as there is close attention to monitoring and evaluation of this approach.

7.7.2 IRS

- Budgets for IRS programmes must include the following elements:
- Purchase of sufficient amounts of an effective insecticide, as well as adjunct commodities (e.g. spray pumps, protective equipment for sprayers, etc.) while avoiding unnecessary stocks that might become obsolete.
- Recruitment, training and salaries for sufficient number of sprayers to cover target areas prior to the transmission season.
- Logistics and funds for the supply, management, storage and distribution of the insecticide so that it is not kept in warehouses at central level. Transport costs for both the insecticide and sprayers must be incorporated in the proposal.
- Education and communication materials and campaign activities to sensitize communities to the importance of IRS, particularly where activities are employed for the first time or are being widely scaled-up.
- Funds must be made available for insecticide resistance monitoring and for proper monitoring of the insecticide residual duration on sprayed surfaces
- Where IRS is employed for the first time, funds for initial geographical reconnaissance studies to determine target areas and structures as well as entomological studies to ensure selection of an effective insecticide.
- Only limited data is available on the relative cost-effectiveness (CE) of IRS and LLINs,

and this indicates that their relative cost-effectiveness depends on various biological and programmatic contextual factors. In some places, the infrastructure for IRS already exists, and in these places it may be more cost-effective than LLINs. In many other places, it is likely that LLINs will tend to be more cost-effective. On the whole, it may be expected that LLINs will tend to be more cost-effective in locations where there is more than 6 months of transmission per year.

7.8. Monitoring & evaluation

- For both IRS and LLINs, specialized teams are required for entomological evaluation. The entomological skills needed for this work need to be maintained, and must be built or re-built if they are lacking. .
- Routine entomological monitoring must include insecticide resistance testing in multiple locations (see above), and vector abundance and sporozoite prevalence in one or more sentinel sites.
- Programmes should be prepared to carry out immediate investigations in response to reports of any unexpected variations in impact, or any local resurgence in cases that is larger than would normally be expected for that season. The aim of the investigations is to establish whether this increase is likely to be due to an intended gap in coverage, or to insecticide resistance, or to a combination of these factors.
- LLIN coverage (ownership and usage) should be reported through routine records of delivery operations, and should also be estimated through standard household survey methods, such as the Malaria Indicator Survey (MIS). IRS coverage should be reported through the collation of household spray records kept by spray teams and supervisors, and should also be checked or separately estimated through follow-up household surveys.
- A new recommendation is that LLIN durability should be monitored closely; provision should be made in the budget for active longitudinal monitoring at six-monthly intervals of LLINs in a one or two sentinel sites. This monitoring should be regarded as a “good practice” routine for every large scale procurement of LLINs. It should include a variety of LLIN products in order to inform subsequent procurement rounds. Standard methods have just been published (http://whqlibdoc.who.int/publications/2011/9789241501705_eng.pdf).

7.9 Conclusion

- Either IRS or LLINs can be used in most areas, as long as full coverage is achieved and maintained, depending on the objectives of the malaria programme, and on the behaviour and insecticide resistance of the local vectors.
- **In unstable malaria areas**, IRS has the advantage of a strong and rapid impact, and it also provides more opportunities than LLINs for managing insecticide resistance, e.g. through rotational use of unrelated insecticides. Capacity for rapid deployment of IRS in outbreaks and other emergency situations (e.g. climatic events) should be developed and maintained at national level. LLINs offer a more sustained level of suppression, as long as they are used.
- **In stable malaria areas**, the priority should normally be given to LLINs, with the immediate objective of achieving and sustaining full coverage of the whole community. If resource limitations mean that this cannot be done in all endemic areas, then the most vulnerable risk groups (i.e. pregnant women and children under 5 years) should be given priority.
- Insecticide resistance management is now a high priority issue for all malaria control programmes

8. SURVEILLANCE, MONITORING AND EVALUATION for high-burden countries

8.1. Background

In high-burden malaria countries, four main antimalarial interventions are used to reduce malaria burden: 1) long-lasting insecticidal nets (LLIN), 2) appropriate diagnostic testing (e.g., rapid diagnostic tests [RDT] or microscopy) and treatment (e.g., artemisinin-based combination therapy [ACT]), 3) insecticide residual spraying (IRS), and 4) intermittent preventive therapy (IPT) in pregnant women and infants (in Africa). In 2007, WHO recommended universal coverage for LLIN (LLIN use by all persons in all households, regardless of age). WHO also recommends adequate laboratory testing (by RDT or microscopy) of all suspected malaria cases, regardless of age. Surveillance and M&E provides key management data to continually assessment performance and improve program management. Surveillance and M&E indicators should match the interventions mentioned above to measure stock (inputs), coverage, and impact.

