Global Fund concept note development

WHO POLICY BRIEF

2014
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>2</td>
</tr>
<tr>
<td>Case management (malaria diagnosis and treatment)</td>
<td>4</td>
</tr>
<tr>
<td>Supply management for malaria diagnostic testing and treatment</td>
<td>8</td>
</tr>
<tr>
<td>Community case management of malaria</td>
<td>13</td>
</tr>
<tr>
<td>Malaria in pregnancy</td>
<td>16</td>
</tr>
<tr>
<td>Intermittent preventive treatment in infancy (IPTi)</td>
<td>19</td>
</tr>
<tr>
<td>Seasonal malaria chemoprevention</td>
<td>21</td>
</tr>
<tr>
<td>Monitoring antimalarial drug efficacy</td>
<td>22</td>
</tr>
<tr>
<td>Malaria vector control including insecticide resistance</td>
<td>26</td>
</tr>
<tr>
<td>Surveillance, monitoring and evaluation: for high-burden countries</td>
<td>34</td>
</tr>
<tr>
<td>Malaria elimination</td>
<td>40</td>
</tr>
</tbody>
</table>
INTRODUCTION

In recent years, visibility and political support for malaria has continued to increase dramatically. This policy brief is a summary of WHO’s recommended technical strategies to combat the disease. Its purpose is to present, in one concise document, a summary of WHO guidance that will assist countries to develop funding proposals, including concept notes for the Global Fund. It will also help countries to appropriately select intervention strategies and to budget for them. Key intervention areas include: malaria case management (malaria diagnosis and treatment); malaria vector control; malaria prevention for special groups (pregnant women, children and infancy); and surveillance, monitoring and evaluation. The document highlights technical areas and implementation activities that countries should ensure are included in proposals, with appropriate funding for 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 a concise overview to be used in conjunction with a separate document entitled, Malaria: Compilation of WHO reference documents, 2014.

Access to prompt diagnostic testing and effective treatment can prevent the majority of deaths from malaria by shortening the duration of the illness and by preventing its progression to severe life-threatening disease. Access to malaria diagnostic testing and treatment should therefore be seen not only as a component of malaria control, but as a fundamental right for 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 that is consistent with WHO guidelines and recommendations. It is recognized that antimalarial treatment policies will vary between countries depending on the epidemiology of the disease, on the patterns of drug resistance, and on 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 in febrile patients (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.

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, thus reducing transmission and lowering mortality and morbidity from the disease. The two main operational interventions for malaria vector control: long-lasting insecticidal nets (LLINs), and indoor residual spraying of insecticide (IRS), are the main focus of vector control in this document. However, other complementary vector control measures that are applicable in some context-specific situations are also highlighted. 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.

For malaria control and for the eventual elimination of malaria, all main operational interventions – case management and vector control (IRS or/and LLINs) – are essential and strategic priorities. Complimentary to these, and dependent on the contextual setting, are Intermittent Preventive Treatment in pregnancy (IPTp), Seasonal Malaria Chemoprevention (SMC), and Intermittent Preventive Treatment in infancy (IPTi). However, regardless of which 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.
Costing is rarely mentioned in this document. However, since figures vary among programmes (and among countries) and over time, local information on operational costs, which are critical to reach intervention targets, must be included in funding proposals. This should include items such as transportation and distribution costs, supervision, quality assurance, monitoring, community sensitization, and salaries/incentives for the health workers who will be carrying out the interventions. The cost of commodities, such as medicines and insecticides, must also be included.
SECTION 1. CASE MANAGEMENT (MALARIA DIAGNOSIS AND TREATMENT)

Malaria treatment guidelines

Malaria case management, encompassing prompt diagnosis and treatment with an effective antimalarial, is one of the key strategies for 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.

The ongoing implementation of this recommendation is leading to a progressive shift from presumptive treatment towards parasitological confirmation prior to treatment. This is a major paradigm change, particularly in areas of high malaria transmission for children under five years of age. It has required an increase in the procurement and use of rapid diagnostic tests, as well as 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, and should include: the training of health workers; consumer education; supervision; and quality assurance services.

Malaria treatment

Uncomplicated P. falciparum malaria

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

- infants;
- people living with HIV/AIDS;
- 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
- artemunate + amodiaquine
- artemunate + mefloquine
- artemunate + sulfadoxine-pyrimethamine
- dihydroartemisinin + piperaquine

A second-line treatment for uncomplicated falciparum malaria is an alternative effective ACT (since the efficacy of ACTs partially depends on the efficacy of the partner medicine, it is possible to use two different ACTs as 1st and 2nd-line options).

Fixed-dose combination (FDC) formulations are strongly preferred and are recommended over co-packaged or loose tablet combinations in order 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.


2 Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible.
Oral artemisinin-based monotherapy medicines

In order to contain the risk of development of resistance to 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, these recommendations were endorsed by all WHO Member States at the sixtyeth 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 website.

Antigametocyte medicine

The addition of a single dose primaquine (0.25mg/kg) to ACT treatment for uncomplicated falciparum malaria as an antigametocyte medicine, is recommended as a component of pre-elimination or of an elimination programme. The safety of use of primaquine in a G6PD deficient individual must always be considered.

Pregnancy

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

1\textsuperscript{st} trimester:

- quinine + clindamycin (an effective ACT should be used if quinine + clindamycin is not available or if it is programatically difficult to ensure compliance of a seven-day treatment with quinine + clindamycin.

2\textsuperscript{nd} and 3\textsuperscript{rd} trimesters:

- any of the recommended ACTs as listed above.

Severe \textit{P. falciparum} malaria

Initial treatment

Parenteral artesunate (IV or IM) is the medicine of choice for severe malaria in all age groups, and in all trimesters of pregnancy. Artesunate significantly reduces the risk of death, and lowers the risk of treatment-associated side effects including hypoglycaemia.

- Artemether or quinine are acceptable alternatives if artesunate is not available.

