Global **Malaria** Programme

# A framework for malaria elimination

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# Contents

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# Glossary

This glossary comprises all key terms relevant for *A framework for malaria elimination*. The definitions are extracted from those approved by the WHO Malaria Policy Advisory Committee in September 2015. As the terminology is reviewed continuously, readers should visit the WHO GMP website at http://apps.who.int/iris/bitstream/10665/208815/1/WHO_HTM_GMP_2016.6_eng.pdf for updated definitions or more malaria-specific terms.

| | |
|---|---|
| **Case detection** | One of the activities of surveillance operations, involving a search for malaria cases in a community<br><br>*Note: Case detection is a screening process in which the indicator is either the presence of fever or epidemiological attributes such as high-risk situations or groups. Infection detection requires use of a diagnostic test to identify asymptomatic malaria infections.* |
| **Case detection, active** | Detection by health workers of malaria cases at community and household levels, sometimes in population groups that are considered at high risk. Active case detection can consist of screening for fever followed by parasitological examination of all febrile patients or as parasitological examination of the target population without prior screening for fever.<br><br>*Note: Active case detection may be undertaken in response to a confirmed case or cluster of cases, in which a population potentially linked to such cases is screened and tested (referred to as "reactive case detection"), or it may be undertaken in high-risk groups, not prompted by detection of cases (referred to as "proactive case detection").* |
| **Case detection, passive** | Detection of malaria cases among patients who, on their own initiative, visit health services for diagnosis and treatment, usually for a febrile illness |
| **Case investigation** | Collection of information to allow classification of a malaria case by origin of infection, i.e. imported, indigenous, induced, introduced, relapsing or recrudescent<br><br>*Note: Case investigation may include administration of a standardized questionnaire to a person in whom a malaria infection is diagnosed and screening and testing of people living in the same household or surrounding areas.* |

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| **Case, imported** | Malaria case or infection in which the infection was acquired outside the area in which it is diagnosed |
| **Case, index** | A case of which the epidemiological characteristics trigger additional active case or infection detection. The term "index case" is also used to designate the case identified as the origin of infection of one or a number of introduced cases. |
| **Case, indigenous** | A case contracted locally with no evidence of importation and no direct link to transmission from an imported case |
| **Case, induced** | A case the origin of which can be traced to a blood transfusion or other form of parenteral inoculation of the parasite but not to transmission by a natural mosquito-borne inoculation<br><br>*Note: In controlled human malaria infections in malaria research, the parasite infection (challenge) may originate from inoculated sporozoites, blood or infected mosquitoes.* |
| **Case, introduced** | A case contracted locally, with strong epidemiological evidence linking it directly to a known imported case (first-generation local transmission) |
| **Case, locally acquired** | A case acquired locally by mosquito-borne transmission<br><br>*Note: Locally acquired cases can be indigenous, introduced, relapsing or recrudescent; the term "autochthonous" is not commonly used.* |
| **Case, malaria** | Occurrence of malaria infection in a person in whom the presence of malaria parasites in the blood has been confirmed by a diagnostic test<br><br>*Note: A suspected malaria case cannot be considered a malaria case until parasitological confirmation. A malaria case can be classified as indigenous, induced, introduced, imported, relapsing or recrudescent (depending on the origin of infection); and as symptomatic or asymptomatic. In malaria control settings, a "case" is the occurrence of confirmed malaria infection with illness or disease. In settings where malaria is actively being eliminated or has been eliminated, a "case" is the occurrence of any confirmed malaria infection with or without symptoms.* |
| **Case, relapsing** | Malaria case attributed to activation of hypnozoites of *P. vivax* or *P. ovale* acquired previously<br><br>*Note: The latency of a relapsing case can be > 6–12 months. The occurrence of relapsing cases is not an indication of operational failure, but their existence should lead to evaluation of the possibility of ongoing transmission.* |

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| **Entomological inoculation rate** | Number of infective bites received per person in a given unit of time, in a human population<br><br>*Note: This rate is the product of the "human biting rate" (the number of bites per person per day by vector mosquitoes) and the sporozoite rate (proportion of vector mosquitoes that are infective). At low levels of transmission, the estimated entomological inoculation rate may not be reliable, and alternative methods should be considered for evaluating transmission risk.* |
| **Focus, malaria** | A defined and circumscribed area situated in a currently or formerly malarious area that contains the epidemiological and ecological factors necessary for malaria transmission<br><br>*Note: Foci can be classified as active, residual non-active or cleared.* |
| **Malaria elimination** | Interruption of local transmission (reduction to zero incidence of indigenous cases) of a specified malaria parasite species in a defined geographical area as a result of deliberate activities. Continued measures to prevent re-establishment of transmission are required.<br><br>*Note: The certification of malaria elimination in a country will require that local transmission is interrupted for all human malaria parasites.* |
| **Malaria eradication** | Permanent reduction to zero of the worldwide incidence of infection caused by all human malaria parasite species as a result of deliberate activities. Interventions are no longer required once eradication has been achieved. |
| **Malaria reintroduction** | Malaria reintroduction is the occurrence of introduced cases (cases of the first-generation local transmission that are epidemiologically linked to a confirmed imported case) in a country or area where the disease had previously been eliminated<br><br>*Note: Malaria reintroduction is different from re-establishment of malaria transmission (see definition).* |
| **Malaria-free** | Describes an area in which there is no continuing local mosquito-borne malaria transmission and the risk for acquiring malaria is limited to infection from introduced cases |
| **Mass drug administration** | Administration of antimalarial treatment to every member of a defined population or every person living in a defined geographical area (except those for whom the medicine is contraindicated) at approximately the same time and often at repeated intervals |

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| **Population at risk** | Population living in a geographical area where locally acquired malaria cases have occurred in the past three years |
| **Receptivity** | Receptivity of an ecosystem to transmission of malaria<br><br>*Note: A receptive ecosystem should have e.g. the presence of competent vectors, a suitable climate and a susceptible population.* |
| **Recrudescence** | Recurrence of asexual parasitaemia of the same genotype(s) that caused the original illness, due to incomplete clearance of asexual parasites after antimalarial treatment<br><br>*Note: Recrudescence is different from reinfection with a parasite of the same or different genotype(s) and relapse in P. vivax and P. ovale infections.* |
| **Transmission, re-establishment of** | Renewed presence of a measurable incidence of locally acquired malaria infection due to repeated cycles of mosquito-borne infections in an area in which transmission had been interrupted<br><br>*Note: A minimum indication of possible re-establishment of transmission would be the occurrence of three or more indigenous malaria cases of the same species per year in the same focus, for three consecutive years.* |
| **Transmission, residual** | Persistence of transmission after good coverage has been achieved with high-quality vector control interventions to which local vectors are fully susceptible<br><br>*Note: Both human and vector behaviour is responsible for such residual transmission, such as people staying outdoors at night or local mosquito vector species displaying behaviour that allows them to avoid core interventions.* |
| **Vectorial capacity** | Number of new infections that the population of a given vector would induce per case per day at a given place and time, assuming that the human population is and remains fully susceptible to malaria |
| **Vulnerability** | The frequency of influx of infected individuals or groups and/or infective anopheline mosquitoes<br><br>*Note: Also referred to as "importation risk". The term can also be applied to the introduction of drug resistance in a specific area.* |

# Abbreviations and acronyms

| | |
|---|---|
| **ACD** | active case detection |
| **ACT** | artemisinin-based combination therapy |
| **CEP** | Certification Elimination Panel |
| **G6PD** | glucose-6-phosphate dehydrogenase |
| **GMP** | Global Malaria Programme |
| **GTS** | *Global technical strategy for malaria (2016–2030)* |
| **IRS** | indoor residual spraying |
| **ITN** | insecticide-treated mosquito net |
| **LLIN** | long-lasting insecticidal net |
| **MPAC** | Malaria Policy Advisory Committee |
| **PCD** | passive case detection |
| **RCD** | reactive case detection |
| **RDT** | rapid diagnostic test |
| **SDG** | Sustainable Development Goal |

# Preamble

The intention of this document is to provide malaria-endemic countries with a framework for malaria elimination. It gives guidance on the tools, activities, and dynamic strategies required to achieve interruption of transmission and to prevent re-establishment of malaria. It also describes the process for obtaining WHO certification of malaria elimination. The framework is meant to serve as a basis for national malaria elimination strategic plans and should be adapted to local contexts.

The document emphasizes that all countries should work towards the goal of malaria elimination, regardless of the intensity of transmission. Countries should establish tools and systems that will allow them to reduce the disease burden (when and where transmission is high) and progress to elimination of malaria as soon as possible. While malaria elimination should be the ultimate goal for all malaria-endemic countries, the guidance given here is intended mostly for areas of low transmission that are progressing to zero.

**Section 1** describes the key principles underlying malaria elimination, which should be tailored to local contexts. **Sections 2 and 3** describe the interventions and activities recommended in areas of low transmission that are progressing to zero transmission (elimination). The steps required to eliminate malaria serve to prepare programmes and health systems to maintain elimination (see **section 4**). **Section 5** gives an overview of the process for obtaining malaria-free certification from WHO.

# What is new?

This document builds on the WHO document *Malaria elimination - A field manual for low and moderate endemic countries (1)*, published in 2007. Many of the principles outlined in the original document remain relevant; key changes are listed below.

- This framework builds on progress during the past decade, when most countries demonstrated that they can scale up their control programmes and achieve significant reductions in disease burden and, in some cases, eliminate malaria.
- The framework is designed for **all malaria-endemic countries**. It outlines the work required across the spectrum of malaria transmission intensity around the world, in order to end malaria, in alignment with Sustainable Development Goal (SDG) 3.3.
- The programme actions along **the continuum of malaria transmission, from very high to very low**, are highlighted, with emphasis on planning for successive steps. Thus, the distinct categories of "control", "consolidation", "pre-elimination" and "elimination", which are based solely on epidemiological criteria, are not used; rather, the framework suggests that iterative planning with anticipation of transitions and evolving approaches is critical. In addition, it stresses the importance of adapting and tailoring interventions to certain areas in the same country.
- The **requirements for achieving and maintaining elimination** are described.
- Greater emphasis is given to **health systems requirements and programmatic aspects essential** for achieving malaria elimination.
- The role of **information systems and surveillance** as an intervention is highlighted; with modern information and communications technology available to all programmes, information collection and exchange are more rapid and dynamic than previously considered possible.
- Additional emphasis is placed on (i) planning the systems required for **documenting** elimination; (ii) the new role of **verification** (country-specific documentation of subnational elimination) and (iii) the importance of acknowledging **incremental** progress in reducing incidence, illness, severe disease and mortality.
- **Acceleration** and the **speed of change** (rapidly lowering transmission and documenting the impact) are discussed. As they can be more rapid than anticipated, each step towards elimination must be planned early.
- **Rapid diagnostic tests** (RDTs) **and light microscopy are both recommended for malaria diagnosis** in areas and countries that are eliminating malaria.
- The **classification of foci has been simplified**, with three instead of seven types of focus and an emphasis on defined, but adaptable, intervention packages for each focus type.
- **Updated strategies** are based on current WHO recommendations, including the use of mass drug administration. Further updates will be reflected regularly in the online version of this document.

- The process for WHO certification of malaria elimination is **simplified**, with a key role for a WHO malaria Certification Elimination Panel (CEP), a final recommendation by the WHO Malaria Policy Advisory Committee (MPAC) to the WHO GMP and a final decision by the WHO Director-General, who will officially inform the national government.
- A careful national investigation and consultation with WHO will be required before a country loses its malaria-free certification. The **minimum threshold for possible re-establishment of transmission** would be the occurrence of three or more indigenous malaria cases of the same species per year in the same focus for three consecutive years.

# Introduction

## Malaria biology

Malaria is caused by the protozoan parasite *Plasmodium,* which is transmitted by female *Anopheles* mosquitoes, which usually bite between sunset and sunrise. There are four human malaria parasite species – *P. falciparum, P. vivax, P. malariae* and *P. ovale*. Of the non-human malaria parasite species, *P. knowlesi* has recently been reported to infect humans in South-East Asia with increasing frequency, but there is no evidence so far of human-to-human transmission.[1] Of the human malaria parasite species, *P. falciparum* and *P. vivax* pose the greatest threat. *P. falciparum* remains the most dangerous and is responsible for the majority of malaria-related deaths. Outside sub-Saharan Africa, *P. vivax* malaria accounts for about half of malaria cases and predominates in countries that are prime candidates for elimination; the parasite accounts for more than 70% of malaria cases in countries with fewer than 5000 cases each year *(2)*. In contrast to *P. falciparum*, which does not cause persistent liver-stage infection, *P. vivax* can stay dormant in the liver for many months or even years after inoculation and can cause repeated relapses. Thus, the elimination of *P. vivax* malaria is particularly challenging and may in some settings require new tools and strategies *(2)*.

Of about 515 *Anopheles* species, only 30–40 are considered important malaria vectors. Multiple species can coexist within one geographical area, each with its own biting and resting pattern and preferred human or animal host; thus, species vary widely in their transmission efficiency and in their susceptibility to existing or potential anti-mosquito interventions. For more information on the biology of malaria, see **Annex 1**.