8.2. Targets

Below, we list targets from the World Health Assembly and the RBM Partnership. In addition, the UN Secretary-General on World Malaria Day, April 2008, called for universal coverage of locally appropriate interventions for prevention and case management by 2010. This call for universal coverage was reconfirmed in RBM's Global Malaria Action Plan. Previously, the World Health Assembly targets were for >80% coverage. For ITNs, universal coverage implies 100% use and access for persons of all ages.

Morbidity

- >50% reduction by 2010 and >75% reduction by 2015 compared to 2000.

Mortality

- >50% reduction by 2010 and >75% reduction by 2015 compared to 2000.
- Near zero malaria deaths by 2015 (revised RBM target, 2011)

The full version of the revised RBM Objectives, targets, and milestones are listed below:

Objective 1. Reduce global malaria deaths to near zero¹⁵ by 2015

Target 1.1 Achieve universal access to case management in the public sector.

By end-2013, 100% of suspected cases receive a malaria diagnostic test and 100% of confirmed cases receive treatment with appropriate and effective antimalarial drugs. Milestone: None, as the target is set for 2013.

Target 1.2 Achieve universal access to case management, or appropriate referral, in the private sector.

By end-2015, 100% of suspected cases receive a malaria diagnostic test and 100% of confirmed cases receive treatment with appropriate and effective antimalarial drugs. Milestone: By end-2013, in endemic countries, 50% of persons seeking treatment for malaria-like symptoms in the private sector report having received a malaria diagnostic test, and 100% of confirmed cases have received treatment with appropriate and effective antimalarial drugs.

Target 1.3 Achieve universal access to community case management (CCM) of malaria.

By end-2015, in countries where CCM of malaria is an appropriate strategy, 100% of fever (suspected) cases receive a malaria diagnostic test and 100% of confirmed uncomplicated cases receive treatment with appropriate and effective antimalarial drugs, and 100% of suspected and confirmed severe cases receive appropriate referral. Milestone 1: By end-2012, all countries where CCM of malaria is an appropriate strategy have adopted policies to support

¹⁵ In areas where public health facilities are able to provide a parasitological test to all suspected malaria cases, near-zero malaria deaths is defined as no more than one confirmed malaria death per 100 000 at-risk population.

CCM of malaria (including use of diagnostic testing and effective treatment). Milestone 2: By end-2013, in all countries where CCM of malaria is an appropriate strategy, 80% of fever cases receive a malaria diagnostic test and 80% of confirmed cases receive treatment with effective antimalarial drugs.

Objective 2. Reduce global malaria cases by 75% by end-2015 (from 2000 levels)

Target 2.1 Achieve universal access to and utilization of prevention measures.¹⁶

By end-2013, in countries where universal coverage and utilization have not yet been achieved, achieve 100% coverage and utilization for all at-risk populations with locally appropriate interventions. Milestone: None, as the target is set for 2013.

Target 2.2 Sustain universal access to and utilization of prevention measures.⁷

By 2015 and beyond, all countries sustain universal coverage and utilization with an appropriate package of preventive interventions. Milestone: From 2013 through 2015, universal access to and utilization of appropriate preventive interventions are maintained in all countries.

Target 2.3 Accelerate development of surveillance systems.

By 2015, all districts are capable of reporting monthly numbers of suspected malaria cases, number of cases receiving a diagnostic test and number of confirmed malaria cases from all public health facilities, or a consistent sample of them. Milestone: By 2013, 50% of malaria-endemic countries have met the 2015 target.

Objective 3. Eliminate malaria by end-2015 in 10 new countries (since 2008) and in the World Health Organization European Region

Milestone: By end-2013, malaria is eliminated in three new countries.

8.3. Routine information plus survey data

A strong national surveillance and M&E system would utilize both 1) routine information systems to continuously monitor logistics and impact and 2) survey data. Surveys would be used intermittently to supplement routine information-both filling gaps (e.g., measurement of ITN use) and providing population estimates (for example, for coverage, biological indicators, and all-cause child mortality).