Follow-on treatment

Once the patient recovers sufficiently and can tolerate oral treatment, or after at least 24 hours of parenteral treatment, a full course of an effective ACT should be administered to complete the treatment of the patient.

Pre-referral treatment

The risk of death from severe malaria is greatest in the first 24 hours. Since isolated rural communities often have poor timely access to health care facilities and to effective treatment, these populations are most at risk of dying from severe malaria.

WHO recommends that if there is delay between referral and arrival at a health facility able to administer parenteral anti-malarial treatment, children under 5 years of age should receive a pre-referral dose of rectal artesunate that must be followed up with further antimalarial treatment on arrival at a health care facility (if transfer to a health facility is delayed more than 12 hours, a further rectal dose may be given). If rectal artesunate is not available, artesunate, artemether or

---

3 http://apps.who.int/gb/ebwha/pdf_files/WHA60/A60_R18-en.pdf
5 ACT should be used if it is the only effective antimalarial treatment available.
quinine can be given intramuscularly. In adults, options for pre-referral treatment include artesunate (IM), artemether (IM) or quinine (IM).

**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*.

In mild to moderate G6PD deficiency, primaquine 0.75 mg base/kg BW may be given once a week for eight 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 by all stakeholders, and continuous stewardship by the ministry of health.

The decision on whether an existing treatment policy needs to be changed or not is based on the therapeutic efficacy of the antimalarial drugs that are already in use, and an assessment is made in line with standard WHO protocol. 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 when the medicine has an average cure rate of >95% as assessed in therapeutic efficacy studies.

**The process of implementing a new treatment policy**

The following areas and activities are critical to the effective implementation of a revised and/or expanding policy. They 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.

2) Provision for procurement and distribution of supplies. To include:

- Estimation of needs (medicines and rapid diagnostic tests);
- Procurement costs for antimalarials and diagnostic tests. This should also include the cost of insurance, transportation, delivery, stock management within the country, etc.;
- Drug storage and distribution systems;
- Resources for purchase of microscopes and malaria rapid diagnostic tests.

---

6 See section on *Therapeutic efficacy monitoring for details on protocols.*
7 See section on supply chain management for details on quantification and procurements.
3) Provision for orientation and training of all health workers in public and/or private sector. To include:
   • 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 and data collection tools for monitoring case management.

4) Provision for behaviour change communication strategy. To include:
   • Production and pre-testing of IEC, BCC and advocacy materials;
   • Implementation of education, information, behaviour change communication and advocacy activities targeting various groups (communities, health workers, leaders at different levels and partners);
   • Activities to enhance compliance with diagnostic test results and ACT treatment.

5) Quality assurance. To include:
   • 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. To include:
   • 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. These should be conducted as an essential part of a malaria control programme (See Section 6 for complete information).

7) Pharmacovigilance. To include:
   • 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.

Challenges

Estimating quantities of required antimalarial medicines and rapid diagnostic tests, especially in those countries that lack a reliable supply information system, is a challenging task. If the pipeline is already filled and reliable stock management records are available, requirements can be estimated using the consumption method. If, however, past consumption cannot serve as a guide to the future, the standard morbidity method should be applied. This would include situations where: previous budgets were too low; prescribing patterns have changed substantially; new treatments are being introduced; or successful malaria control interventions have decreased or are decreasing drug consumption over time. In most situations a combination of both methods is applicable. The estimations of needs should be adjusted to programme delivery capacity, and should take 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.

SECTION 2. SUPPLY MANAGEMENT FOR MALARIA DIAGNOSTIC TESTING AND TREATMENT

Malaria diagnostic testing

Background

Clinical diagnosis of malaria has poor accuracy and leads to over-diagnosis, with resultant inappropriate management of non-malarial febrile illness and wastage of antimalarial medicines. As such, evidence of the presence of malaria parasites prior to treatment with antimalarial medicines is fundamental and 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 or quality-assured RDTs, depending on the setting / area of intended use.

Microscopy

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 employ competent and motivated staff, who are supported by effective training and supervision to promote a high level of 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 that result in poor performance; and 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 as an essential part of funding for malaria case management.
Rapid diagnostic tests (RDTs)

It is the responsibility of each national malaria control programme to select well performing RDTs that are adequate for the intended setting. To guide the selection and procurement of these, a Malaria RDT Product Testing Programme was launched in 2008. This programme, coordinated by WHO and the Foundation for Innovative New Diagnostics, provides comparative performance data through the evaluation of products against well-characterized, cryopreserved, native and cultured *P. falciparum* and *P. vivax* samples. Testing is conducted at US CDC. Five rounds of testing have been undertaken since 2008. Round 4 results were published in December 2012 and Round 5 results are expected in the second quarter of 2014. A summary of results of the rounds is available on the web, and comprises the basis for the WHO procurement recommendations explained in the *Information note on recommended selection criteria for procurement of malaria rapid diagnostic tests (RDTs).* Based on the results of WHO malaria RDT product testing, procurement requirements are the following:

1. For the detection of *Plasmodium falciparum* (Pf) in all transmission settings, the panel detection score (PDS) against Pf samples should be at least 75% at 200 parasites/μL.
2. For the detection of *Plasmodium vivax* (Pv) in all transmission settings, the panel detection score (PDS) against Pv samples should be at least 75% at 200 parasites/μL.
3. The false positive rate should be less than 10%.
4. The invalid rate should be less than 5%.

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

- Stability requirements at temperatures of intended storage, transport and use;
- Ease of use and training requirements for health workers;
- Supplier production capacity and lead times;
- Delivery schedules, box size and shelf life;
- Product registration requirements of the national regulatory authorities.

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), programmatic needs, and price. It must be stressed that price alone should not be the determining factor for the procurement of RDTs.

The above information, as well as further guidance, can be obtained from the WHO manual on *Good practices for selecting and procuring rapid diagnostic tests for malaria.*

The Foundation for Innovative New Diagnostics (FIND) has developed a web-based interactive guide to inform RDT selection on the basis of target malaria species, minimum panel detection score for both *P. falciparum* and *P. vivax*, invalid rate, false positive rate, and test format. The guide is available on the web.