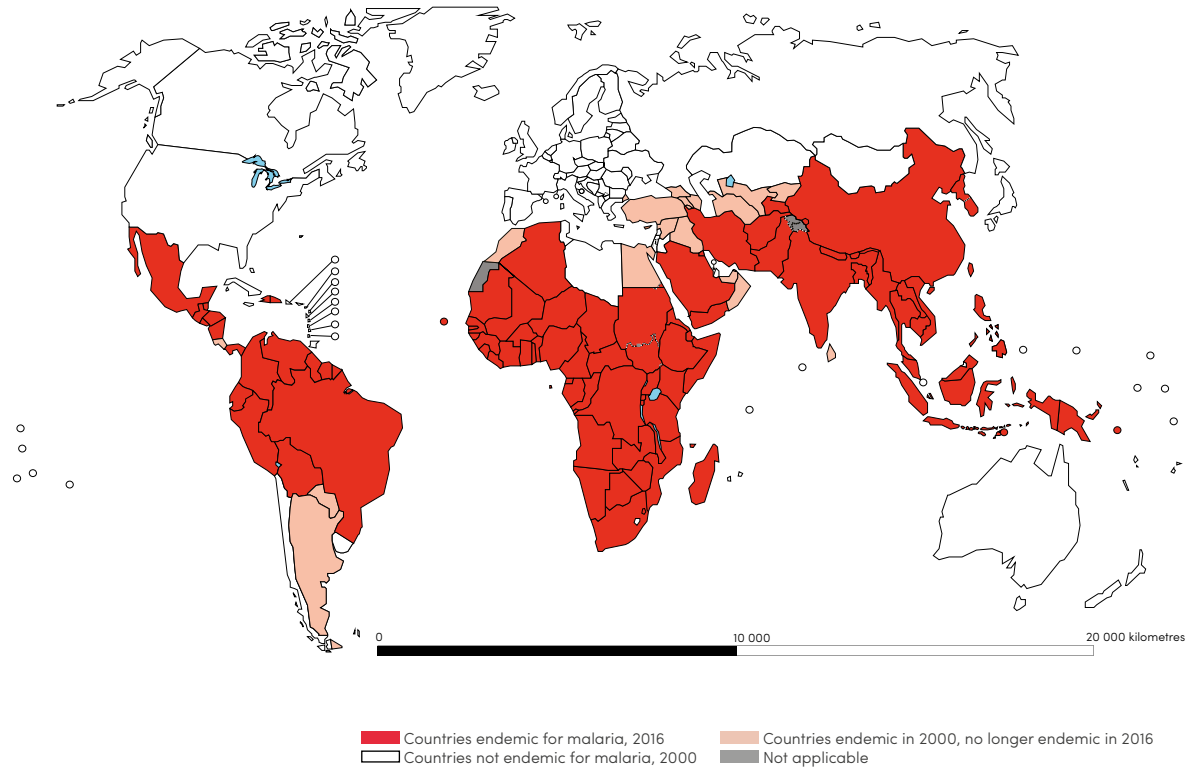
## Recent gains in malaria control

Wide-scale malaria interventions have led to major reductions in overall malaria mortality and morbidity. At the beginning of 2016, an estimated 3.2 billion people in 91 countries and territories *(3)* were at risk of infection with *Plasmodium*. This reflects a remarkable change since 2000. Between 2000 and 2015, the rate of new malaria cases declined globally by an estimated 37%, and the global malaria death rate fell by 60%, with 6.2 million lives saved *(4)*.

Since 2000, 17 countries and territories have been declared no longer endemic or had zero indigenous malaria cases in 2015 (**Fig. 1**). These are: Argentina, Armenia, Azerbaijan, Costa Rica, Georgia, Iraq, Kyrgyzstan, Morocco, Oman, Paraguay, Sri Lanka, Syrian Arab Republic, Tajikistan, Turkey, Turkmenistan, United Arab Emirates and Uzbekistan.

[1] Certification of malaria elimination by WHO requires the elimination of all four human parasite species, and does not require elimination of the non-human parasite *P. knowlesi*.

FIG. 1.
**Countries endemic for malaria in 2000 and in 2016**




Source: *World Malaria Report* 2016 *(3)*

## *Global technical strategy for malaria 2016–2030*

Building on the unprecedented progress achieved over the previous decade, WHO developed a *Global technical strategy for malaria 2016–2030* (GTS) *(5)*, endorsed by the World Health Assembly in 2015, which sets global targets for 2030, with milestones for measuring progress in 2020 and 2025. All countries, including those with high burdens in Africa and elsewhere, will set their own national or subnational targets and will accelerate activities for eliminating malaria transmission and preventing its re-establishment. Progress towards malaria-free status is continuous: countries, subnational areas and communities are at different stages on the path to malaria elimination, and intervention packages can be tailored for use in different settings within a country.

The GTS is an overarching approach based on three pillars and two supporting elements (**Fig. 2**) to guide the design of tailored country programmes, while *Action and investment to defeat malaria 2016–2030 (6)*, developed by the RBM Partnership, builds a strong case for investment to mobilize collective action and resources for the fight against malaria.

The GTS sets the most ambitious targets since those of the Global Malaria Eradication Programme over 50 years ago: by 2030, mortality from and the incidence of malaria should be reduced by at least 90% from the levels in 2015, and malaria should be eliminated in at least 35 countries in which it was transmitted in 2015 (**Table 1**).

FIG. 2.
**GTS framework: pillars and supporting elements**

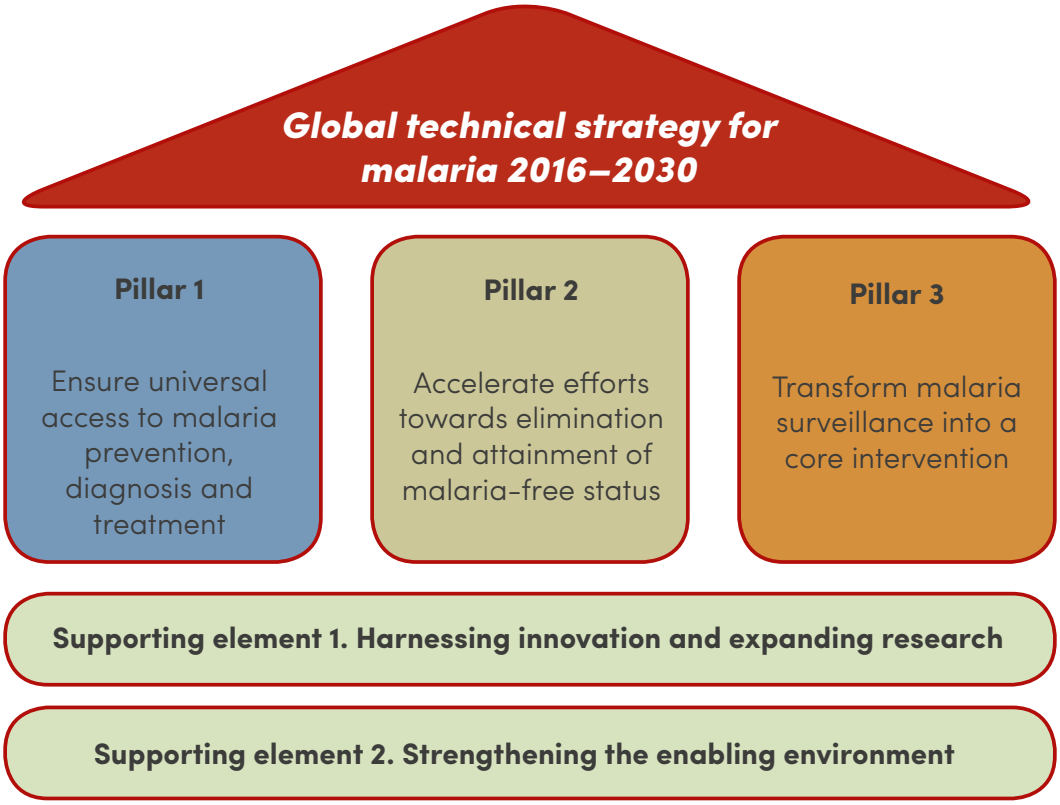



TABLE 1.
**Goals, milestones and targets of the *Global technical strategy for malaria 2016–2030***

**Vision – a world free of malaria**

| GOALS | MILESTONES | | TARGETS |
|---|---|---|---|
| | 2020 | 2025 | 2030 |
| Reduce malaria mortality rates globally compared with 2015 | At least 40% | At least 75% | At least 90% |
| Reduce malaria case incidence globally compared with 2015 | At least 40% | At least 75% | At least 90% |
| Eliminate malaria from countries in which malaria was transmitted in 2015 | At least 10 countries | At least 20 countries | At least 35 countries |
| Prevent re-establishment of malaria in all countries that are malaria-free | Re-establishment prevented | Re-establishment prevented | Re-establishment prevented |

## New guidance for malaria elimination

Since 2007, a number of policies for malaria control have changed, including universal coverage of long-lasting insecticidal nets (LLINs) and diagnostic testing and updated malaria treatment guidelines (see **Box 1**). The previous guidance *(1)* published in 2007 had to be revised to include **all** countries and epidemiological settings, wherever they lie along the continuum to malaria elimination, while providing updated guidance for countries or areas with moderate to very low malaria transmission.

This framework is intended primarily for national malaria programme managers. It will also inform the governments of endemic countries, partners, donor agencies and field workers about malaria elimination and how it is adapted and adopted in settings with different malaria epidemiology and health systems.

BOX 1.
**Key policy changes and reviews since 2007**

**Changes**

- 2007: Universal coverage of insecticide-treated mosquito nets (ITNs) is recommended.
- 2010: Malaria treatment guidelines recommend prompt parasitological confirmation by microscopy or with an RDT for all patients with suspected malaria before treatment is started.
- 2012 (reviewed in 2015): In low transmission areas, a single dose of 0.25 mg/kg body weight of primaquine with ACT should be given to all patients (except for pregnant women, infants aged < 6 months and women breastfeeding infants < 6 months) with *P. falciparum* malaria.

**Reviews**

- 2014: WHO policy recommendation on malaria diagnostics in low transmission settings *(7)*;
- 2015: Guidelines for the treatment of malaria, 3rd edition *(8);*
- 2015: The role of mass drug administration, mass screening and treatment, and focal screening and treatment for malaria *(9)*; and
- 2015: Risks associated with scale-back of vector control after malaria transmission has been reduced *(10)*

# 1. Principles and practice of malaria elimination

This section gives an overview of the principles of malaria elimination, from the moment a country decides to set elimination targets to the point at which the country is certified malaria-free by WHO. These principles are summarized in **Box 2** and further detailed in subsequent sections.

BOX 2.
**Key principles of malaria elimination**

- National malaria elimination is defined as country-wide interruption of local mosquito-borne transmission of a specified malaria parasite species (reduction to zero incidence of indigenous cases).
- WHO certification of malaria elimination in a country requires proof that local transmission of all human malaria parasites has been interrupted, resulting in zero incidence of indigenous cases for at least the past three consecutive years. Measures to prevent re-establishment of transmission are required indefinitely until eradication is achieved.
- No single intervention or package of interventions will achieve malaria elimination in all countries; rather, a set of interventions should be identified and used appropriately for the malaria transmission intensity and dynamics in each country to achieve and maintain elimination. Because of variation in the effectiveness of interventions by place and time, effectiveness should be evaluated regularly to guide adaptation of the country's malaria programme.
- Excellent surveillance and response are the keys to achieving and maintaining malaria elimination; information systems must become increasingly "granular" to allow identification, tracking, classification and response for all malaria cases (e.g. imported, introduced, indigenous).
- Elimination requires that the health system in a country have both strong leadership and the capacity to reach fully into communities (e.g. with systems to ensure access, deliver quality services, track progress and rapidly and effectively respond to epidemiological challenges).
- Operational research on tools, strategies and delivery should generate knowledge to improve guidelines and future elimination activities.
- Every country, including those with a high burden of malaria, may consider malaria elimination as a goal and adjust interventions to accelerate progress towards elimination. Therefore, understanding of the process and requirements for WHO certification of malaria elimination should be global.
- Any country may set subnational elimination targets as internal milestones to maintain public and political commitment and to increase the funding required for attaining national certification.

As further discussed in **section 5**, malaria elimination in a country is officially recognized by WHO certification. In order to be certified malaria-free, a country must show beyond reasonable doubt that local malaria transmission has ended in the country, resulting in zero incidence of indigenous malaria cases for at least the past three consecutive years. This requires that a good-quality surveillance and response system is in place for rapid detection, diagnosis and treatment of any case of locally transmitted malaria. It is essential that countries embarking on malaria elimination establish such systems early in the programme so that they can achieve and maintain their status. Countries should be aware of the requirements for documentation of proof of malaria elimination to be certified as malaria-free.

A country that plans to set subnational elimination targets should establish internal systems to verify malaria-free areas within its borders (see **section 5**). Subnational verification is conducted by countries, including evaluation of candidate subnational areas. Subnational verification not only contributes to strengthening surveillance and response but also provides opportunities for attaining milestones as the country progresses towards elimination, reinforcing national commitment and advocacy for continued or additional funding.

## 1.1 The starting-point: understanding malaria transmission intensity and country stratification

Every country can accelerate progress towards elimination through evidence-based strategies, regardless of the current intensity of transmission and the malaria burden they may carry.

Accurate stratification of malaria transmission intensity is essential for effective targeting of interventions. In settings with high transmission, the malaria control programme usually stratifies subnational areas such as districts or provinces, sometimes by population surveys. As countries progress towards elimination, finer-scale mapping is required, and stratification should be more specific, ideally at the level of localities or health facility catchment areas *(11,12)*. Accurate local stratification requires reliable case detection through a surveillance system in which health facilities routinely receive reports of confirmed malaria cases at specified intervals (weekly, monthly) *(13)*.

As described below and in greater detail in **section 2**, stratification involves classification of geographical units according to their current transmission intensity and, once transmission intensity has been reduced, according to their vulnerability and receptivity to malaria, i.e. the risk for importation of malaria cases and the inherent potential of their vector-human ecosystem to transmit malaria.

Transmission intensity is usually assessed as the incidence of cases or the prevalence of infection. Most countries have information on the annual parasite incidence[2] (number

of new parasitologically confirmed malaria cases per 1000 population per year) from routine surveillance and/or on the parasite prevalence from surveys, often conducted during or just after periods of peak transmission.

The following categories of transmission intensity are indicative and meant to provide an adaptable framework in which each country can conduct a stratification exercise to classify geographical units according to local malaria transmission (see **section 2.2**).