8.3.1 Indicators for routine information systems

WHO-recommended indicators for routine information systems were published in September 2008 in the World Malaria Report 2008 and updated in World Malaria Report 2010. Core indicators were designed such that they were simple and limited in number (for example, limited enough to fit within an integrated national health information system [HMIS]), yet provided enough logistic information on all main malaria interventions as well as impact data. Below, in brief, we list the recommended indicators measured by routine information systems:

Impact

- Confirmed malaria cases (microscopy or RDT), per 1000 persons per year
- Inpatient malaria cases per 1000 persons per year
- Inpatient malaria deaths per 1000 persons per year (if number deaths are few, then 100 000 persons per year)
- Outpatient malaria test positivity rate (positivity rate of RDT or microscopy)

¹⁶ Universal access to and utilization of prevention measures is defined as every person at risk sleeping under a good-quality insecticide-treated mosquito net or in a space protected by indoor residual spraying, and every pregnant woman at risk receiving at least one dose of intermittent preventive treatment during pregnancy (IPTp) during each of the second and third trimesters (in settings where IPTp is appropriate).

Quality of surveillance

- Annual blood examination rate (percentage of suspected malaria cases that were tested with RDT or microscopy over total population at risk)

Diagnostic testing and treatment

- Percentage of suspected malaria cases that receive parasitological testing
- Percentage of outpatient malaria cases treated with ACT (number of patients treated with ACT compared to number expected to be treated according to national policy)

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Prevention

- Proportion of population at risk potentially covered by nets distributed
- Percentage of first-visit ANC clients that received an LLIN (number of LLIN distributed to ANC clients divided by number of first ANC visits)
- Percentage of pregnant women attending ANC that received at least two doses of IPT
- Proportion of health facilities without stock-outs of ACT, RDT, and LLIN by month
- Percentage of population at risk protected by IRS
- Percentage of targeted households that were sprayed with at least one round of IRS

Completeness of reporting:

- Completeness of monthly health facility reports

8.3.2 Indicators from population surveys

Population surveys can provide data on the following indicators:

Coverage indicators: Insecticide-treated nets (ITNs) and indoor residual spraying (IRS)

Primary indicators

- Use: ITN use by persons of all ages. "Use" is defined as "slept under an ITN last night" recorded during a household survey. Target: 100%, universal coverage. Most important indicator.
- Access:
 - a) ITNs per person (of all ages) or ITNs per sleeping place. Target: 2.0 persons per ITN or 0.5 ITNs per person; 1.0 ITN per sleeping place.
- The target of 2.0 persons per ITN is a provisional estimate of the ratio which allows use of ITNs by everyone in the community; it is based on limited data and will need to be reconsidered as additional data becomes available. Where there is local data on the ratio needed for full coverage in local conditions, countries may use this to define a country-specific target (see vector control section for further comments on procurement quantification)
- ITNs per sleeping place (bed, mat, etc.) is likely to be a preferable indicator, but adequate data about the number of sleeping places in the household has not been collected in most surveys. Further experience is needed both with the question about the number of sleeping places in a household and this indicator (ITNs per sleeping place).
 - b) Proportion of households with at least one ITN
 - c) Proportion of households with at least one ITN and/or sprayed by IRS in the last 12 months.

Secondary indicators

- Proportion of children under 5 years old and pregnant women who slept under an ITN the previous night
- Prompt and effective treatment and use of diagnostics
- Proportion of children under 5 years old with fever in last 2 weeks who received any antimalarial treatment.
- Proportion of children under 5 years old with fever in last 2 weeks who had a finger prick

or heel prick

- Proportion of children under 5 years old with fever in the last 2 weeks who received antimalarial treatment according to national policy within 24 hours from onset of fever.
- Prevention and control of malaria in pregnant women
- Proportion of pregnant women who slept under an ITN the previous night.
- Proportion of women who received intermittent preventive treatment for malaria during ANC visits during their last pregnancy.

Other indicators from surveys

- Biological indicators (selected surveys)
- Parasite prevalence in children <5 years old
- Percentage of children <5 years old with anemia (<8 grams/dl of haemoglobin)
- All-cause child mortality (selected surveys)

8.4. Routine information systems for malaria-operational aspects

Strong routine systems are needed to ensure that adequate stocks of essential commodities (ACT, RDT, LLIN) are present every day in all health facilities. In addition, continuous monitoring of impact using disease surveillance is needed at health facility, district, and national levels.