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 with a panel detection score lower than 75% on a large scale should proceed with pre- or post-shipment lot testing (see RDT lot testing programme)

---

12 Panel detection score (PDS): The PDS is a composite index, considering the positivity rate as well as inter-test and inter-lot variability. The percentage reflects the malaria samples in the panel that give 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.
13 Proportion of tests deemed invalid, i.e. without visible control band.
below) and strongly consider moving to an RDT that meets WHO procurement criteria recommendations (>75% panel detection score at low parasite densities) in the near future.

Any plans to replace RDTs should be made taking into consideration all corresponding training and programmatic requirements.

**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 by lot testing, prior to large-scale deployment in the field, and that a process of monitoring RDT performance in the field should be put in place. This should be applied to all RDTs. WHO-FIND Lot testing services are available free of charge and results are provided within five days of RDTs being received at the testing laboratory. Full information on WHO-FIND procedures for RDT lot testing is available on the web.\(^\text{15}\)

**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 and have a relatively short shelf life of 2–3 years.

WHO provides guidance on how to select and procure safe and effective quality medicines with its manual on good procurement practices for artemisinin-based antimalarial medicines,\(^\text{16}\) which is based on new, stringent and internationally agreed quality assurance criteria.

**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 the WHO treatment guidelines, after review approval by a 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.

Fixed-dose combination (FDC) formulations are strongly preferred and recommended over blistered co-packaged or loose tablet 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 sulfadoxine-pyrimethamine (SP).

In case products should be procured, which do not meet with the above mentioned quality criteria, the following partial quality criteria should be applied to guide procurement; all three points must be fulfilled:

1. GMP compliance certified after inspection by WHO or by a SDRA for the dosage form concerned; and
2. Submission of the product dossier to the WHO PQ Programme or to a SDRA, and acceptance of the corresponding organization to review the dossier;

\(^\text{15}\) [http://www.finddiagnostics.org/programs/malaria-afs/malaria/rdt_quality_control/lot_testing/](http://www.finddiagnostics.org/programs/malaria-afs/malaria/rdt_quality_control/lot_testing/)

and
3. Acceptance of the product after technical review by an Expert Review Panel (ERP) convened by WHO.

**Procurement of quality medicines**

Detailed information on each step of the procurement cycle (from estimation of requirements, to tender-related procedures and pre-/post-shipment quality control, to monitoring and evaluation) of antimalarial medicines can be derived from the 16 steps procurement checklist in the manual on *Good procurement practices for artemisinin-based antimalarial medicines* available on the web.17

**Plan of activities for budgeting purposes**

To allow for adequate budgeting, it is essential to make a comprehensive list of activities for which funding is required. Below is an example of such a list. This is not exhaustive and should be modified and customized according to the country’s specific needs:

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, and 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.
   - 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: The necessary technical equipment (e.g. for distribution and storage, and RDT waste management) need to be taken into account, together with maintenance costs.
   - Staff: Costs of tender related procedures (preparation of tender documents, tender invitation and bid evaluation by sufficient staff with appropriate expertise) must also be included.

5) The implementation and ongoing running of sound quality assurance systems for medicines as well as diagnostics (pre-/post-shipment quality control systems for medicines and pre-/post-shipment lot testing for RDTs). Quality assurance materials and services for microscopy and 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).

Table 1: A summary outline of components of a budget for a malaria diagnosis programme

Table 4. Components of the budget for a malaria diagnosis programme

<table>
<thead>
<tr>
<th>Component</th>
<th>Activities specific to microscopy</th>
<th>Activities specific to RDTs</th>
<th>Activities for management of (malaria and non-malaria) fevers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparation of technical guidelines, standard operating procedures and checklists</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guidelines</td>
<td>Laboratory supervision*</td>
<td>RDT transport and storage</td>
<td>Fever management algorithm</td>
</tr>
<tr>
<td>Standard operating procedures for diagnostic testing</td>
<td>Microscopy performance</td>
<td>RDT performance</td>
<td>Other tests used at primary care level</td>
</tr>
<tr>
<td>Other standard operating procedures</td>
<td>Proficiency testing, validation of routine slide results</td>
<td>RDT storage</td>
<td></td>
</tr>
<tr>
<td>Training material</td>
<td>Training manual for microscopy</td>
<td>Training manual for RDTs</td>
<td>Training manuals for integrated management of fevers</td>
</tr>
<tr>
<td>Checklists for supervision</td>
<td>Laboratory visits*</td>
<td>Health facility visits</td>
<td></td>
</tr>
<tr>
<td>Procurement and supply of commodities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnostic tests</td>
<td>Microscopes and related supplies</td>
<td>RDT kits</td>
<td>Urine dipsticks, haemoglobin meter, hemotocrit meter, glucometer</td>
</tr>
<tr>
<td>Medicines</td>
<td>ACTs</td>
<td></td>
<td>Antibiotics, zinc, inhaled salbutamol, rehydration salts</td>
</tr>
<tr>
<td>Other commodities</td>
<td>Gloves, lancets, alcohol, cotton wool, timers, sharps boxes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distribution of commodities to the field</td>
<td>All items listed above</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality management system</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-shipment testing</td>
<td>Lot-testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Training of focal people</td>
<td>Quality management system focal people</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring the quality management system</td>
<td>Quality monitoring supervision visits and compilation of health information management data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Training of health workers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Training of tutors</td>
<td>Expert microscopists</td>
<td>Tutors for RDT performance outside laboratories and clinical management of fever cases</td>
<td></td>
</tr>
<tr>
<td>Training of health workers</td>
<td>Microscopists</td>
<td>Health workers</td>
<td>Clinicians</td>
</tr>
<tr>
<td>Training of supervisors</td>
<td>Laboratory supervisors*</td>
<td>Clinical supervisors</td>
<td></td>
</tr>
<tr>
<td>Supervision</td>
<td>Laboratory visits*</td>
<td>Health facility visits</td>
<td></td>
</tr>
<tr>
<td>Advocacy, communication and social mobilization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Design of strategies and material</td>
<td>Communication on the need for malaria testing</td>
<td>Communication on other causes of fever</td>
<td></td>
</tr>
<tr>
<td>Dissemination of key messages</td>
<td>Through each delivery channel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring and evaluation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Updating the health information management system</td>
<td>Add row for RDTs in laboratory report and column for malaria test results in clinicians' book</td>
<td>Column for other test results in clinicians’ book</td>
<td></td>
</tr>
<tr>
<td>Train health workers in the new health information management system</td>
<td>Training of person in charge or focal person for reporting on health information management in health facilities</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* To simplify, activities specific to laboratories have been mentioned under 'Microscopy', although both microscopy and RDT are generally performed in laboratories.