- Areas of **high transmission** are characterized by an annual parasite incidence of about 450 or more cases per 1000 population and a *P. falciparum* prevalence rate of ≥35%.[3]
- **Moderate transmission** areas have an annual parasite incidence of 250–450 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* malaria of 10–35%.
- Areas of **low transmission** have an annual parasite incidence of 100–250 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* of 1–10%. It should be noted that the incidence of cases or infections is a more useful measure in geographical units in which the prevalence is low, given the difficulty of measuring prevalence accurately at low levels *(15)*.
- **Very low transmission** areas have an annual parasite incidence of < 100 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* malaria > 0 but < 1%.

The relation between parasite incidence, parasite prevalence and the number of cases presenting to a health facility per week can be estimated in models *(16)*. For case investigation and focus investigation, local programmes must know the number of cases per health facility per week, as these activities are possible only if health workers see few cases and have sufficient time to conduct investigations within a reasonable workload. Generally, only in areas with "very low transmission" is the number of cases small enough (perhaps fewer than two or three cases per week per health facility) to permit investigation and follow-up. Training and preparation for this work must precede this stage.

Differences in transmission from one area to another may be due to geographical characteristics, such as altitude, temperature and humidity, rainfall patterns, proximity to water bodies, land use, vector distribution, socio-demographic characteristics, access to anti-malarial treatment and implementation of vector control. In most endemic areas, seasonal patterns of transmission are seen, with high transmission during part of the year. Both the intensity and timing of transmission are important considerations in designing elimination strategies.

[2] "Incidence" is the number of new events or cases of disease that develop in a population of individuals at risk during a specified interval *(14)*; here, it is the annual number of new malaria cases per 1000 population at risk.
[3] This rate typically applies only to *P. falciparum*, as such high levels are not usually achieved in *P. vivax* infections.

## 1.2 Aligning country field actions with the *Global technical strategy for malaria 2016–2030*

On the basis of the results of accurate stratification of transmission intensity and understanding of the epidemiological, ecological and social features of each area, national malaria programmes can determine the appropriate package of interventions to be used in each area. The choices should be reassessed regularly. **Fig. 3** presents an indicative set of interventions, aligned with the pillars and supporting elements of the GTS and the WHO vision of malaria elimination, for deployment and enhancement over time as malaria transmission intensity is systematically reduced.

### 1.2.1 Component A: Enhancing and optimizing vector control and case management

Vector control strategies, such as use of insecticide-treated mosquito nets (ITNs/LLINs[4]) and indoor residual spraying (IRS), together with case management (prompt access to diagnosis and effective treatment) are critical for reducing malaria morbidity and mortality, and reducing malaria transmission. In all areas, especially as programmes approach elimination, it is essential to *"Ensure universal access to malaria prevention, diagnosis and treatment"* for at-risk populations (GTS pillar 1).

In many countries, continued access to core malaria prevention will be required even as transmission is markedly reduced: a large proportion of the reduction in receptivity is due to vector control. Once elimination has been achieved, vector control may be "focalized" rather than scaled back, i.e. the intervention should be made available for defined at-risk populations to prevent reintroduction or resumption of local transmission.

### 1.2.2 Component B: Increasing the sensitivity and specificity of surveillance to detect, characterize and monitor all cases (individual and in foci)

According to the GTS pillar *"Transform malaria surveillance into a core intervention"*, countries should upgrade surveillance of parasitologically confirmed malaria to a core intervention, irrespective of their stage of malaria elimination. This is essential for tracking cases and responding to data received.

In this programme step, activities should be started early, even in settings where the intensity of transmission is high or moderate, so that systems are in place for characterizing, classifying and investigating each malaria case and focus as transmission intensity is reduced. For example, early steps to strengthen the surveillance system so that it becomes an actual intervention against malaria include:

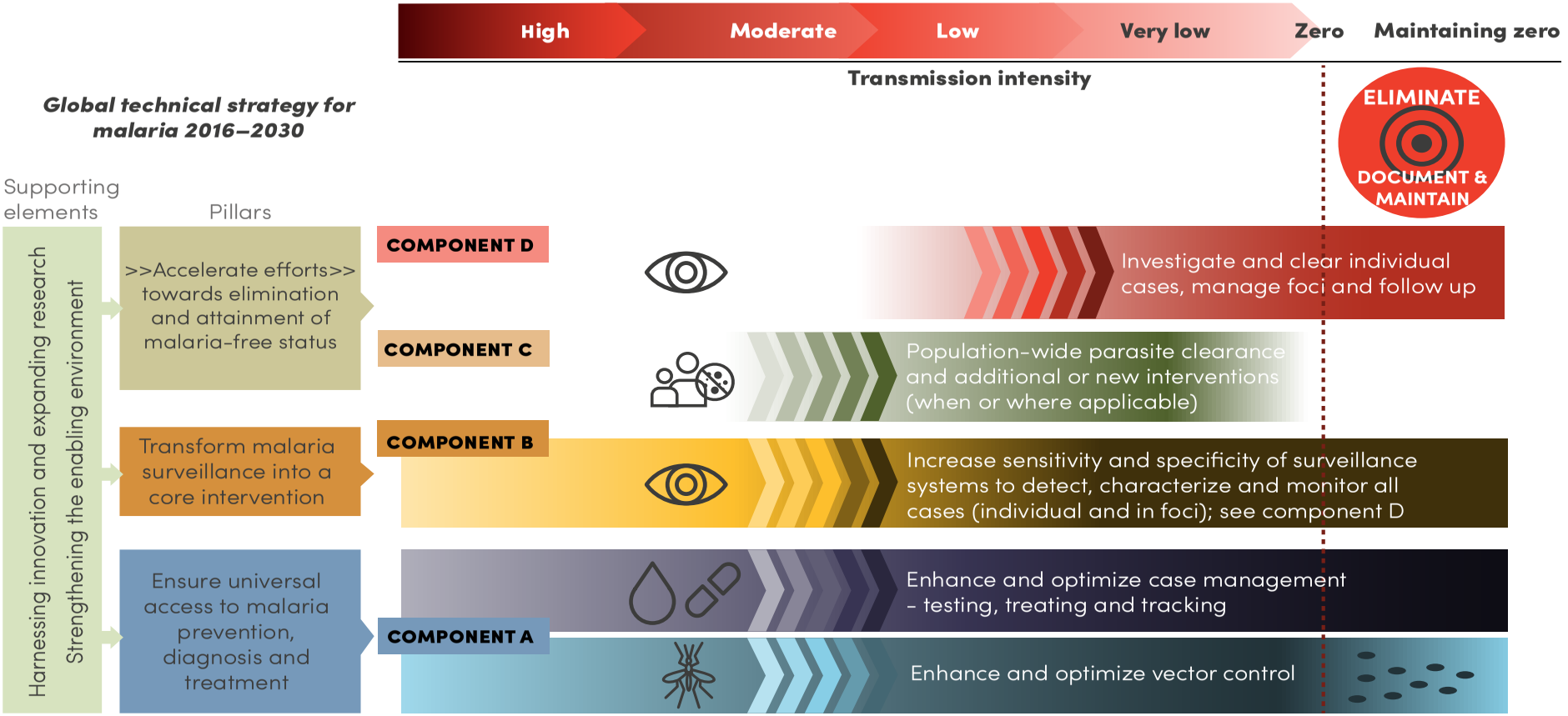
- testing all individuals with suspected malaria and recording all confirmed cases;
- enhancing the quality and timeliness of case reporting through training, supervising and retraining (in case of staff turnover);
- including community case detection, confirmation and reporting of malaria cases;

[4] Since 2007, the ITNs distributed have been LLINs; however, the number of ITNs is still used as an indicator of standard coverage and use. Consequently, and to avoid confusion, this vector control intervention is referred to as "ITN/LLIN" throughout this document.

FIG. 3.

**Illustrative intervention package**

This package of intervention strategies can be adapted for different geographical areas in a country. The choice of interventions should be based on transmission intensity (from "high" to "very low" to zero and maintaining zero) and also on operational capacity and system readiness. The diagram should be seen as illustrative rather than prescriptive, as the onset and duration of interventions will depend on local circumstances. The shading in the boxes showing components indicates the enhancements and quality required as programmes progress towards elimination, with darker colours indicating more intense actions and shading from light to dark indicating enhancement of the quality and scale or focus of the work.




**Acceleration – as represented by arrow bars (>>>>>) here - relates to time-limited efforts made across all components in order to (1) achieve universal/optimal coverage in malaria prevention and case management (**Component A**), and increase sensitivity and specificity of surveillance systems so they are able to detect, characterize and monitor all malaria cases and foci (**Component B**); and (2) bring malaria transmission to sufficiently low levels (with or without population-wide parasite clearance and other strategies, **Component C as an option**) where remaining cases can be investigated/cleared and foci can be managed and followed up (**Component D**).*

- including cases detected by all parts of the health system (e.g. public, private, nongovernmental organizations, military); and
- developing reference laboratory capacity for verification of parasitological diagnosis of malaria, which is required for decision-making.

As transmission is reduced and the number of cases decreases, the information obtained should be more and more detailed and dynamic. Surveillance not only provides information to determine which interventions are required but is also a pivotal component for complete interruption of transmission (see **section 2**). This includes the response triggered by case and focus investigation:

- building systems for reactive case investigation;
- collecting relevant information on travel to determine or estimate whether malaria infections are local or imported; and
- documenting elimination through continuous surveillance and reporting and ensuring that reintroduction does not occur (see below).

All countries that have eliminated malaria have established strong information systems and maintained them to prevent or contain re-establishment of the disease.

### 1.2.3 Component C: Accelerating transmission reduction

As part of the GTS pillar "*Accelerate efforts towards elimination and attainment of malaria-free status*", component C refers to the speed at which universal coverage with core malaria interventions is achieved for at-risk populations and at which surveillance systems generate detailed, dynamic information. Depending on the local context, component C may also include deployment of additional, timely, efficient interventions to reduce transmission intensity to sufficiently low levels that the few remaining infections can be found, treated and cleared as soon as they arise.

Possible means of acceleration include strategies such as population-wide parasite clearance by mass drug administration, which is currently recommended for consideration in areas approaching elimination *(9)*, and potential strategies such as additional vector control and vaccines, if and when they become available. Decisions to use such means of acceleration are made for each location after careful assessment of factors such as transmission intensity and system readiness (see **section 2.7** for more information).

### 1.2.4 Component D: Investigating and clearing individual cases, managing foci and following up

Component D is the other part of the GTS pillar "*Accelerate efforts towards elimination and attainment of malaria-free status*", which can be implemented effectively once a programme has attained a very low intensity of malaria transmission through acceleration strategies. The programme must be capable of finding the few remaining infections and any foci of ongoing transmission and investigating and clearing them with appropriate treatment and possibly additional vector control (see **section 2**).

Documentation of zero infections and no local transmission is critical to verify (in local health facility catchment areas or at district level) and ultimately certify (at national level) that elimination has been achieved. Once elimination has been achieved, surveillance (identifying cases or foci and responding to them) becomes the mainstay of future health system work to maintain elimination. This is the case in every country in which malaria has been eliminated: these countries continue to maintain surveillance and information systems and the ability to detect any introduced or imported cases and ensure no local transmission. **Box 3** describes the case-based method for documenting elimination of malaria.

When a programme achieves and maintains zero cases of malaria, high quality and coverage of the intervention package of components A, B and D must be maintained.

BOX 3
**Documenting malaria elimination *(17)***

Determination of elimination relies principally on a high-quality, comprehensive system for case-based surveillance and outreach, with systematic documentation of the absence of locally transmitted malaria over time, such as the three years before verification or certification of malaria elimination. The case-based measures are the following.

- All cases of suspected malaria are tested with quality-assured methods (RDTs* or microscopy).
- All tested cases are negative or are positive[5] with probable exposure to malaria outside the area.
- All test-positive imported cases are followed and shown not to generate secondary cases transmitted locally.

* The diagnostic performance of currently available RDTs is adequate for the detection of low-density parasitaemia (in the range of 100–200 parasites/μL) caused by *P. falciparum*[6] and *P. vivax* and evaluated by the WHO Product Testing Programme *(18)*. However, RDTs are not evaluated for detection of *P. malariae* and *P. ovale* because of lack of sources of suitable mono-species infections with these parasites. Published data suggest that the sensitivity of RDTs for detecting these species is significantly poorer than that for *P. falciparum* and *P. vivax*. Therefore, negative findings of RDTs targeting all non-*falciparum* infections should be supported by use of more sensitive and specific techniques (i.e. expert microscopy).

As a country creates malaria transmission-free areas, documentation may initially be necessary only for the communities in the catchment areas of one or a group of health facilities. As elimination is extended, the groupings may include full districts, groups of districts, provinces and regions. Such measurement and documentation capacity is necessary for subnational verification and for ultimate certification.

[5] If combination Pf/pan RDTs are used, tests with a positive pan-line and a negative Pf-line require confirmatory testing for species identification by expert microscopy or polymerase chain reaction.

[6] This refers to *P. falciparum* parasites that express HRP2 antigen.

# 2. Strategies and interventions for malaria elimination

## 2.1 Introduction

This and subsequent sections describe the work required as countries approach malaria elimination, moving from low to no local transmission. Key strategies and interventions for malaria elimination are summarized in **Box 4**. Before elimination is attempted, a core set of interventions should already be in place, including optimal coverage of vector control, high-quality, timely case management, and an ever-improving information and surveillance system capable of confirming and characterizing cases, intervention coverage and transmission dynamics.