WHO recommends that routine data collection and analysis should occur monthly at all levels health facility, district, and national levels. Quarterly information systems are not adequate for monitoring stock-outs of essential commodities or for disease surveillance for a disease (malaria) that can be strongly seasonal with dramatic month-to-month differences and have areas with risk of epidemics.

8.4.1 Core data elements needed to monitor routine core indicators

The following are a minimal set of core data elements needed to monitor routine core indicators.

- Disease surveillance: inpatient: malaria cases, malaria deaths; out-patients: suspected, tested, confirmed.
- Logistics
- ACT: number of patients treated with ACT, no. patients expected to be treated according to national policy (this data element comes from outpatient surveillance data)
- LLIN: number of LLIN distributed at ANC visits, number of ANC first visits
- IPT: number of ANC clients receiving 2nd dose of IPT, number of ANC first visits
- IRS: number of households with at least one round IRS/no. households targeted
- Stock-outs: number of health facilities with stock-out of ACT, RDT, LLIN
- Completeness of reporting
- Number of health facilities that reported, no. expected to report
- Number of districts that reported, no. expected to report

8.4.2 Core analyses from core data elements needed to monitor routine core indicators.

WHO recommends the following seven core graphs or tables that can be updated at all levels and discussed at monthly and quarterly performance assessments and during supervisory visits:

- Graph of malaria test positivity rate, <5 years old and all ages.
- Double-axis graph of in-patient malaria and non-malaria cases and deaths in children <5 years old
- Double-axis graph of out-patient confirmed malaria cases and percentage of suspected malaria cases tested with parasite-based test or annual blood examination rate.
- Double-axis graph with out-patient all-cause cases and suspected malaria cases, all ages

- Logistics graph. Percentage coverage with patients treated with ACT (of expected), ANC clients receiving ITN, and IPT2
- Logistics graph of stock-outs. Percentage of health facilities with stock-outs of ACT, RDT, and LLIN.
- Graph of completeness of reporting. Percentage of health facilities that reported.

8.4.3 Interpretation of core analyses

- Disease surveillance
 - Available evidence indicates that all countries and districts with low or moderate transmission should be able to achieve >50% reduction in in-patient malaria cases and deaths within 12 months of mass distribution of LLIN that achieves household possession >60% and ITN use in children of >50%. Declines <50% suggests an investigation is needed.
 - Available evidence indicates that countries and districts with high-transmission require much higher levels of ITN coverage to achieve >50% reduction in inpatient malaria cases and deaths. The target should be near 100% household possession and >80% ITN use in all persons (not just those <5 years old and pregnant women).
 - Peak-season and annual malaria test positivity rate (RDT or microscopy) should decline progressively. Available evidence indicates that annual malaria test positivity rate should decline to <10% in countries starting with moderate or low transmission.
- Quality of surveillance
 - Percentage of suspected malaria cases that are tested should reach 100%
- Logistics
 - Percentage of confirmed or probable malaria cases treated with ACT in public facilities should reach 100%
 - Percentage of women visiting ANC receiving an LLIN should reach 100%
 - Stock-outs of ACT, RDT, and LLIN should be eliminated at national and health facility levels
- Completeness of reporting
 - Completeness of district reporting should reach 100%
 - Completeness of health facility reporting should exceed 90%

8.4.4 Analysis, feedback, and use of data for program improvement

National malaria plans of action should describe how each level should convene for analysis of indicators and use of data for action. For example, all levels – health facility, district, and national level – should be updating graphs and tables every month to monitor progress on core indicators. During regular (monthly) meetings of health facility staff with district team, district teams with provincial malaria focal points (quarterly), and provincial focal points at the national level (quarterly), analyses of these core indicators should be discussed. Peak-season and annual malaria test positivity rate should progressively decline at all levels.

National-level feedback bulletin. National malaria programs should publish a monthly bulletin showing logistics and disease surveillance indicators nationally and by district.

Supervision. National malaria plans should also describe how supportive supervision will be supported from provincial and district levels to build high-quality information system with near 100% health facility completeness of reporting and support regular (monthly) analysis of indicators for action.

Quality assurance program for laboratory testing for malaria. All countries should have a quality assurance program for laboratory testing for malaria, including both RDT and microscopy, covering all health facilities in the country.