---

SECTION 3. COMMUNITY CASE MANAGEMENT OF MALARIA

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, including at community level. 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 recommendations on community case management of malaria

Community case management of malaria should be implemented in the context of the integrated community case management (iCCM) strategy. In 2012 WHO and UNICEF released a Joint Statement on integrated Community Case Management, which presents the latest evidence on iCCM, describes the necessary programme elements and support tools for effective implementation, and lays out actions that countries and partners can take to support the implementation of iCCM at scale. The malaria component of iCCM is based on: diagnosis of fever (WHO strongly recommends the use of RDTs at the community level as part of the iCCM programme, provided appropriate training and adequate quality assurance measures for RDTs are in place) in children under 5 years of age; treatment with the national first-line medicine (ACTs) for uncomplicated malaria; and rectal artesunate as pre-referral treatment for severe malaria. In addition to diagnostics and medicines for malaria, the iCCM strategy package includes diagnostic tools for pneumonia, and medicines for pneumonia and diarrhoea (respiratory rate timers, antibiotics, ORS and zinc).

In order to ensure health service coverage to areas beyond the easy reach of health facilities (hard to reach populations) the following commodities should be made available:

4. Quality-assured RDTs to confirm/rule out malaria infection in children presenting with fever/history of fever;
5. First-line oral antimalarials (ACTs) for treatment of uncomplicated malaria cases;
6. Pre-referral treatments (rectal artesunates) for all children with fever/history of fever unable to swallow oral medicines and/or other signs of severe disease;
7. Tools for the diagnosis of pneumonia, such as respiratory timers;
8. Antibiotics (preferably amoxicillin), ORS and Zinc for the treatment of pneumonia and diarrhoea.

These should be provided at the community level along with the following essential components of a community delivery platform for iCCM:

a. Identifying, training and providing appropriate remuneration for community treatment providers (CHWs);
b. Implementing a reliable supply system for medicines and diagnostics to the community workers;
c. Implementing a supportive communication strategy (IEC, BCC and advocacy) to create demand and encourage appropriate care-seeking;
d. Implementing a rigorous system for monitoring and supervision of all activities by the health facility level.
e. The necessity to build and sustain a functional referral system is critical to the successful implementation of iCCM.

To adequately facilitate access to essential treatment at the community level, countries need to recognize iCCM as a service delivery point and incorporate its activities in 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 quality assured treatment services and essential commodities for iCCM at community level:

- Supportive policies facilitating the use of ACTs, antibiotics, ORS, zinc and RDTs at community level;
- A system for procurement, delivery and distribution of all essential commodities at all levels to include delivery at the community level;
- A system for information dissemination through implementation of IEC and BCC activities in communities;
- Identified key community service providers (including private providers);
- Training of all service providers at community level using training manuals on integrated management with the provision of necessary job tools;
- Adequate information systems to support implementation, including pharmacovigilance and surveillance systems;
- The development and maintenance of a functional monitoring, supervision and patient referral system.

**Implementation requirements**

In countries that do not have any experience of community based malaria case management, it is recommended that implementation be undertaken in a phased manner in order to allow the country to build up experiences and document best practices. Reference can be made to the iCCM Benchmarks Matrix, which lays out the necessary steps to be taken across the various critical programme components of iCCM. Opportunities to learn from best practices in neighbouring countries that have experience with iCCM should also be considered.

In order to scale up malaria case management as part of an iCCM strategy, the following steps need to be undertaken and should have clear and specific budget lines:

- Sensitization of all stakeholders at national, sub-national, district and community levels;
- Development of integrated training materials for community based providers;
- Development of behaviour change communication strategies and materials to improve community participation and mobilization;
- Training of selected community based providers on iCCM, including malaria case management, diagnostics and medicine handling, and reporting;
- Procurement and distribution of 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;
- Development of a monitoring and supervision system for community-based interventions and activities for quality assurance.

WHO recommends that community case management of malaria 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 and zinc, the setting up of community structures (including the training, supervision, and supply chain systems for community delivery of case management through an iCCM platform) may be conducted under Global Fund Grants. Experience has shown that implementation of the full iCCM package is associated with an increase in rational use of antimalarials, and countries are strongly encouraged to secure
funds for the procurement of all commodities needed for iCCM, including antibiotics, ORS and zinc.

**Working through the private sector**

As much as possible, countries should explore involving the private sector in the provision of ACTs by using existing, commonly used providers in a public-private mix. Drug shop owners could be sensitized in order to solicit their co-operation in selling the recommended ACT medicines. While recognizing the greater challenge of deploying RDTs in the private as compared to the public sector, their use in the private sector should nonetheless be strongly encouraged.

Countries should develop and explore innovative models for organizing and engaging the private sector in order 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. The public sector should subsequently 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 public health facilities is rapidly increasing, many countries are still in the initial stages of using ACTs and RDTs, or the full iCCM package, at the community level. Some of the key challenges include:

- Limited experience of ACT and RDT use at the community level by CHWs;
- Limited experience and/or regulatory challenges with regard to the use of antibiotics by CHWs;
- Current high cost of these medicines and diagnostics;
- Challenges in procurement and supply of case management commodities;
- Limited penetration into the private sector;
- High costs associated with setting up 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;
- Low utilization of community treatment services compared to expected burden of illness.