BOX 4
**Strategies and interventions for malaria elimination: key points**

- Most countries have diverse transmission intensity, and factors such as ecology, immunity, vector behaviour, social factors and health system characteristics influence both the diversity of transmission and the effectiveness of tools, intervention packages and strategies in each locality.
- To manage the inherent complexity of addressing transmission intensities in different geographical areas, malaria programmes should stratify their national maps of malaria distribution into discrete areas.
- Stratification should, if possible:
    - differentiate receptive from non-receptive areas;
    - identify receptive areas in which malaria transmission has already been curtailed by current interventions;
    - distinguish between areas with widespread transmission and those in which transmission occurs only in discrete foci;
    - differentiate strata by transmission intensity, particularly if different intensities are being addressed by different sets of interventions; and
    - determine geographical variations and population characteristics that are associated with vulnerability.
- Stratification allows better targeting and efficiency, with assignment of specific packages of interventions and deployment strategies to designated strata.
- Stratification packages may include:
    - further enhancement and optimization of vector control;
    - further strengthening of timely detection, high-quality diagnosis (confirmation) and management and tracking of cases;

- strategies to accelerate clearance of parasites or vectors in order to reduce transmission rapidly when possible; and
- information, detection and response systems to identify, investigate and clear remaining malaria foci.

- Optimal coverage of ITNs/LLINs or IRS should be ensured and maintained in strata that are both receptive and vulnerable to malaria transmission.
- Vector control interventions should be conducted in addition to ITNs/LLINs and/or IRS according to the principles of integrated vector management and evidence-based, WHO-recommended strategies.

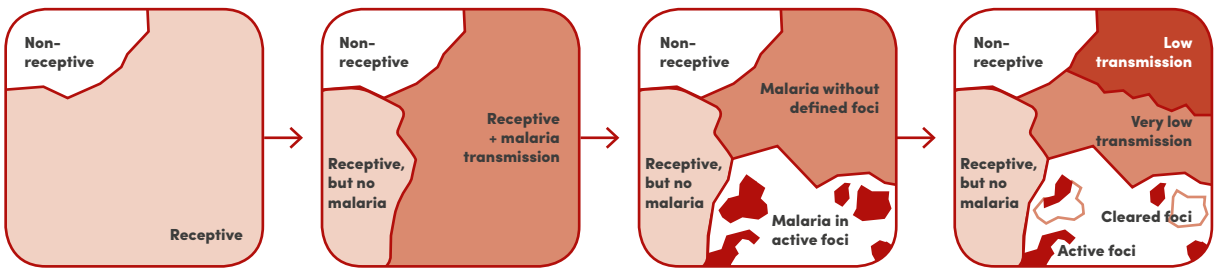
National malaria programmes have tools (e.g. insecticides to kill vectors, methods to prevent vector–human contact, diagnostics to detect infections and document clearance of infections, a variety of medicines to kill parasites in humans) and strategies to use those tools (e.g. spraying insecticides on walls or distributing ITNs/LLINs, managing clinical illness or proactively seeking infected people or at-risk populations to ensure clearance or prophylaxis of malaria infections). As described in **section 6**, new tools and strategies will become available in the future; nevertheless, even current tools and strategies can dramatically reduce the malaria disease burden and transmission; many countries have already eliminated malaria with existing tools. In order to define optimal intervention packages, current and evolving transmission intensities and the ecological and epidemiological features of the areas of a country must be understood.

## 2.2 Local stratification by malaria transmission intensity

As elimination activities are expected to change the epidemiology of malaria rapidly and profoundly, the stratification of national malaria maps should be revised frequently, for example at the end of each transmission season or at an appropriate month of each year.

Geographical units are categorized on the basis of their receptivity (defined as the ability of an ecosystem to allow transmission of malaria) and the intensity of transmission (as described in **section 1**). Stratification should initially be done at the lowest geographical level for which operational decisions can be made, such as a district, sub-district, village or health facility catchment area. Stratification begins with categorization of each selected geographical unit into a stratum, according to the sequence shown in **Fig. 4**.

FIG. 4.
**Sequential stratification according to receptivity and transmission intensity of a diffuse or focal geographical area targeted for malaria elimination**




**1st stratification**
Receptive vs non-receptive

**2nd stratification**
Receptive with and without transmission

**3rd stratification**
Transmission with or without foci

**4th stratification**
Degree of transmission in diffuse or focal areas

The first categorization differentiates receptive from non-receptive areas; the second distinguishes receptive areas without malaria transmission as a result of interventions; the third identifies receptive areas with widespread transmission and areas with transmission only in discrete foci; and the fourth stratifies areas with persistent transmission by transmission intensity to guide targeting of interventions.

Areas with no vectors are not receptive to malaria and should be categorized as such. In practice, in some settings, non-receptive areas are identified as those that have had no vector control and no locally transmitted malaria cases but have had high-quality surveillance for several years. In some countries, certain areas can be categorized as non-receptive on the basis of their landscape. If the smallest geographical unit of stratification comprises both receptive and non-receptive areas, it must be classified as receptive. While vector control is not required in non-receptive areas, cases may still be imported; therefore effective case management will always be required.

At sites in which there is some malaria receptivity but no current transmission, continued measures may be required to prevent re-establishment of transmission. The extent of such measures should be commensurate with the risk for reintroduction of malaria from elsewhere; this risk is known as the "vulnerability" of an area. Vulnerability can be measured directly as the incidence of imported cases in an area or estimated indirectly as the population flow from endemic areas. Receptivity and vulnerability are discussed further in **section 4**.

The progression from low transmission to elimination passes through a phase in which fewer, more discrete malaria foci are identified, investigated and cleared. In "low transmission" areas, transmission may still be too high for observation of discrete foci; in this case, an appropriate package of interventions should be used, comprising either better quality and coverage or the addition of new interventions, to further reduce transmission. In settings with "very low" transmission, cases will increasingly be clustered, and the surveillance system must be sufficiently sensitive to identify such clustering in health facility catchment areas or individual villages, to characterize it fully and to clear the infections and remaining transmission. The surveillance programme must be strengthened well in advance so that the staff and systems are fully prepared to undertake this work, which is required for the achievement and documentation of elimination.

## 2.3 Enhancing and optimizing vector control

Two core vector control strategies are currently recommended by WHO: universal access to and use of ITNs/LLINs or universal access to IRS for populations at risk for malaria.

### 2.3.1 Core vector control interventions

ITNs/LLINs and IRS are core interventions for reducing the human biting rate and vector survival, which significantly reduce vectorial capacity and transmission. ITNs/LLINs provide protection for the occupants of houses against biting malaria mosquitoes by killing them before they can take a blood meal, whereas IRS kills mosquitoes that rest indoors after they have taken a blood meal.

While the effectiveness of both these interventions is maximal with high coverage and use, their impact is temporary and depends on their maintenance. Premature withdrawal of ITNs/LLINs and IRS can result in a rebound of malaria transmission to pre-existing levels (see **section 2.3.4**).

Optimal coverage of ITNs/LLINs or IRS should be maintained in strata that are both receptive and vulnerable to malaria transmission. The receptivity of an area is not static but is affected by determinants such as environmental and climate factors. The many anopheline vectors around the world differ in the efficiency with which they transmit malaria. Thus, some, such as the nocturnal indoor-biting and indoor-resting mosquitoes in sub-Saharan Africa, are more amenable to control by indoor interventions. Earlier and/or outdoor biting and resting anophelines in other continents may be less so, although some will enter houses and be killed by the interventions. Thus, ITNs/LLINs and IRS continue to be relevant both in sub-Saharan Africa and elsewhere.

#### 2.3.1.1 ITNs/LLINs

High coverage of ITN/LLIN can be achieved and maintained most rapidly by a combination of mass free-distribution campaigns and continuous distribution channels *(19)*. Distribution campaigns with a target of one net for every two people or one net for every sleeping space can rapidly achieve high coverage. As many households have an odd number of occupants, an overall ratio of 1 ITN/LLIN for every 1.8 people in the targeted population should be used to calculate overall ITN/LLIN procurement *(20)*. The frequency of mass campaigns should be decided on the basis of net durability, and only WHO-recommended ITNs/LLINs should be procured and distributed. Programmes should consider maintaining stocks of ITNs/LLINs for local replacement, which requires a modest additional number of ITNs/LLINs over that calculated for the campaign and continuous distribution schemes.

Continuous or routine distribution channels include: antenatal, child health and vaccination services; schools, places of worship and community networks; work sites (e.g. plantations, military facilities, mines and farms) and the private or commercial health sector.

#### 2.3.1.2 IRS

All programmes for malaria elimination should establish and maintain their capacity to conduct IRS for rapid clearance of transmission foci and as an adjunct or targeted control measure, even where ITNs/LLINs are the core vector control strategy, especially in areas in which the vectors are resistant to pyrethroids. A significant advantage of IRS for the containment of malaria foci is that it does not require human behavioural change, except when people refuse access to their houses or re-plaster their walls soon after spraying; such problems can sometimes be solved by using a more acceptable insecticide. Unlike ITNs/LLINs, which remain effective during several transmission seasons, IRS may be effective for only two to six months, depending on the insecticide formulation and spray surface.

Failure to achieve high coverage and high-quality implementation of either ITNs/LLINs or IRS should not be compensated by adding the other intervention *(5)*. Continued use of ITNs/LLINs is recommended even in areas where vectors are moderately resistant to the ITN/LLIN insecticide. In areas with vectors resistant to pyrethroids, where ITNs/LLINs are the primary intervention, IRS with application in rotation of different classes of insecticide should be used to manage resistance *(21)*.

### 2.3.2 Supplementary vector control strategies

While factors that may limit the effectiveness of existing vector control interventions must be addressed, even full implementation of core interventions cannot halt malaria parasite transmission in all settings. Evidence from various areas indicates that residual malaria parasite transmission occurs even with good access to and use

of ITNs/LLINs or well-implemented IRS, as well as in situations where ITN/LLIN use or IRS are not practical *(22)*. The behaviour of both humans and vectors is responsible for residual transmission, such as when people live in or visit forest areas or do not sleep in protected houses or when local mosquito vector species have one or more characteristics that allow them to avoid the IRS and ITN/LLIN intervention tools.

Additional vector control interventions should be practised to supplement ITNs/LLINs and/or IRS on the principle of integrated vector management and evidence-based, WHO-recommended strategies. Such supplementary interventions can accelerate a reduction in transmission intensity. They should be implemented concurrently with, but not in lieu of, optimal coverage with ITNs/LLINs or IRS.

#### 2.3.2.1 Larval source management

Larval source management consists of the management of water bodies that are potential sites for anopheline oviposition *(23)* in order to reduce the production of adult vectors, either temporarily or permanently. This intervention is recommended in areas where larval habitats are "few, fixed and findable" *(24)*, i.e. close to houses; such conditions are likely to exist when transmission has become increasingly focal. Effective larval source management requires understanding of the ecology of larval habitat productivity and effective monitoring of both the larval and adult stages of the vector in order to determine the effectiveness of the intervention. Larval source management can be categorized as habitat modification, habitat manipulation, biological control or chemical larviciding (including the use of insect growth regulators). Use of the last three categories can temporarily reduce vectorial capacity and contribute to malaria elimination in some settings; however, permanent removal of larval habitats (habitat modification) will reduce potential re-establishment of transmission once malaria has been eliminated, by permanently reducing the density of the vector population and proportionally reducing vectorial capacity. Reintroduction of malaria parasites into an area with effective habitat modification will be less likely to result in local malaria transmission.

#### 2.3.2.2 Additional strategies

Additional strategies may be required to reduce the disease burden caused by vectors that feed outdoors or early in the day or are resistant to insecticides. The value of innovation and research in creating such strategies and in the development of new insecticides for ITNs/LLINs, IRS and larval source management and the means for their implementation are recognized as one of two supporting elements in the GTS, Harnessing innovation and expanding research. Use of new vector control strategies and new products that are under development (see **section 6**) may be considered once information on their effectiveness is available and the products are approved for use in programmes.

### 2.3.3 Vector control activities in active transmission foci

As malaria incidence falls and elimination is approached, increasing heterogeneity in transmission will result in foci with ongoing transmission, in which vector control should be enhanced *(25)*. Such foci may be due to particularly intense vectorial capacity, lapsed prevention and treatment services, changes in vectors or parasites that make the current strategies less effective, or reintroduction of malaria parasites by the movement of infected people or, more rarely, infected mosquitoes.

The vector species should be identified and their susceptibility to currently used insecticides evaluated. Supplementary vector control may be justified in some settings,

such as for vectors that are not vulnerable to ITNs/LLINs or IRS due to physiological or behavioural resistance. Supplementary vector control should be based on WHO-recommended strategies and with products approved by the WHO Pesticide Evaluation Scheme (http://www.who.int/whopes/en/).

### 2.3.4 Vector control activities after elimination or prevention of re-establishment *(10)*

Soon after elimination has been achieved, vector control coverage should be maintained in receptive areas where there is a substantial risk for reintroduction (vulnerable areas). An assessment in 2015 by the WHO Vector Control Technical Expert Group indicated that discontinuing vector control increases the risk for malaria resurgence, even in areas with substantially reduced transmission, and the risk increases with increasing receptivity and importation rates and low coverage of active disease surveillance and case management. WHO therefore recommends the following.

- In areas with recent local malaria transmission (residual non-active foci), a reduction in vector control is not recommended. Optimal coverage with effective malaria vector control (including the use of new tools when they become available) of all people in such areas should be pursued and maintained.
- In areas where transmission has been interrupted for more than three years (cleared foci), any reduction in vector control should be based on a detailed analysis, including assessment of the receptivity and vulnerability of the area and the capacity for active disease surveillance and response.
- Countries and partners should continue to invest in health systems, including continuous support for malaria surveillance; when receptivity is reduced, a reduction in vector control may be considered in some geographical areas.

Vector control programmes should assess the receptivity of a geographical area from data predating increased use of ITNs/LLINs and IRS and should also consider the dynamic nature of receptivity. Changing land use patterns (including urbanization), climate, housing quality and use of strategies that permanently reduce vectorial capacity (e.g. environmental modification) may dramatically reduce malaria receptivity. Changes that increase receptivity may be less common but might include the introduction of agricultural, mining or forestry activities that multiply vector breeding sites.