8.5 Malaria programme review brief

Purpose, objectives and timing

The Malaria Program Review is a joint periodic performance evaluation of a malaria program with the aim of improving performance and refocusing the strategic direction of the delivery of anti-malaria interventions. The MPR is conducted by the NMCP and partners.

The main objectives of an MPR are to review and update malaria epidemiology; to review the policy and programming framework for malaria control in the country; to assess progress towards achievement of global, regional and national targets; to review the current programme performance by intervention and service delivery levels; to define the next steps to improve programme performance and/or redefine the strategic direction.

Countries should consider conducting a malaria program review as part of mid-term or end-term evaluation of the malaria strategic plans; when there is evidence of epidemiological transition or a country is considering a major investment in malaria control.

Methodology

The MPR is generally done in four phases:

Phase I: Consensus, consultation, planning, and preparation – technical consultative meetings are held and an MPR steering committee (SC) and technical working group (TWG) are constituted. MoH and partners are part of the SC and TWG.

Phase II: Desk review – this is where documents are assembled, thematic groups by intervention area constituted, information gathered and analyzed before compilation of reports.

Phase III: Field review – this is where consultative meetings between internal and external reviewers are conducted as well as technical briefings and consolidation of the MPR thematic reports. Other activities include field observations and interviews at central, provincial and district levels; in-depth discussion of key strategic and operational issues; as well as providing feedback to the MOH top management, partners and stakeholders. A draft MPR report is presented to the key partners and the MOH who sign an aide memoire as a sign of commitment to the MPR recommendations.

Phase IV: Follow-up – this is where a costed work plan for the implementation of the recommendations is agreed upon. Also, the findings of the MPR are disseminated including finalization of the MPR report.

The MPR cost generally ranges between USD 150, 000 to USD 300,000 depending on the country size and the availability of local expertise.

Outputs of the malaria programme reviews

- The immediate outputs of the MPR are the thematic review reports, the MPR Report and aide memoire to be signed by malaria partners at country level. The MPR can lead to new stratification of the malaria problem
- The MPR is also an important step in the development of a new evidence-based strategic plan with comprehensive budget and funding gap analysis, detailed implementation plan as well as a comprehensive M&E plan
- MPR represents a good platform for partners alignment around one national strategic plan, one M&E framework and one coordination mechanism
- MPR will facilitate resource mobilization for the national strategic plan including proposal writing for the Global Fund as well as the evaluation of phase 1 and preparation for phase 2 for existing grants. MPR can also be an ideal entry point for grant consolidation or NSA development

Reference: WHO – *Manual for malaria program performance review*, Geneva 2010 <http://www.who.int/malaria/publications/atoz/whomprmalariaprogramperformancemanual/en/index.html>

9. MALARIA ELIMINATION

9.1 Introduction: malaria elimination vs. eradication

Malaria *elimination* is the complete interruption of local mosquito-borne malaria transmission in a defined geographical area. This is in contrast to the definition of *eradication*, which is the permanent reduction to zero of the *worldwide* incidence of an infection caused by a specific agent as a result of deliberate efforts.

Malaria elimination programmes target the parasites and the localities where they are transmitted (so-called foci). For malaria to be eliminated, the malaria reproduction rate, i.e., the number of new infections generated by one single case over the duration of infection has to be maintained at less than one. Elimination is achieved when there are zero locally acquired cases over a period of three or more years, and the surveillance systems in place to prove it. *However even after elimination has been achieved, continued intervention measures are required for as long as the area remains receptive to resumption of transmission and exposed to importation of parasites from abroad*¹⁷. Failure to sustain malaria control and elimination, resulting in resurgence of malaria -- as has happened in the past, must be avoided.

9.2 Malaria elimination in geographical Africa

In 1997, the five African countries north of the Sahara decided jointly to aim for the elimination of malaria from the region. In 2008, only 3 locally acquired malaria cases were reported in these five countries combined, in Algeria. Other areas that have successfully eliminated malaria are Mauritius and La Réunion, relatively outlying African islands which coupled a rigorous elimination programme with overall socio-economic development.

There is as yet no evidence to indicate, given the current resources, prevailing health care systems, and using the existing tools, that malaria elimination can be achieved in high transmission areas with unrelentingly high vectorial capacities, nor that a "malaria-free" status can be sustained in such areas. However, history shows that incremental improvements in socio-economic development, infrastructure, health services, housing, etc. will contribute to decreases in the malaria reproduction rate and improve the possibilities for malaria elimination over the longer time.