A number of these challenges require operational research projects at country level to address some of the issues, and countries are encouraged to include the resources for this in their funding requests.
SECTION 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, who carry the greatest burden of malaria, there has been less investment in the linkages between Malaria Programmes and Maternal, Newborn and Child Health (MNCH) 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. MNCH service delivery points provide an opportunity not only to scale up disease specific interventions but also to improve 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; and 3–8% of infant deaths. 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.  

Key policy issues

WHO recommends that all endemic countries provide a package of interventions for the 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 (IPTp_SP) 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 a 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 three doses of SP as IPT at scheduled antenatal care visits (at least one month apart). The first dose should be given at first contact in the 2nd trimester and the last dose can be given as late as possible in the 3rd trimester, irrespective of the expected delivery date of the mother. IPT-SP should be taken under direct observation (DOT) during the ANC visit.

Implementation issues

Antenatal clinics provide 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 LLINs to pregnant women should occur through ANCs, supplemented by campaign approaches. The nets should be handed out during the very first ANC visit, together 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.

**Exploiting linkages to improve the delivery of 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 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 skilled 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.

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

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 calculated at about five percent (5%) of the total population times at least three doses of SP (three tablets per dose) per pregnant woman.
- 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 LLINs through ANCs, 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 warehouses 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 that target 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 programmes.

- 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. In addition, there should be pharmacovigilance to monitor the safety of the medicines used for treatment of malaria in pregnancy.
SECTION 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 sulfadoxine-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 ≤50%.

**Considerations and caveats for implementation**

- In situations where 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 ≤ 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.

**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.

**Issues to be considered in the development of GF 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 programmes. Support for capacity building of personnel for improving quality of care, with resources, staff training and supervision included, should be part of the Global Fund proposal. Specific items to be included in the proposal and budget, include:

- Medicines for IPT (sulfadoxine 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.
SECTION 6. SEASONAL MALARIA CHEMOPREVENTION

Seasonal malaria chemoprevention (SMC), previously termed intermittent preventive treatment in children, is defined as the intermittent administration of full treatment courses of effective antimalarial medicines during the malaria season to prevent malarial illness. The objective of SMC is to maintain therapeutic antimalarial drug concentrations in the blood throughout the transmission season, which is the period of greatest malarial risk. SMC has been studied most frequently in areas with seasonal malaria transmission where the main burden of malaria is in children, rather than in infants, and the main risk of clinical malaria is restricted to a few months each year. In these settings SMC has been shown to prevent approximately 75% of severe malaria episodes.

SMC with amodiaquine plus sulfadoxine-pyrimethamine (AQ+SP) for children aged 3–59 months in areas of highly seasonal malaria transmission is recommended across the Sahel subregion in Africa. SMC is not currently recommended for countries in southern and eastern Africa, even though there are some locations in those regions where the transmission pattern would suggest suitability. This is because of the high level of P. falciparum resistance to AQ and/or SP, and the absence of adequate efficacy and safety data for other potential anti-malarial regimens for use in SMC.

An implementation manual for SMC developed by WHO-GMP was issued in December 2012.

Considerations and caveats for implementation

The following criteria should be used to determine the suitability of deploying SMC in any setting:

- Malaria seasonality: Highly seasonal malaria transmission;
- Efficacy of SP and AQ: High > 90% therapeutic efficacy (last available study results);
- Pharmacovigilance systems: needed to monitor potentially serious adverse reactions should be strengthened;
- Surveillance of parasite resistance to SP should accompany the implementation of SMC as a surrogate measure of its efficacy.

Contra-indications

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

Issues to be considered in the development of GF 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 (AQ+SP), which are a fairly inexpensive commodity. Provision should be made for the delivery of this intervention through community delivery programmes. 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 SMC (AQ+SP);
- Logistics for distribution of medicines to facilities;
- Education and communication materials and campaign activities to improve acceptability and use of SMC;
- Strengthening the capacity of health workers/community health workers to deliver SMC through appropriate training and supervision.
SECTION 7. 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* or GPARC (WHO 2011). In that document, the need to monitor antimalarial drug efficacy is one of the four pillars of the response to this public health threat.

**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 a 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 results in country and among countries in the same region.

Routine monitoring of the therapeutic efficacy of artemisinin-based combination therapies (ACTs) is essential for timely changes to treatment policy and can help to detect early changes in *P. falciparum* sensitivity to artemisinins. WHO currently recommends monitoring the efficacy of first line and second line ACTs every two years in all sentinel sites, and changing antimalarial treatment policy when the treatment failure rate of a 28- or 42-day follow-up study (depending on the medicine) exceeds 10%. The proportion of patients who are parasitemic on day 3 is currently the best available indicator used in routine monitoring to measure *P. falciparum* sensitivity to artemisinins. If $\geq 10\%$ of patients treated with an ACT are parasitemic on day 3, the area will be considered Tier I, and, consistent with recommendations in the GPARC, containment activities should begin immediately. Carefully controlled research studies using oral artesunate monotherapy should also be initiated to further confirm and investigate the presence of artemisinin resistance in the area. Confirmation of artemisinin resistance should not delay containment activities.

**Organization and survey outline**

**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.
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 a 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 necessary 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, 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 at 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.

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 low transmission areas;
- Absence of severe malnutrition;
- Parasitaemia: limits of parasite count for inclusion are 2000–200 000/µl in areas of intense transmission, and 1000–100 000/µl for low-moderate transmission area;
Absence of general danger signs or signs of severe and complicated falciparum malaria according to the definition given by WHO; \(^\text{20}\)

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 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 analysing 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 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 a 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 2–3 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.
SECTION 8. 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 free LLIN mass campaigns and continuous distribution (ANC and immunizations) before, during and after mass campaigns are needed to sustain this coverage – see latest recommendation from WHO.\(^{21}\) When there are temporary gaps in LLIN coverage, protection of risk groups, especially young children and pregnant women in high transmission areas, should be given preference. This is a temporary measure to minimize deaths from malaria and should not replace the goal of universal coverage. WHOPES-approved LLINs should be used – refer to the updated list as of 29 October 2013.\(^{22}\) While the insecticide on an LLIN should be retained for at least three years, recent data shows that, in fact, 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 three to six months, but occasionally up to nine months, depending on the insecticide that is used, the type of surface sprayed, and the seasonality of transmission. See the list of recommended insecticides for IRS.\(^{23}\)

**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 are 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 (especially those funded with public health funds) or highly subsidized, and should be 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.