### 2.3.5 Monitoring and evaluating vector control

Monitoring the coverage, quality and impact of vector control interventions is essential to maintain the effectiveness of control (see illustrative list of indicators in **Annex 3**). Each programme should identify and use relevant indicators according to their priorities, especially process indicators, in accordance with strategic and operational plans. Any indicator measured should generate data that can be used for response. Monitoring and evaluation of vector control should include all ecological and epidemiological scenarios, including areas from which malaria has been eliminated but which remain at risk for re-establishment of transmission.

The numbers of ITNs/LLINs distributed and of houses sprayed and vector breeding sites should be determined by geo-positioning and mapping in order to evaluate intervention coverage and its effect. Interventions directed at either the adult or

the larval stage should be evaluated by monitoring relevant changes in vector characteristics, such as susceptibility to the insecticide, vector density and the behaviour of the adult vector population. Malaria vector control programmes should quickly detect and respond to such changes if necessary.

- The effectiveness of anti-larval campaigns should be evaluated by their impact on adult mosquito populations; larval surveys alone are not sufficient *(23)*.
- The effectiveness of ITNs/LLINs and IRS depends on the timing and location of blood meals. Strategies for sampling adult vectors are not effective for all vector species and do not work equally well indoors and outdoors, with the exception of human landing catches.[7] Paired (indoor and outdoor) all-night landing catches at the times of peak vector population enable simultaneous determination of the relative frequency of outdoor- and indoor-biting and the time of biting. The samples collected can be used to determine the vector species present, to estimate survivorship and to determine susceptibility to insecticides.
- Residual malaria transmission can occur even with good access to and use of ITNs/LLINs or well-implemented IRS as well as in situations where ITN/LLIN use or IRS are not practical. Good understanding of the behaviour of local vector species (feeding, resting and breeding preferences) and of the human population (sociocultural factors such as mobility, extent of uptake of preventive measures by vulnerable populations such as forest workers, and difficulty in achieving optimal adherence to anti-malarial treatment) should be the basis of a plan to control malaria in such areas of residual transmission.

## 2.4 Enhancing and optimizing case detection and case management

As transmission decreases, it becomes essential to enhance[8] case detection and case management to find all suspected malaria cases, test for confirmation of malaria infection, treat all cases according to national treatment policies to clear infections, characterize and classify infections by their most likely place of origin and report cases and actions taken to the national surveillance system.

### 2.4.1 Case detection

Cases can be detected by passive case detection (PCD), when patients seek care for their illness from health workers; active case detection (ACD), which requires extension of testing with or without screening to high-risk, vulnerable groups, hard-to-reach populations or low-transmission settings; and reactive case detection (RCD), which involves an active response to a case detected by either PCD or ACD. Testing should be conducted with a high-quality diagnostic test and the case reported after confirmation. When people are screened for symptoms before testing, cases are suspected when they occur in people with fever or a recent history of fever, a history of malaria, anaemia of unknown cause or splenomegaly. In areas with low, very low or

[7] Human landing catches do not increase the risk of the collectors for malaria over that of the general adult population when collection is undertaken by recommended practices; e.g. collectors are provided with prophylaxis and are recruited from the local adult population. Human landing collections are not recommended in areas with active arbovirus transmission.

[8] The concept of "enhanced" interventions suggests tailoring access to and coverage and use of an intervention to address the epidemiological situation optimally. Even if all health facilities have the capacity to confirm diagnoses and treat cases, the need for and opportunity to extend the services to communities should not be ignored. "Optimization" requires local assessment of what can be done and planning to achieve the best possible results aggressively.

no transmission, a history of travel to an endemic area is a strong criterion for testing. Examples of the information required on cases are given in **Annex 7**.

#### 2.4.1.1 Passive case detection

Clinical malaria cases are usually initially identified by health workers in health facilities or by community health workers in villages by PCD, as part of the routine diagnostic and treatment services provided to the population. If the population has good access to health care workers, PCD can result in early identification and treatment of cases and reduce the risk for ongoing transmission.

Effective PCD services have become much more common and less costly since RDTs and electronic data recording and transmission became available. The services can be provided by health workers or volunteers in health facilities or in the community and are a priority for all malaria programmes. PCD in areas in which elimination is being undertaken should cover the entire population, including people living in remote areas, to increase the probability that any case of illness that might be malaria will be rapidly tested, treated and reported. Programmes should identify, by mapping or another means, any communities in receptive areas that are far from public health facilities and add additional health posts or community health workers to those locations to extend the reach of the PCD network. Imported malaria cases can occur in non-receptive areas and should also be correctly managed.

Confirmed cases should receive the full recommended treatment (including radical treatment for *P. vivax* to clear persistent liver-stage parasites and single-dose primaquine for *P. falciparum* to clear gametocytes) and be followed up at recommended intervals to ensure complete cure. All confirmed cases must be reported to health information systems (see **Annex 7**). It is advisable that both negative and positive results be reported to demonstrate whether testing is sufficient in all at-risk populations.

#### 2.4.1.2 Active case detection

ACD requires extra effort to find malaria cases among people who do not present to health facilities, for various reasons, including living in a remote area, populations such as migrants and refugees who may not use or have access to routine health care and asymptomatic infections. ACD can play an important role in elimination programmes by detecting infected people who may risk transmitting malaria but are not detected by PCD. As in PCD, all patients with confirmed malaria should receive the full recommended treatment, be followed up to ensure that the infection is cleared and be reported to health information systems.

If ACD is conducted because of limited or under-utilization of health care services, it may comprise initial screening for symptoms, followed by appropriate laboratory confirmation. In low-transmission settings or as part of a focus investigation, ACD may consist of testing of a defined population group without prior symptom screening (population-wide or mass testing) in order to identify asymptomatic infections.

ACD has limited benefit for *P. vivax* malaria, because liver-stage hypnozoites cannot be detected with current testing methods. In subtropical areas (and, more markedly in the past, in temperate climates), *vivax* malaria often has a seasonal pattern. Intensified case detection could be a rational choice for ensuring detection of relapses and delayed primary attacks during those seasons.

### 2.4.1.3 Reactive case detection

ACD may also be conducted in a targeted, reactive fashion after identification (by either PCD or ACD) of a local or imported case. The rationale is that, at low transmission intensity, malaria cases are highly aggregated; thus, where there is one, there will be more. RCD is an important component of an elimination strategy at low transmission intensity and is related to the concept of focus investigations. The type of RCD is determined by how the case is identified, how wide the net is cast around the index case and who is tested; the strategy chosen for a given area depends on local epidemiology and the health system. **Table 2** illustrates the roles of different types of case detection.

TABLE 2.
**Roles of different types of malaria case detection**

| TYPE OF CASE DETECTION | WHERE MOST APPLICABLE | HOW CASES ARE IDENTIFIED | USEFULNESS |
|---|---|---|---|
| Passive case detection (PCD) | Areas with good access to and use of health care services in either facilities or the community | Testing of symptomatic individuals seeking treatment | Usually the easiest type of case detection and that best suited to higher levels of transmission. PCD is not sensitive enough to be the only means of detecting cases as areas approach elimination, but information from PCD may be useful in low-transmission settings for identifying areas with ongoing transmission. |
| Active case detection (ACD) | • Areas or populations with limited access to health care<br>• Populations that under-use health care services (e.g. migrants and other hard-to-reach populations)<br>• "High-risk" settings such as refugee camps<br>• Areas approaching elimination<br>• For detection of asymptomatic infections | One of two approaches, depending on the context:<br>• Where there is limited access to or under-use of health care services, ACD may include initial screening for symptoms and/or risk factors, followed by testing.<br>• When the goal is identification of all infections, including those that are asymptomatic, ACD involves testing all individuals. | ACD may not be feasible when transmission intensity is high, but it may be the only method available for identifying cases in areas or populations for whom health care services are not available or are under-used. As areas approach elimination and asymptomatic infections are targeted, ACD becomes increasingly important. ACD can be used to map transmission in a focus or identify high-risk groups. |
| Reactive case detection (RCD) | After identification of a local or imported case in a receptive area where transmission intensity is low or assumed to be interrupted | • Testing of family members, neighbours and community members in a specified radius, co-workers, people in areas recently visited by the index case or others as appropriate, irrespective of symptoms.<br>• May be initiated as a component of a focus investigation. | Not feasible at higher transmission intensity but is particularly important as intensity decreases. The most efficient, sensitive, feasible radius for testing around the index case will depend on the epidemiology and health system. |

### 2.4.2 Parasitological diagnosis

Malaria infection is detected in symptomatic cases primarily in blood by RDTs or microscopy.

- RDTs allow detection of parasite antigens, and some tests differentiate species. They are easy to use in communities by both health workers and trained volunteers.
- Microscopy allows direct visualization of parasites, determination of species and stages and quantification of the density of parasites. It requires well-trained staff and laboratory support.

Therefore, RDTs should be available at all levels in health facilities and community services, while quality-assured microscopy should be available in hospitals and designated laboratories. RDTs should be available even at health facilities with good laboratories, because they allow rapid diagnosis when laboratory personnel are absent. RDTs and microscopy can be used to detect almost all symptomatic infections and many but not all asymptomatic infections.[9]

More sensitive diagnostic methods, such as polymerase chain reaction and other molecular techniques, are used to detect asymptomatic infections with very low parasite densities. These tests may be useful in surveys for mapping submicroscopic infections, but their value depends on the epidemiological significance of low-density infections, which is not yet sufficiently defined. Currently, most molecular methods can be performed only in laboratories with sophisticated equipment and skilled personnel; they are not recommended for routine case management or surveillance.

Both RDTs and microscopy must be supported by a quality assurance programme. More information on malaria diagnosis in low-transmission settings is given in reference *(26)*.

### 2.4.3 Treatment

Malaria treatment should follow national policies and WHO guidelines *(8)*. Treatment that fully clears malaria infection is required in the context of malaria elimination. Thus, for cases due to *P. vivax* or *P. ovale*, in addition to clearance of the blood infection, anti-relapse therapy (primaquine) is required to clear liver-stage parasites; and, for all infections caused by *P. falciparum*, a gametocytocidal drug (primaquine) should be administered in addition to treatment for the blood stage to reduce and eventually halt transmission.

Treatment should be provided through all channels of service delivery: public facilities, private facilities and community outreach. The optimal mix will depend on the country. As transmission and malaria incidence are reduced, increased coverage and better access to high-quality care should be ensured through all three channels.

#### 2.4.3.1 The public health sector

All health institutions in the public sector should serve as diagnosis and treatment centres for malaria. Free-of-charge malaria testing and treatment should be

[9] RDTs may be less sensitive for detecting *P. ovale* and *P. malariae* than *P. falciparum* and *P. vivax*; microscopy should be considered for detection of these infections when necessary.

encouraged in order to cover all population groups with malaria who contribute to ongoing transmission, including illegal residents.

#### 2.4.3.2 The private health sector

This sector comprises a wide range of health care providers: medical practitioners, licensed pharmacies, unlicensed drug vendors, authorized services for the employees of private companies and not-for-profit services, such as nongovernmental organizations and faith-based organizations. Depending on national policies and regulations, all may be involved in malaria diagnosis, treatment and surveillance. Their engagement requires that the public sector invest in communication, training, monitoring and, in many cases, provision of quality-assured diagnostics and medicines. The not-for-profit private sector often provides high-quality services. The informal private sector, however, may be a major source of irrational treatment, substandard medicines and under- or no reporting of malaria cases. When elimination targets are set, the informal private sector may require specific attention. Each country should develop a strategy for determining the most appropriate role for various types of private providers.

#### 2.4.3.3 Community services

Many countries have well-established community case management services that provide diagnosis, treatment and reporting of clinical cases of malaria free of charge. Technically, community service providers are part of public services, but the providers themselves are often volunteers, who depend on support from health workers in peripheral health facilities, their community or nongovernmental organizations. In some countries, community workers receive regular remuneration. Because community services are often the best solution for people living in remote areas, countries should consider how to ensure high-quality community outreach that includes testing and treatment for malaria.

The quality of care relies on appropriate diagnosis, treatment and counselling of patients and carers, applied with clear protocols and monitoring systems. The administration of medicines under supervised treatment (sometimes referred to as directly observed treatment, or DOT) may improve patient adherence to treatment and allows close patient monitoring during treatment. Until more evidence is available, programmes should apply the supervised treatment that is most appropriate to their context.

Strategies and treatment guidelines for *P. falciparum* and *P. vivax* malaria are described in **Annex 2**.

#### 2.4.3.4 Detecting and treating asymptomatic infections

A complex set of factors and mechanisms, such as innate or acquired immune response, a functioning spleen, genetic factors, including deficiency for glucose-6-phosphate dehydrogenase (G6PD) and haemoglobinopathy, determine the timing and extent of malaria symptoms after infection.

In general, in areas of high transmission, people usually experience repeated infections from early in life and develop a significant degree of immunity with increasing age

and exposure. That is why, in such areas, the risk of clinical malaria and death tends to be concentrated in younger children. Acquired immunity tends to limit parasite replication but rarely leads to sterilizing immunity. As such, in areas with significant levels of acquired immunity, a high proportion of the population can harbour parasites in the absence of significant clinical manifestations. This same epidemiologic picture applies to areas that have only recently reduced transmission as acquired immunity to malaria can last for many years.

In contrast, in areas of very low transmission where the risk of infection throughout life is low, few people develop any significant level of immunity. Those infected, even at very low parasite densities, will exhibit clinical signs and symptoms. Therefore, the proportion of the population infected in the absence of clinical manifestations would tend to be very low.

While all malaria elimination programmes must provide timely diagnosis and treatment for all malaria cases, they should consider the local transmission dynamics and determine whether, when and where to seek and treat asymptomatic individuals, who do not present to health facilities for care. Such an approach should be considered only in the context of persistent transmission in spite of intensified vector control and efficient surveillance systems.