9.2.1 First step: consolidate the gains

Recent years have seen significantly decreasing malaria incidence and mortality among children and adults in some countries in Africa south of the Sahara which previously suffered from high and stable malaria transmission. As countries achieve such marked reductions in the levels of transmission, malaria control strategies need to be reviewed and adjusted. WHO advises such countries to observe a "consolidation period" preceding a possible decision to proceed with programme re-orientation towards elimination. This consolidation period has the following objectives:

- a) sustain achievements even in the face of limited malaria transmission
- b) allow health services to adapt to the new clinical and epidemiological situation, and
- c) Strengthen surveillance systems to respond rapidly to new cases.

9.3 Global Fund support for elimination

The 2007 declaration by Bill and Melinda Gates of an ultimate goal of malaria eradication has resulted in an immediate and widespread declaration of elimination as a country goal in Global

¹⁷ Receptivity refers to the abundant presence of *Anopheles* vectors and other ecological and climatic factors favouring malaria transmission. Importation of parasites from abroad (resulting in "vulnerability" to resumption of transmission) is of particular concern in countries that immediately border highly endemic areas, or otherwise experience heavy, uncontrolled population exchange with such areas.

Fund applications. However, countries doing so risk weakening their application if they do not link their epidemiology to appropriate activities with targets. Some problematic areas for over-optimistic applications with “pre-elimination/elimination” proposals to the Global Fund were identified by the TRP in a recent meeting with WHO and other partners.¹⁸ These include:

- d) Countries apply for support for malaria elimination/pre-elimination programmes without having satisfied the programmatic and epidemiological prerequisites for programme transition to an elimination approach. In other words, countries not eligible for such an approach are adopting it.
- e) Countries seek support for pre-elimination/elimination proposals without including the appropriate key intervention strategies of malaria elimination. In other words, the strategies proposed often better match control than elimination, for instance by failing to concentrate on identification of cases and foci of transmission.
- f) Most proposals seeking pre-elimination/elimination are submitted by individual countries often with no coordination with neighbouring endemic countries. Aspects of elimination proposals may best be implemented through a regional approach. Applicants need to be aware that regional applications have the additional burden of proving that the regional approach will be more effective than the same strategies applied by the individual countries in the application. Regional approaches should not undermine the process of building capacity at the country level – they should not supplant the country health systems or create duplicate health systems.

In sum: Countries seeking funding for pre-elimination/elimination proposals should make sure their epidemiological and programmatic realities clearly merit (a transition to) an elimination approach, duly explore coordination with neighbouring endemic countries, and make sure that activities in the proposal are in line with WHO recommended pre-elimination/elimination strategies (*see references below*).

9.3.1 Main contents of a malaria elimination proposal

Most countries introduce malaria elimination in a geographically phased manner, expanding the programme area over time. The WHO publication *Malaria elimination - a field manual for low and moderate endemic areas* (2007) describes the principles, practice, tools and approaches, as well as monitoring and evaluation requirements for malaria elimination.

Approaches that are particularly relevant to malaria elimination are: case detection, prevention of onward transmission (including through the immediate, full treatment of all parasite carriers), and management of malaria foci and parasite importation.

Programmes that re-orient their programmes towards an elimination approach must begin by improving the quality and targeting of systems, including:

- Immediate notification and investigation of all malaria cases
- GIS-based information on all cases and transmission foci
- Quality-assured diagnostic services aiming at 100% laboratory diagnosis
- Full engagement of the private sector, phasing out the "over-the-counter" sale of antimalarial medicines
- Entomological surveillance and effective vector control in transmission foci

To date, all successful elimination programmes have been driven by highly competent, dedicated expertise at the national level; where this is not available, it must be built up.

9.3.2 Role of international support versus domestic funding

Multi-lateral funding aims to support elimination programme systems through investments in human resource development, curative and preventive health services and surveillance. However, experience shows that international donors are reluctant to cover the running costs of malaria elimination programmes, which become increasingly high relative to the remaining, dwindling local malaria burden. All countries that have over the last decades achieved malaria elimination

¹⁸ Round 9 Technical Review Panel Debriefing with Partners, Ramada Park Hotel, Geneva, 15 December 2009

have done so with very significant domestic funding, in the context of a national/regional development plan.