**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 interven-

---

tion, 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 behaviours, dynamics of transmission (rhythm and intensity), and 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 rests 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 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 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 to these, must be determined through geographical reconnaissance prior to decision-making and planning.

**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 of which to use 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 also when deployed correctly on a large scale, both have an impact on decreasing the vector population and therefore malaria transmission intensity.

**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 continuous ITN distribution can easily be integrated into existing health systems such as routine EPI and/or ANC;
In areas where the specialized 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 of buildings that need to be sprayed is excessive and where 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.

**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 humanitarian emergencies (e.g. displaced populations and refugee settings, climatic events, etc.) where there are house structures for IRS;
- 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 level of protection 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 deployment, is the availability of the programmatic capacity (planning, logistics and supervision) necessary to ensure an IRS 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 exophilic and exophagic (i.e. tend to bite and rest outdoors, respectively).

**When should IRS and LLINs be combined?**

IRS and LLINs may be deployed in combination as a means of resistance management. Since all nets are treated with pyrethroids and given that coverage of LLINs is high in most malaria areas, rotational use of IRS with non-pyrethroids is a logical choice to manage resistance (preserve pyrethroids). If this strategy is well implemented, it will make a return to pyrethroids possible. Combining IRS and LLINs in order to compensate for programmatic failure or challenges in deploying one or other of the interventions effectively on its own is not recommended. As such,
the general 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, as this is likely to produce excessive selection for pyrethroid resistance; conversely

**Do select insecticides other than pyrethroids for IRS** where the intervention is to be implemented together with LLINs: This is believed to be one of the more promising of the available resistance management methods.

Until enough evidence is collected on the epidemiological benefit and value of combining the two interventions, such a strategy should be restricted mainly to managing insecticide resistance. WHO will continue to update these recommendations as more evidence becomes available.

As previously stated, the use of an IRS/LLIN 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.

**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.24

- For IRS, the minimum resistance management policy is to alternate between insecticide classes in a 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 previously 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 is 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 using molecular genotyping methods. It is recommended that funds for these activities be included in proposals. 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.

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 their effective use. Evidence suggests that about 90% of the population with access to a mosquito net actually uses it. In areas where LLIN use is identified as being lower, WHO recommends the roll-out of behaviour-change communication programmes, including information, education and communication (IEC) campaigns.

- Some LLIN distribution campaigns have successfully used follow-up field operations to support and promote use of nets after a campaign. There is also 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. To-date., 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.

Timing and sustaining coverage

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, the insecticide used and the surfaces sprayed, one or two spray cycles per year may be required. Large-scale implementation requiring more than two 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.

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.

Continuous distribution strategies are needed to avoid gaps in LLIN coverage

WHO has long recommended both mass campaigns and continuous distribution 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 mass campaigns but not continuous distribution through routine ante-natal care (ANC) and immunization (EPI) systems, WHO has adjusted its guidance on this issue: the current recommendation is that LLIN distribution through continuous distribution channels should be given as much priority as mass net campaign distribution in national plans, before, during and after campaigns. Delivery through ante-natal care (ANC) as well as through immunization (EPI) channels is especially valuable because (1) it ensures a continuous flow of nets into the population, partially balancing the continuous loss of nets through wear and tear, and (2) 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 other country/specific distribution channels, may be more successful in sustaining high coverage.

**Budget considerations**

For all procurement of vector control products (LLINs and insecticides), pre-and post-shipment testing for quality control is mandatory.\(^{25}\)

**ITNs**

- In planning for procurement quantities, the aim should be to distribute enough LLINs to achieve 100% coverage, with one net for two people. There must be a clear plan as to how this is to be achieved at household level. A good way to do this is to give nets to households at the rate of one net for every two 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 one 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, must be in place. Opportunities to give a greater role to manufacturers and/or procurement agents to deliver LLINs up to final destination, e.g. district level should be explored.
- Adequate and efficient planning of distribution methods (e.g. through ANC clinics, integrated with immunization campaigns, etc.) is 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.
- 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, should be included in the budget.
- Funds for insecticide resistance monitoring and for proper monitoring of effective biological activity and physical durability of LLINs should be included in the budget.
- 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. 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.

**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 a 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;

• Insecticide resistance monitoring and proper monitoring of the insecticide residual duration on sprayed surfaces;

• Where IRS is being employed for the first time, 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 six months of transmission per year.

**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. See recent WHO recommendations on capacity building for entomology and vector control.

• 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 of LLINs at six-monthly intervals in one or two sentinel sites. This monitoring should be regarded as a “good practice” routine for all large-scale procurements of LLINs. It should include a variety of LLIN products in order to inform subsequent procurement rounds. Standard methods have just been published. There is also a recent WHO recommendation on how to estimate the longevity of LLINs under field conditions, which can be found on the web.

---


**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 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, for as long as they are in use.

- **In stable malaria areas**, 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.
SECTION 9. SURVEILLANCE, MONITORING AND EVALUATION: FOR HIGH-BURDEN COUNTRIES

Background

In high-burden malaria countries, four main antimalarial interventions are used to reduce malaria burden: (1) long-lasting insecticidal nets (LLINs), (2) appropriate diagnostic testing (e.g. rapid diagnostic tests [RDT] or microscopy) and treatment (e.g. artemisinin-based combination therapy), (3) insecticide residual spraying (IRS), and (4) intermittent preventive therapy (IPT) in pregnant women and infants (in Africa). Surveillance and M&E provide key management data to continually assess performance and improve programme management. Surveillance and M&E indicators should match the interventions mentioned above to measure inputs, coverage, and impact.