If local malaria transmission persists despite intensive vector control and universally good case management, the programme may consider undertaking special studies to evaluate the distribution and frequency of infections in the asymptomatic population.

If the programme decides that all symptomatic and asymptomatic infections in an active focus must be cleared, the work must be well planned and all efforts made to reach the entire targeted population, including ill and apparently healthy people, young and old. Special consideration should be given to the treatment of specific populations (e.g. pregnant women, newborns, mobile populations).

The following points should be considered.

- Currently available point-of-care tests for malaria have little capacity to detect low-density infections; thus, consideration should be given to treating the entire population, regardless of test results and regardless of symptoms.
- All people should be treated with safe, effective anti-malarial medicines that will clear all *asexual* stage parasites.
- For *P. falciparum* infections, treatment to clear sexual stage parasites (gametocytes) should also be given. Currently available artemisinin-based combination therapy (ACT) is effective against developing stages 1–4 gametocytes but not the infectious stage 5 gametocytes, which require a gametocytocide (i.e. single-dose primaquine at 0.25 mg/kg of body weight) *(27)*,[10] which can prevent the transmission to mosquitoes of sexual stage parasites present in the blood.

[10] The recommendation includes the following: In low-transmission areas, give a single dose of 0.25 mg/kg of body weight primaquine with an ACT to patients with *P. falciparum* malaria (except pregnant women, infants aged < 6 months and women breastfeeding infants aged < 6 months) to reduce transmission. Testing for G6PD deficiency is not required.

- For confirmed *P. vivax* (and the much less common *P. ovale*), treatment should include both schizontocidal medicine and anti-relapse therapy to clear their dormant liver-stage parasites (hypnozoites). Ideally, treatment should be administered only after G6PD testing is performed; the appropriate dose and duration of primaquine can then be selected (see **Annex 2**). Such treatment dramatically reduces the frequency of relapses and their contribution to transmission.

## 2.5 Role of quality assurance and reference laboratories in malaria elimination *(28,29)*

Quality assurance within national malaria control programmes and national malaria reference laboratories ensures high-quality laboratory diagnosis and treatment of malaria in a country.

### 2.5.1 Quality assurance *(30)*

As malaria programmes seek elimination, consistent quality of work is essential, particularly for detecting, confirming, treating, tracking and reporting on malaria cases. The core of this work is preparation of standard operating procedures and training, including re-training and continuing education, and supervision, including monitoring of performance. Various examples of guidance for ensuring the quality of care in health service delivery are available on the WHO website (http://www.who.int/management/quality/en/). Specific guidance for malaria programmes emphasizes high-quality laboratory testing for malaria.

### 2.5.2 Malaria reference laboratories

Reference laboratories are essential for ensuring the quality of malaria services. They are generally identified by the ministry of health and may be based in a research institute, a medical school or a large hospital; they collaborate closely with the national malaria elimination programme. A national reference laboratory should have the necessary laboratory space, equipment, reagents and consumables and a sufficient number of expert microscopists and should participate in international external quality assessment programmes. WHO has established a programme for testing the proficiency of national reference laboratories for several diseases, including malaria *(31)*.

Examples of activities carried out by national reference laboratories include:

- developing and using guidelines for diagnostic policy, with supportive training, accreditation and supervision;
- preparing standard operating procedures for testing, laboratory techniques and equipment specifications, disseminating them to national or regional laboratory networks and providing technical assistance for national use;
- overseeing internal and external quality assurance, including comparing the sensitivity, specificity and predictive value of all tests used in the country and evaluating diagnostics for all human malaria parasite species (**Annex 2** shows evaluations for *P. falciparum* and *P. vivax* infections);
- coordinating the servicing and maintenance of equipment in the laboratory network;

- liaising with procurement agencies and tender boards to ensure that the diagnostic equipment and reagents procured meet the recommended minimum criteria and arrive on time;
- coordinating the referral of samples from district laboratories and providing confirmatory testing and special testing services (e.g. molecular and serological tests, expert microscopy); and
- establishing and standardizing information management protocols and practices for collecting laboratory data in multiple information systems (i.e. DHIS2).

Reference laboratories could also participate in operational research or activities such as assessing the diagnostic performance and utility of new tools and supporting programmes in their introduction and dissemination.

## 2.6 Surveillance

This section describes the core elements of a surveillance system that will allow countries to achieve malaria elimination. Surveillance of malaria infection in the human population is the backbone of malaria elimination.[11] Identifying where transmission is occurring with increasing accuracy will permit targeted, effective responses where they matter most. Steady improvements in the quality, timeliness and use of surveillance information must begin early in malaria programmes to ensure that elimination work is well directed and monitored. Ultimately, surveillance will become part of the intervention, focused on case characterization, treatment and investigation and on identification, management and clearance of transmission foci.

Malaria surveillance systems are described extensively in operational manuals on malaria elimination *(32)* and malaria control *(33)* issued by WHO. Both manuals will be revised in 2017; see the WHO GMP website for updated information.

### 2.6.1 Increasing sensitivity of surveillance systems for elimination

In areas of high and moderate transmission intensity, aggregated data are usually sent from level to level (health facility to district to province to national level), and most analysis of distribution and trends is done at higher levels.

As case-loads are reduced and capacity is built, surveillance should include data on individual cases, characterized and classified according to their most likely place of origin. Cases should be geo-located to understand where transmission is occurring. Staff at all levels should be trained to examine and evaluate surveillance data, on both disease and operations, and to monitor programme progress, target interventions and detect problems that require action.

The surveillance system must be sufficiently robust to capture all infections (probably with increasing community outreach) as the number of cases falls and clinical cases and asymptomatic infections are identified, and sufficiently sophisticated to fully characterize each infection and direct local investigations and clearance of transmission.

[11] Monitoring of vectors and vector control is also important and is described in **section 2.3.5**; this section addresses malaria infections in humans.

### 2.6.2 Surveillance as an intervention to eliminate malaria

Surveillance was recognized as an intervention for malaria eradication in and of itself in the initial Global Malaria Eradication Programme. In elimination settings, malaria surveillance comprises a set of responses that should allow (i) detection of all malaria infections (symptomatic and asymptomatic) as early as possible; (ii) prevention of onward transmission from each case through rapid, radical treatment and vector control; and (iii) identification, investigation, classification and management of all transmission foci with appropriate measures to terminate transmission as soon as possible.

The key activities of elimination surveillance systems are:

- ensuring that an entire area (national or subnational) targeted for elimination is covered, with particular attention to areas with on-going or recent transmission;
- quality-assured diagnostic testing;
- testing of all cases of suspected malaria, reporting of all confirmed cases, investigation of all cases and foci and recording of all tests and investigations;
- case detection activities to:
    - ensure rapid, complete treatment for parasite clearance in as many cases as possible to minimize the time during which cases can infect vectors; and
    - provide information to monitor the programme's progress;
- following standard operating procedures for all components of surveillance and monitoring compliance in real time; and
- participation of all health care providers treating malaria cases in the surveillance system.

For malaria elimination programmes to use surveillance as an intervention, there are certain requirements.

- There are sufficiently few cases and an adequate health staff to characterize, classify and follow up each one; the manageable number is likely to be two or three or fewer cases of confirmed malaria per health centre per week but will vary by location and the available staff.
- Cases have become clustered such that it is possible to identify and characterize discrete foci of transmission.
- The surveillance system covers cases detected by all health providers.
- Malaria is a notifiable disease by national legal requirements.

After interruption of transmission, surveillance for malaria may become part of the broad responsibility of the general health services; however, it should be supported by regular training and monitoring activities in a national programme to ensure the surveillance of changes in receptivity and vulnerability. Compulsory, immediate notification must be maintained.

### 2.6.3 Case characterization, classification, follow-up and response

Each parasitologically confirmed malaria case should be evaluated. A case investigation form is completed for each confirmed malaria case (see example in **Annex 7**), which includes characterization of the case: patient demographics, history of the current illness, including diagnostic test results and treatment, as well as travel history to assess how and where the infection might have been acquired and the possibility of onward transmission.

After a case has been characterized, it should be classified as imported, introduced, indigenous, relapsing, recrudescent or induced, according to the definitions given in the **Glossary** (see also **Fig. 8** in **section 4**). Correct epidemiological classification of malaria cases is the basis for selecting appropriate measures and classifying foci (see **section 2.6.4**).

Classification is based on the case characterization and understanding of the different intervals in the life cycle of malaria parasites (see **Table A1** in **Annex 1**). Especially for cases detected by ACD, the final classification depends on data on previous cases in the same locality and a focus investigation. If, for example, the case history is compatible with both importation and local transmission, the presence or absence of other locally acquired cases may determine the classification. Staff responsible for case classification should be trained in classification and investigation during field exercises and by reviewing case histories. After a case has been characterized, the response should be based on the classification, although all cases should be managed according to national treatment guidelines. Additional responses to address transmission for the different classifications are described below.

#### 2.6.3.1 Imported cases

An imported case is one that is acquired outside the area in which it was diagnosed. In the elimination phase, the "area" should usually correspond to a focus. Recording cases imported within the same country may be complicated, as a case may be considered "imported" from a focus or district but "locally acquired" from a province. One solution might be to report such cases as "indigenous" in the area in which they were acquired and not as "imported" in the area in which they were detected. Subsequently, an adequate response should be made to a case detected in a highly receptive area where it could generate secondary cases. In reporting to WHO, only cases imported from other countries should be considered "imported".

The main concern with imported cases is spread in the local area. The household and neighbouring households of a case should be alerted and asked to report any suspected malaria illness. An investigation, with screening and/or testing of people in the case household and possibly neighbouring households, could be undertaken to identify additional infections. The finding of other cases (perhaps characterized as "introduced") suggests local transmission, and activities to stop transmission should be instituted; evaluation of the vulnerability and receptivity of the area should be considered.

#### 2.6.3.2 Local cases

Local cases can be introduced or indigenous. It may be difficult to distinguish between these categories; however, this is not important in the early stages of malaria elimination, because all such cases indicate the presence of recent local transmission. The distinction becomes important during the interval just before certification of

malaria-free status, when the occurrence of some introduced cases (rigorously validated) is not an impediment to certification (see **section 5**).

- An "introduced" case occurs at a biologically plausible spatial and temporal distance from an observed imported case. As noted above, investigation of an imported case may result in identification of cases that were probably introduced. This indicates local transmission, and further activities to stop transmission should be instituted, including evaluating vector control activities and ACD.
- An "indigenous" case is one that was probably derived from locally transmitted cases, with no evidence that it was imported or linked directly to an imported case. Such cases indicate ongoing local transmission, and further work to stop transmission should be instituted (see above).

#### 2.6.3.3 Relapsing or recrudescent cases

Such cases may be imported or locally acquired. A relapsing or recrudescent case that was originally imported is epidemiologically unimportant and should be classified as an imported case.

- In elimination settings, a person infected locally before transmission was interrupted could have a relapse or a late primary attack of *P. vivax* or *P. ovale* malaria. A relapsing case requires radical cure according to national standards, which usually includes an anti-malarial drug for the asexual stage (chloroquine or ACT) and primaquine (after evaluation for G6PD deficiency) at a dose of 0.25–0.5 mg/kg body weight daily for 14 days *(8)*. Further investigations can be undertaken in the case household and neighbourhood, as for imported cases.
- A locally acquired malaria case may be detected after transmission has been interrupted, because of long latency in the blood. Such cases have been described for *P. malariae* and, exceptionally, for *P. falciparum* malaria. If careful investigation of such a case provides strong evidence that it was indeed acquired locally by mosquito infection before the presumed interruption of transmission, it may be classified as "recrudescent", and its occurrence should not preclude certification. Recrudescent cases should be treated according to the national treatment guidelines.

#### 2.6.3.4 Induced cases

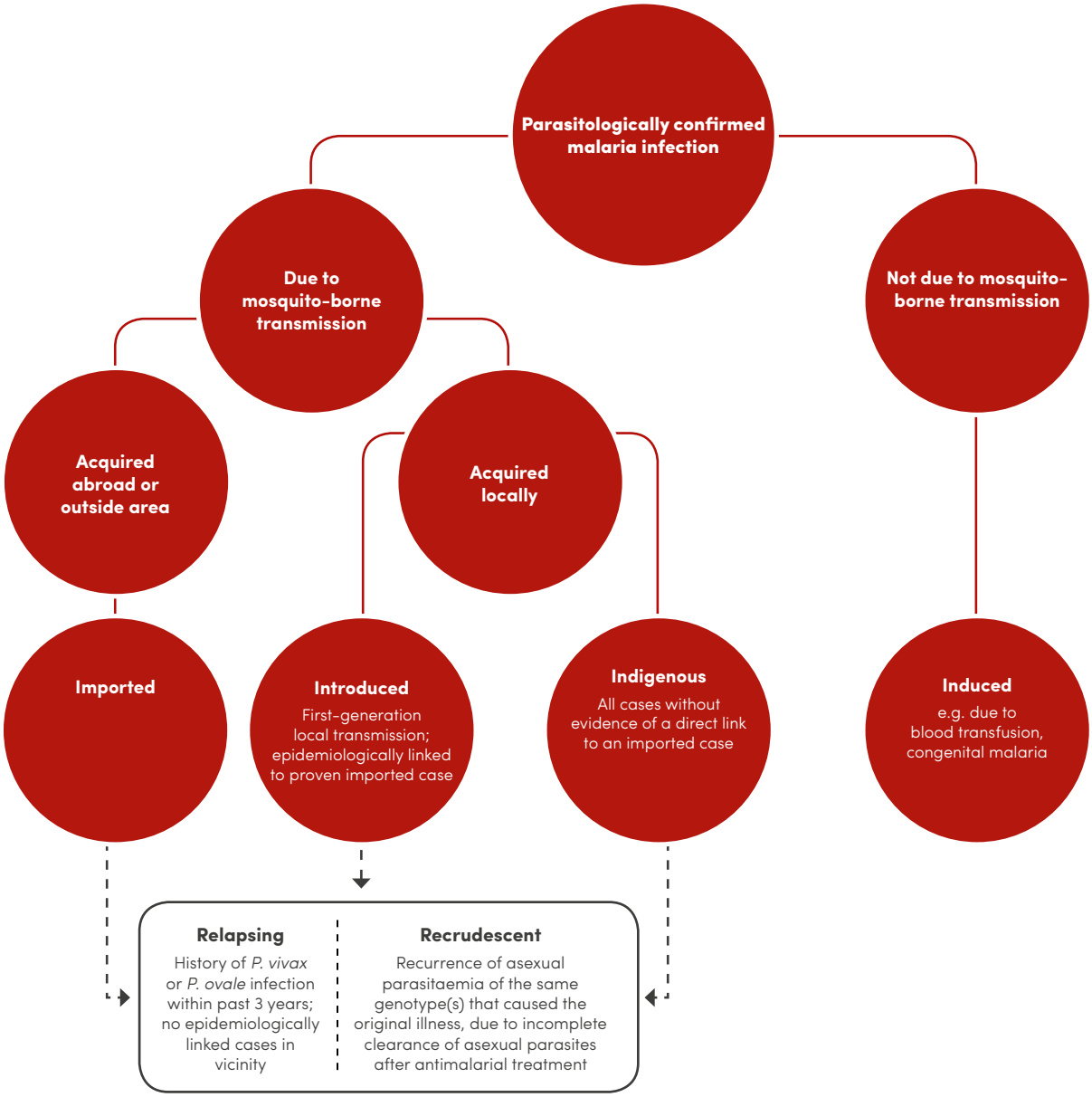
A case the origin of which can be traced to a blood transfusion or other form of parenteral inoculation of the parasite (see **Glossary** for full definition) is not due to mosquito-borne transmission. It should be managed promptly. If there is a risk of ongoing transmission in the area, surveillance staff and the case household and neighbours should be alerted and asked to report any suspected malaria illness.