Targets

Below, we list targets from the World Health Assembly and the RBM Partnership. In addition, the United Nations Secretary-General on World Malaria Day, April 2008, called for universal access to locally appropriate interventions for prevention and case management by 2010. This call for universal access 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

- >75% reduction by 2015 compared to 2000

Mortality

- >75% reduction by 2015 compared to 2000 (WHA target)
- 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 zero\(^{29}\) 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.

---

\(^{29}\) 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.
• **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, 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 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.  

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.

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 these. 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.

**Routine information plus survey data**

A strong national surveillance and M&E system would utilize both (1) routine information systems to continuously monitor impact and (2) survey data to supplement routine information, both to fill gaps (e.g. measurement of ITN use) and to provide robust population estimates (for example, for programme intervention coverage, parasite prevalence, and all-cause child mortality).

**Indicators from routine information systems and household surveys**

WHO-recommended indicators for surveillance and monitoring of malaria programmes were recently updated and published in the *World Malaria Report 2013*. Key indicators were designed

---

30 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).

31 Further information on indicators derived from household surveys can be found in *Household Survey Indicators for Malaria Control*, found at [http://www.rollbackmalaria.org/toolbox/docs/rbmtoolbox/tool_HouseholdSurveyIndicatorsForMalariaControl.pdf](http://www.rollbackmalaria.org/toolbox/docs/rbmtoolbox/tool_HouseholdSurveyIndicatorsForMalariaControl.pdf)
to be simple and limited in number (for example, limited enough to fit within an integrated national health information system (HMIS)), yet able to provide sufficient information on all malaria interventions as well as impact data. Listed in the table below are the recommended key and supporting indicators measured by routine information systems and household surveys. Indicators are linked to the corresponding objective or target in the Global Malaria Action Plan and the relationship between key and supporting indicators is described by the analytic question to be answered.

Table 2: Recommended key and supporting indicators measured by routine information systems and household surveys

<table>
<thead>
<tr>
<th>GMAP Objective or Target</th>
<th>Key Indicator 1</th>
<th>Further Analysis 1</th>
<th>Supporting Indicator 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective 1</td>
<td>Incidence malaria deaths per 1000 persons per year</td>
<td>Has health facility reporting completeness changed over time?</td>
<td>Completeness of monthly health facility reports</td>
</tr>
<tr>
<td>All-cause under 5 mortality rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of suspected malaria cases that receive a parasitological test</td>
<td></td>
<td></td>
<td>Programme coverage indicators in this table (detailed below)</td>
</tr>
<tr>
<td>Target 1.1</td>
<td>Proportion of children under 5 years old with fever in the last two weeks who had a finger or heel stick</td>
<td>Are people seeking advice or treatment for fever and from where?</td>
<td>Proportion of children under 5 years old with fever in the last two weeks for whom advice or treatment was sought</td>
</tr>
<tr>
<td>Proportion of confirmed malaria cases that receive first-line anti-malarial treatment according to national policy</td>
<td></td>
<td></td>
<td>Proportion of health facilities without stock-out of key commodities by month</td>
</tr>
<tr>
<td>Objective 2</td>
<td>Confirmed malaria cases (microscopy or RDT) per 1000 persons per year</td>
<td>has diagnostic test changed over time?</td>
<td>Annual blood examination rate</td>
</tr>
<tr>
<td>Reduce global malaria cases by 75% by end 2015 (from 2000 levels)</td>
<td></td>
<td></td>
<td>Completeness of monthly health facility reports</td>
</tr>
<tr>
<td>Parasite prevalence: proportion of children aged 6-59 months with malaria infection</td>
<td></td>
<td></td>
<td>Malaria test positivity rate</td>
</tr>
<tr>
<td>Proportion of population with access to an ITN within their household</td>
<td></td>
<td></td>
<td>Proportion of children aged 6-59 months with a hemoglobin measurement of &lt;9 g/dL</td>
</tr>
<tr>
<td>Target 2.1</td>
<td>Proportion of population that slept under an ITN the previous night</td>
<td>Are specific population groups using ITNs?</td>
<td>Proportion of children under 5 years old who slept under an ITN the previous night</td>
</tr>
<tr>
<td>Proportion of households with at least one ITN</td>
<td></td>
<td></td>
<td>Proportion of pregnant women who slept under an ITN the previous night</td>
</tr>
<tr>
<td>Target 2.2</td>
<td>Proportion of population protected by IRS within the last 12 months</td>
<td>Are ITNs being used?</td>
<td>Proportion of existing ITNs used the previous night</td>
</tr>
<tr>
<td>Sustain universal access to and utilization of prevention measures**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target 2.3</td>
<td>Proportion of households with at least one ITN and/or sprayed by IRS within the last 12 months</td>
<td>How many households have been reached with at least one vector control method?</td>
<td>Proportion of households with at least one ITN and/or sprayed by IRS within the last 12 months</td>
</tr>
<tr>
<td>Proportion of women who received at least three or more doses of IPTp during ANC visits during their last pregnancy</td>
<td></td>
<td></td>
<td>Proportion of women who received all pregnant women at each scheduled ANC visit</td>
</tr>
<tr>
<td>Objective 3</td>
<td>Proportion of households with at least one ITN and/or sprayed by IRS within the last 12 months</td>
<td>How many households have been reached with at least one vector control method?</td>
<td>Proportion of households with at least one ITN and/or sprayed by IRS within the last 12 months</td>
</tr>
<tr>
<td>Eliminate malaria by end 2015 in 10 new countries (since 2008) and in the WHO European Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of new countries in which malaria has been eliminated</td>
<td></td>
<td></td>
<td>Proportion of women attending ANC who received a minimum of four doses of IPTp</td>
</tr>
</tbody>
</table>

Indicators derived from household surveys are in bold.

* In areas where public health facilities are able to provide a parasitological test for all suspected malaria cases, near zero malaria deaths is defined as no more than 1 confirmed malaria death per 100,000 population at risk.

** Universal access to and utilization is defined as every person at risk sleeping under a quality insecticide-treated net or in a space protected by indoor residual spraying and every pregnant woman at risk receiving a dose of IPTp at each ANC visit after the first trimester (in settings where IPT is appropriate).
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 at all times 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 health facility, district, and national levels. Quarterly information systems are not adequate for monitoring stock-outs of essential commodities or for surveillance of a disease that can be strongly seasonal with dramatic month-to-month differences and areas at risk of epidemics.

Core data elements needed to monitor routine core indicators

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

- Disease surveillance: inpatient – malaria deaths, inpatient malaria cases, total cases – suspected, tested, confirmed.
- ACT: number of patients treated with ACT and the number of patients expected to be treated according to national policy (this data element comes from outpatient surveillance data).
- LLINs: number of LLINs distributed at ANC visits, and number of ANC first visits, number of LLINs distributed at the EPI clinics.
- LLINs: distribution through mass campaigns.
- IPT: number of ANC clients receiving 1, 2, 3 and 4 doses of IPT, and number of ANC first visits.
- IRS: number of households with at least one round IRS, number of households targeted.
- Stock-outs: number of health facilities with stock-out of ACT, RDTs, LLINs.
- Completeness of reporting.
- Number of health facilities that reported, number expected to report.

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

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

- Malaria incidence rates: confirmed malaria cases per 1000; inpatient malaria cases per 10 000; inpatient malaria deaths per 100 000.
- Proportional malaria incidence: slide positivity rate; % inpatient due to malaria; % inpatient deaths due to malaria.
- General patient attendance: outpatients per 1000; inpatients per 10 000; inpatient deaths per 100 000.
- Diagnostic effort: annual blood examination rate.
- Quality of diagnosis and reporting: % health facilities reporting; % suspected cases receiving diagnostic test.
- Species of malaria: % cases due to P.falciparum.

Analysis, feedback, and use of data for programme 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 teams, 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.
National-level feedback bulletin. It may be helpful for national malaria programmes to publish a quarterly bulletin showing key indicators nationally and by district.

Supervision. National malaria plans should also describe how supportive supervision will be conducted from provincial and district levels to ensure 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 programme for laboratory testing for malaria, including both RDT and microscopy, covering all health facilities in the country.

**Malaria programme review brief**

**Purpose, objectives and timing**

The Malaria Programme Review (MPR) is a joint periodic performance evaluation of a malaria programme 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; and to define the next steps to improve programme performance and/or redefine the strategic direction.

Countries should consider conducting an MPR as part of mid-term or end-term evaluation of 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 – documents are assembled, thematic groups by intervention area constituted, and information gathered and analysed before compilation of reports.
- **Phase III:** Field review – 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 who, together with the ministry of health, 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. The findings of the MPR form the basis for updating an existing National Strategic Plan or for the development of a new plan.

The cost of an MPR generally ranges between US$ 150 000 to US$ 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 the 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, a detailed implementation plan as well as a comprehensive M&E plan.
- MPR represents a good platform for partners to align 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.

---

SECTION 10. MALARIA ELIMINATION

Introduction: malaria elimination vs. eradication

Malaria elimination is the complete interruption of local mosquito-borne malaria transmission in a defined geographical area. This is distinguished from eradication, which is defined as 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 can be considered 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. Failure to sustain malaria control and elimination, resulting in resurgence of malaria – as has happened in the past, must be avoided.

Malaria elimination in geographical Africa

Among countries in Africa, six (Lesotho, Libya, Mauritius, Morocco, Seychelles, and Tunisia) have been certified by WHO as malaria free or added to the supplementary list of countries where malaria never existed or disappeared without specific measures. Egypt is at the stage of prevention of re-introduction of malaria and Algeria is currently in elimination programme phase. Cabo Verde is in the pre-elimination stage while the remaining countries in Africa are focused on malaria control.

There is as yet no evidence to indicate, given the current resources, prevailing health care systems, and 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 will improve the possibilities for malaria elimination over the longer time.

Monitoring and evaluation of progress towards malaria elimination

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. As countries progress towards elimination of malaria, two important programme re-orientations are needed: (1) from control programme to elimination programme, and (2) from elimination programme to a programme focused on prevention of re-introduction of malaria. In each re-orientation, substantial changes in activities, priorities and programmatic focus must take place. During each phase, some strategies, activities and specific interventions will be phased out while new are phased in; staff will need to be retrained and new routines established. During these changes, the monitoring and evaluation components of the programme have to be developed to:

- document and guide the reorientation process;

---

34 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.
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 Fund applications. However, countries that do this 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 2009 meeting with WHO and other partners. These include the following issues:

a) 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.

b) 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.

c) Most proposals that seek pre-elimination/elimination are submitted by individual countries, frequently without any 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 summary: 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 document as detailed in the Introduction).

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 for malaria elimination and eventual interruption of transmission are: case detection, prevention of onward transmission (by targeting the mosquito vectors, man-vector contact and the parasites), and management of malaria foci and parasite importation.

Programmes that re-orient 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 anti-malarial medicines;
• Entomological surveillance and effective vector control in transmission foci.

Updated criteria for tracking countries’ progress towards elimination over time have been published in the *World Malaria Report 2012* (p. 67, table R2). These criteria cover (1) the malaria situation in the areas with most intense transmission, (2) case management, and (3) surveillance. They may also be helpful for countries to identify programmatic aspects that need to be addressed for moving forward with elimination.

**Case management**

- All cases in the private and public sector are microscopically confirmed;
- Nationwide microscopy quality assurance system covers public and private sector;
- National Policy for radical treatment with PQ for *P.vivax* is fully implemented;
- National Policy with ACT plus single dose PQ for *P.falciparum* is fully implemented.

**Surveillance**

- Malaria is a notifiable disease nationwide;
- There is a centralized register on cases, vectors and foci;
- There is a National Malaria Elimination Database;
- Active case detection in groups at high risk or with poor access to services is carried out;
- Case and foci investigation and classification are conducted.

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

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