#### 2.6.3.5 Other cases

Certain cases cannot be classified and should be reported separately. These include cases of infection by an infective mosquito inadvertently imported by air or sea and cases due to laboratory accidents.

Classification of cases as imported, locally acquired, relapsing, recrudescent or induced is often difficult. Conservative classification (e.g. classification as indigenous rather than introduced) is recommended, as it ensures that programmes are more responsive. Classification of malaria cases is illustrated in **Fig. 5**.

FIG. 5.
**Classification of malaria cases**




## 2.6.4 Focus identification, characterization, classification and follow-up

"Focus" is defined in the **Glossary**. It should be noted that a focus may not necessarily have active transmission; foci can be identified only in receptive areas. As discussed in **section 2.2**, foci are described and delimited in order to identify areas in which appropriate interventions should be deployed or maintained. As described below, a focus investigation is conducted to determine the response measures necessary to eliminate or prevent re-establishment of transmission.

A focus may be identified in several ways. For example, the investigation of an individual case may lead to the recognition of additional locally transmitted cases around the case household, and further investigation shows that transmission is limited to a geographically defined area. Active investigation of areas previously defined as "at risk" may identify a transmission focus.

Once a focus has been identified, an investigation is launched to delimit and characterize the area and the populations at risk, and a focus investigation form is completed (see example in **Annex 8**). The investigation is more extensive for a new focus, whereas detection of a new case in known active foci will trigger a new focus investigation only if its features (e.g. parasite species or location) differ from those of previously detected cases. The area to be covered is determined by an initial rapid assessment based on the results of ACD and entomological and community social and behavioural investigations. The focus investigation will then identify the main features of the location, including populations at risk, location of actual or potential breeding sites, likely vectors and, if possible, insecticide susceptibility and behaviour. The findings may lead to modification of the initial mapping until a clear, stable picture emerges.

A map should be prepared of the location of case households, geographical features relevant for malaria transmission (e.g. water bodies, forests and altitude), other habitations, health facilities and roads, as well as coverage of all interventions. Although both paper and electronic maps can be used, the increased availability of user-friendly software and geo-coded data favourizes electronic maps.

#### 2.6.4.1 Practical aspects of focus investigation

Standard operating procedures should be used to determine the timing of initiation and completion of focus investigations, including reporting and response. An initial ACD survey, for example, should be completed within seven days of detection of the focus.

Once the field investigation is completed, the team should be able to determine the extent of and factors driving local transmission and to characterize the focus. The local staff member responsible for malaria, in consultation with experts at higher levels, will prepare a response plan according to the results of the investigation.

Copies of the completed case and focus investigation forms and the line-list of records of all cases identified in the focus are sent to the national malaria programme and the reporting health facility. The situation and response plan are communicated to local health staff, community leaders, community volunteers and relevant local actors.

The district malaria focal point is responsible for ensuring that a register of foci is established, all foci are investigated and reports on all foci are available and kept up to date.

### 2.6.4.2 Classification of foci

Once investigated, the focus may be classified into one of the three types listed in **Table 3**.[12]

TABLE 3.
**Types of malaria foci with operational criteria**

| TYPE OF FOCUS | DEFINITION | OPERATIONAL CRITERIA |
|---|---|---|
| Active | A focus with ongoing transmission | Locally acquired case(s) have been detected within the current calendar year. |
| Residual non-active | Transmission interrupted recently (1–3 years ago) | The last locally acquired case(s) was detected in the previous calendar year or up to 3 years earlier. |
| Cleared | A focus with no local transmission for more than 3 years | There has been no locally acquired case for more than 3 years, and only imported or/and relapsing or/and recrudescent or/and induced cases may occur during the current calendar year. |

Foci should be recognized and their classification upgraded immediately after detection of cases. Reclassification should be based on regular review, usually at the end of the calendar year or of the transmission season.

A register of foci is maintained at district and national levels, which is updated with new data on interventions and findings as they are accrued. Focus classification is updated at the end of each calendar year or transmission season, depending on the programme policy.

Residual non-active foci should remain non-active (no indigenous cases) for three consecutive years before a programme applies for malaria elimination certification.[13]

### 2.6.4.3 Response measures

Response measures to active, residual non-active and cleared foci depend on several principles.

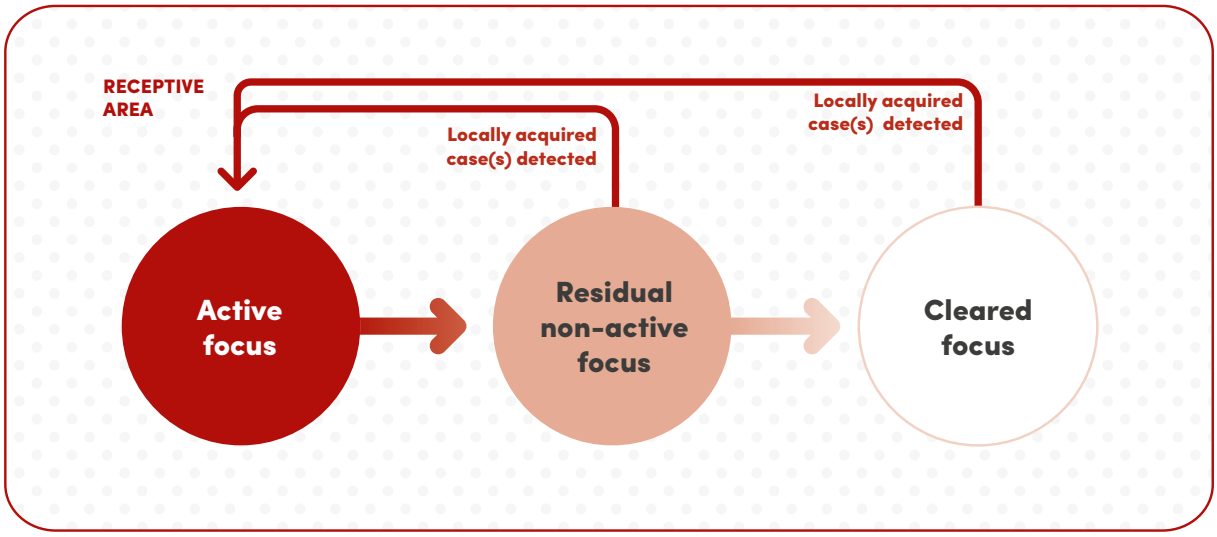
- Vector control measures are assessed for their appropriateness, coverage and use and increased according to the characteristics of malaria in the area, with particular attention to its receptivity.
- PCD services are accessible to all members of the population throughout the year, with supervision at defined intervals.

[12] In a previous WHO document on malaria elimination *(32)*, seven types of focus were identified; however, experience has shown that these posed difficulties at local level and had minimal operational implications. Here, we define three types of focus.

[13] Identification of an introduced case (with no ongoing transmission) in a non-active foci does not preclude certification.

- For active foci, various options exist. First, high coverage of appropriate vector control should be maintained. ACD (with screening and testing or with testing alone) can be considered at appropriate intervals, especially just before or during the transmission season. If testing is chosen and no cases have been found after several rounds of ACD, the frequency of testing may be reduced or the strategy changed to active surveillance for suspected clinical cases that can be tested and managed as necessary. In some circumstances, mass drug administration may be appropriate.
- For residual non-active foci, ACD may be considered at key times (e.g. the mid and late transmission season), and people most likely to have malaria (e.g. those with fever, migrant labourers, those not using prevention) are screened to identify local cases, indicative of ongoing transmission. If several rounds of ACD reveal no cases, the frequency may be reduced. If new introduced or indigenous cases are identified, further evaluation is required to determine whether there is local transmission, which would require additional action (see **Fig. 6**).
- For cleared foci, the programme should rely on the surveillance system to rapidly identify any cases of suspected malaria and determine whether local transmission has resumed.

FIG. 6.
**Characterization, classification and review of malaria foci**




## 2.6.5 Special surveys

In many programmes, it may be necessary to triangulate case detection data with information from other surveys. In the early stages, data from malaria indicator surveys, demographic and health surveys and multiple indicator cluster surveys may provide useful information on disease burden and intervention coverage. As the prevalence of malaria decreases, such surveys play a smaller role in assessing the burden of disease and infection.

The most important surveys or special assessments in the late stages of a programme may be those on operational factors, such as coverage of key prevention interventions, the quality and availability of diagnosis and understanding of how to identify and manage a suspected case and how to investigate a confirmed case.[14] Where appropriate, population-level information on intervention coverage and use can be collected during the process of case and/or foci investigation. Health facility surveys may be used to investigate the quality of diagnosis and treatment of malaria.

### 2.6.6 Data management, analysis, feedback and decision-making

In the final steps of elimination, clinicians and laboratories should consistently and immediately notify the district team and national malaria programme of all confirmed malaria cases by the fastest possible means and include basic demographic, clinical and parasitological data. Case and focus investigation reports are controlled for quality in the district and centrally, and direct feedback is sent to the person or team that prepared the report.

Regular data (immediate, weekly, monthly) should be available at the local level for evaluation and should be disseminated to districts or to intermediate level, the national malaria programme and the national reference laboratory. As a country sets elimination targets, a computerized geo-referenced database should be established that covers all cases, including those seen outside the public health system. This database will support programme management and can be used for in-depth analysis and response.

Repositories of all malaria reports, records of case detection, entomological monitoring of vector behaviour and intervention quality and focus investigations, special surveys, case registers and focus registers, should be maintained at district and central levels. See the operational manual for disease surveillance for malaria elimination published by WHO *(32)* (to be updated in 2017) and **section 5** of this framework.

### 2.6.7 Monitoring drug efficacy

Up-to-date, good-quality data on the efficacy of the recommended malaria treatment ensure that patients are cured and progress is made towards malaria elimination. As countries progress to very low numbers of indigenous malaria cases, monitoring of drug efficacy should be integrated into national malaria case surveillance, replacing regular studies of therapeutic efficacy. Once efficacy monitoring has been integrated into overall case surveillance, treatment should be given to all patients (regardless of age and parasitaemia) under direct observation. At a minimum, the patient should be assessed clinically and parasitologically daily for the first three days and weekly thereafter (until day 28 or day 42 for ACT containing a partner drug with a long half-life). Integration of surveillance of drug efficacy into overall malaria case surveillance facilitates the collection of information on efficacy; complementary information on molecular markers of drug resistance is also useful.

## 2.7 Accelerating activities towards elimination

Progression towards malaria-free status is continuous and not a set of independent stages. Countries, subnational areas and communities are at different stages in malaria elimination; their rate of progress depends on their level of investment, biological determinants (of the affected population, the parasites and the vectors), environmental factors, the strength and performance of the health system and social, demographic, political and economic realities. Thus, the time that each country will take to reach elimination depends strongly on contextual factors. Probably the two most important factors that can be acted upon are a political decision to accelerate activities and ownership and the performance of the national health system and its adaptability to new opportunities. If these two factors are in place, the time a country takes to achieve elimination depends on effective universal health coverage with the core malaria interventions (pillar 1 of the GTS) and an effective health management and

[14] In some settings and in certain research projects, surveys have been conducted with highly sensitive diagnostic tests or serology in certain at-risk populations to obtain complementary information on infection clearance. Pending further evaluation, WHO does not currently recommend these approaches for evaluating elimination but, instead, stresses the quality and the sensitivity of the surveillance system for finding and responding to cases.

information system that allows national malaria control programmes to direct resources, identify gaps in coverage, detect outbreaks and assess the impact of interventions (pillar 3 of the GTS). It is through these approaches that countries such as Sri Lanka have achieved elimination, and often accelerated it.

### 2.7.1 Population-wide medicine-based strategies

There are few additional WHO-endorsed strategies for accelerating a reduction in transmission at population level. Population-wide medicine-based strategies to eliminate parasite reservoirs within a short time are being explored. Currently, only mass drug administration can be considered in a few, specific settings to accelerate *P. falciparum* elimination. This strategy has several key components.

- It should achieve high coverage in the target population, be **time limited**, and be used in the context of high-quality coverage of all other core malaria interventions in the path to elimination.
- It **should not replace** the responsibility for achieving high coverage of all core malaria interventions **or resolve failures** in implementation of those core strategies.
- It should be directed to the entire population at risk in a given location.
- The drug used should have a very high safety profile. The reduction in transmission is expected to be higher if the therapeutic levels of a medicine last longer; therefore, clearance of existing parasites and a prophylactic period render people insusceptible to new infections.
- The drug may be directed against asexual stages (e.g. ACT) or may also target the sexual stage (e.g. low-dose primaquine).

Recent reviews of mass drug administration and MPAC recommendations on its use are available *(34,35)*.

### 2.7.2 Additional interventions to accelerate malaria elimination

Vector control (ITNs/LLINs and IRS) affects the biting rates and survival of vector populations. Beyond ITNs/LLINs and IRS, many new strategies are being developed, but, at present, none has proven wide applicability or the capacity to substantially reduce malaria transmission. Certain vector control tools may be relevant in some locations in which there is local understanding of vector transmission dynamics (see **section 2.3.2**).

Acceleration of elimination of malaria will require strengthening of information and surveillance systems and rapid adaptation for tracking the acceleration effort (see **section 2.6.2** for further information).

In the future, malaria vaccines may have a role in elimination if they specifically reduce transmission. Issues in vaccine development are briefly described in **section 6**.

While other interventions may appear in the future, medicine-based parasite clearing strategies given in combination with vector control, case management and effective surveillance remain the only tested, proven tools available at this time.

# 3. Management and planning

Eliminating malaria requires a well-trained workforce, engagement in multiple sectors, strong community involvement and commitment at the highest levels of leadership. An elimination programme is not an intensified version of the approach of "scaling up for impact". Deployment of interventions becomes more complex, and programmes must increase their understanding of the biological, environmental and social determinants of malaria transmission in order to plan and determine the best mix of interventions for specific areas. Considerations for managing and planning an elimination programme are listed in **Box 5**.

BOX 5.
**Management and planning: key points**

- Planning for elimination should begin with an assessment of the epidemiological, operational, and financial situation of the malaria programme.
- Several plans should be made: strategic, elimination, operational and monitoring and evaluation.
- Strategic plans should be costed to inform and facilitate resource mobilization.
- Elimination programmes must constantly monitor critical metrics, regularly validate and analyse the collected data and adjust programmes in response.
- Elimination programmes require strong management and structures that encourage hiring, training and retention of staff with core skills and reliable supply chains.
- Establishment of an independent national malaria elimination advisory committee is recommended to provide an external view of progress and any gaps.
- Elimination programmes benefit from a supportive enabling environment, which can consist of political commitment from national leaders, the enactment of necessary legislation, strategic partnerships across sectors and community engagement.

## 3.1 Planning process

Planning for elimination should be linked with national and local planning. It should begin with an assessment of the epidemiological, operational and financial situation of the malaria programme, including what is currently working well and any gaps and challenges.

The **epidemiological assessment** addresses the current malaria situation and stratification (see **section 2.2**), including trends over time and the tools that have most influenced them. The assessment should also characterize the affected populations and seek to determine the economic, social and behavioural dynamics that affect disease transmission. It should also confirm and evaluate the effectiveness and cost–effectiveness of malaria control interventions. The effectiveness of the programme can be evaluated in epidemiological surveys and/or in studies of the efficacy of medicines or insecticides.

The purpose of an **operational assessment** is to identify gaps in programmes and what should be strengthened to achieve the desired objectives within the given timeframe. It includes structure, staffing and achievements as well as weaknesses that might prevent achievement of the objectives.

The **financial assessment** should involve a costing of malaria programmes and a review of the funding situation, both current and anticipated. It should include the total budget of the current programme, whether funding is sufficient to implement current operational and strategic plans, whether the available funding could be used more efficiently and how sustained domestic funding could be secured and augmented as required.

### 3.1.1 Strategic planning

Strategic planning is "owned" by the national malaria programme and supported by stakeholders and partners. Strategic plans should be costed to inform and facilitate resource mobilization. Although the aim of all programmes is ultimately to obtain malaria-free status, the time-bound nature of a strategic plan may indicate a different goal, such as reducing the prevalence of malaria below a certain threshold. Different goals may be set for subnational regions with different contexts, such as a highly endemic province or district or one in which malaria transmission is low.

Elimination plans should define the objectives to be achieved along the path to the goal. The objectives may be epidemiological, operational or financial. For each objective, the activities or actions required should then be included in an operational plan, and indicators for assessing progress should be defined in a monitoring and evaluation plan.

### 3.1.2 Operational planning

An operational plan is more detailed than a strategic plan, as it defines who will do what, when and how. The operational plan should delineate all activities and sub-activities to be implemented for each strategic programme component (e.g. vector control), define their geographical scope, assign responsibilities for implementation and set timelines and deadlines.

The documents that will be required are likely to include:

- standard operating procedures;
- a monitoring and evaluation plan, which defines indicators and targets for measuring programme progress and the system used to collect and report them;
- national diagnosis and treatment guidelines;
- vector control guidelines and the insecticide resistance monitoring plan;
- a surveillance manual;
- the procurement and supply management plan, which defines the systems and processes for procuring and supplying all commodities necessary for the interventions; and
- a communications and advocacy plan.

### 3.1.3 Resource mobilization

An elimination programme will require a short-term infusion of funding to intensify activities and a commitment to longer-term funding to ensure continued surveillance and control even after malaria has been eliminated, to prevent reintroduction and resurgence.

An increase in the overall malaria budget may also be necessary to achieve programme goals. All objectives in the strategic plan should be costed in detail to inform the resource mobilization strategy, which should include both advocating for increased domestic contributions and applying for external funds. Traditional and new donors in the public and private sectors should be targeted, and innovative financing mechanisms to expand the donor base should be explored. Domestic financing may be more sustainable, especially as malaria transmission is reduced; this is recommended where possible.

## 3.2 Informed decision-making

Decisions on programme policies, strategies, approaches, structures and priorities must be based on the best available evidence to ensure maximum impact with the available resources, improve the results that programmes can achieve and enhance accountability. An elimination programme should monitor metrics constantly and measure various components of programme performance, including input indicators (e.g. the fraction of targeted households that received IRS, the number of ITNs/LLINs purchased), intermediate indicators (e.g. impact of an intervention on vectors) and outcome indicators (e.g. malaria incidence) to produce data for decision-making. Processes should be set up to validate the collected data regularly, analyse it and adjust programmes in response.

Leaders at all levels of the malaria programme should be empowered to collect and analyse data regularly. Centrally, programme managers require information on overall performance to track progress and report to their government and donors; they also require measures of the availability of commodities to ensure timely distribution of pharmaceutical products and avoid stock-outs. At provincial level, malaria managers require analysis of intervention coverage in order to hold implementers accountable, adjust strategies to cover underserved areas and evaluate the effectiveness of tools. Individual health facilities should receive feedback on their testing and reporting rates and how they compare with those elsewhere. All staff should be trained in recognizing the importance of data, and the results of analyses should be shared with the people who collected the data in order to demonstrate its value.

### 3.2.1 Monitoring and evaluation

As for control programmes, monitoring (systematic tracking of programme actions over time, including budget allocations and adherence to standard operating procedures) and evaluation (examining progress and its determinants) are essential for measuring how well an elimination programme is operating over time and whether it is achieving its milestones and goals. In the context of "scale-up for impact", monitoring and evaluation consist of evaluating the reduction in burden. As transmission is reduced, however, monitoring and evaluation with strong surveillance systems (see **section 2.6.6**) should consist of detecting infections and measuring transmission dynamics *(12)*. A detailed monitoring and evaluation plan should include a manageable set of the most important indicators, determined according to programme goals and interventions used. While the coverage indicators used in

control programmes remain useful, some will have to be adapted and new indicators introduced. Some recommended indicators for elimination programmes are listed in **Annex 3**. Planning of monitoring and evaluation should include the sources of data that will be used to measure the indicators, how and when metrics will be reported and how the programme will verify the accuracy of reported information and ensure accountability for timely, complete reporting.

### 3.2.2 Data quality

Monitoring and evaluation can be compromised if poor-quality information is provided for decision-making, thus preventing programme managers from seeing programme strengths and weaknesses and reducing confidence in the data. The six components of data quality are:

- validity: Do the data accurately reflect the intended measure?
- reliability: Are the data collected regularly, with the same method?
- integrity: Have the data been manipulated in some way, consciously or unconsciously?
- precision: Are the measurements reproducible and free of excessive random error?
- timeliness: Are data collected and reported within appropriate time lapses? This is especially important in elimination programmes, as reported data must be analysed rapidly to assess trends over time and place, particularly as transmission decreases and the distribution of cases of infection becomes increasingly focal.
- completeness: Are data missing?

Data quality can be maximized by ensuring strong, well-functioning information systems that facilitate the collection and reporting of the required information by programme staff. Procedures for reviewing data at all levels and performing regular audits of quality should be specified. Technological solutions can be helpful; for example, reporting by mobile phone can increase timeliness, while electronic data entry can minimize later transcription errors and obviate the entry of contradictory information.

### 3.2.3 Data management

The data management system influences both the quality of the information collected and the ease with which it can be analysed and used for decision-making. A high-quality data management system facilitates entry of indicators by field workers, improves quality by allowing data checks and validation, ensures rapid, faithful transmission to central levels, allows cross-referencing and analysis of metrics from various programme components and ensures feedback to all levels of the data collection system to encourage participation and improve performance. As mentioned in **section 2.6.6**, elimination programmes are advised to establish a computerized, geo-referenced database that includes all cases.

The collection of data directly in electronic form, such as on mobile phones, tablets or computers, tends to be more rapid and results in fewer errors than use of paper forms, questionnaires or registries. Not all electronic systems are user-friendly, however, and if electronic devices break, run out of power or are stolen, monitoring may break down. The local context must be carefully considered in designing any system, and no one system is suitable everywhere.

Data entered into the system should be checked regularly, including for:

- completeness: Have all the required fields been filled, and have all staff and facilities reported?
- consistency: Are contradictory results reported in different fields (e.g. a patient is reported to have no travel history but the case is classified as imported), which call the metric into question?
- plausibility: Are the values (e.g. patient age) within the expected range?
- duplication: Has each report been entered only once, and are reports referring to the same individual or household properly linked?

When all data are stored locally rather than on a "cloud", procedures should be established for backing them up.

## 3.3 Programme structure and management

The structure of a malaria programme varies from country to country; however, all programmes require a central structure to provide technical leadership, set policies and guidelines, coordinate national training, communicate with donors and evaluate overall progress. Regardless of the structure, accountability should be ensured at each level. If milestones are not met, processes must exist for detecting and responding to challenges and ensuring that similar problems do not occur again. If operations are conducted by provincial programmes, a system should be in place to ensure that they are aligned with the national strategy and well coordinated by the central leadership. Health care systems can be strengthened; integration with existing systems, especially at the community level and across multiple national and subnational regional levels will be important in the structure and management of elimination *(36,37)*.

### 3.3.1 Programme management

Programme management involves managing the people, processes and resources that contribute to achievement of a strategic goal. Good management is necessary at all levels of a health system and especially in an elimination programme, as operations will have to be adjusted over time in response to changing circumstances. Anticipating challenges before they arise, planning time to account for inevitable delays and strong internal and external communication will be required.

### 3.3.2 Programme staffing

The achievement of goals requires a programme structure designed to support execution of the operational plan, including clear understanding of roles and responsibilities in the malaria programme. The staffing requirements for a malaria programme are likely to vary according to context; nevertheless, a core set of staff required in nearly every malaria programme can be considered:

- a programme manager or director: an experienced person to oversee the national programme, with the authority and freedom to make decisions without political interference;
- an epidemiologist: an expert in monitoring and evaluating patterns in malaria prevalence and its causes and in assessing the effectiveness and cost–effectiveness of interventions;

- an entomologist: an expert on the mosquito vectors of malaria, who can ensure that the optimal interventions are being used and who can monitor the impact of the interventions on vectors and their behaviour to ensure a continued impact;
- laboratory technicians: people with skills at various levels, according to the national policies for diagnostic testing and its quality assurance;
- an expert in information systems: a person with thorough knowledge of geographical information systems, who can set up a national platform for mapping malaria cases, foci, population movement and other risk factors, and identify operational progress and gaps;
- a data systems specialist: an expert in data systems who can ensure that information from surveillance flows appropriately and is readily available to the programme;
- a communications specialist: an expert in health education and public relations who can oversee outreach to communities and others;
- a logistician: an administrator who can oversee accounting, procurement, transport and other systems;
- operational staff: depending on the interventions used, these may include IRS spray personnel, surveillance officers, environmental health officers, sanitary engineers, community health workers, net distribution teams, drug distribution teams and district elimination coordinators; and
- health care workers: doctors, nurses and other health facility staff and, in countries with problems of access to health care, community health workers.

Depending on the overall programme structure, some of these positions may be duplicated at central, provincial and district levels.

### 3.3.3 Training and retaining staff

Targeted training and continuous mentoring and supervision will ensure that staff understand their roles in the elimination programme and the importance of their activities for success. Rather than train entire cadres of staff at routine intervals with a standard curriculum, tailored training should be conducted in accordance with the heterogeneity of malaria transmission intensity in the country or when guidelines are changed. Between formal courses, routine supportive supervision and targeted feedback can be effective for honing staff skills and empowering them to trust the tools and systems they are using.

To ensure that experienced staff who are of great value to the programme are retained, they should be paid sufficiently attractive salaries for their jobs, to motivate them to continue. Retention programmes, including incentives and career promotions to discourage attrition, should be considered. If staff are advised of the expected tenure of the position before they are hired, they may be encouraged to stay with the programme longer. Training many staff to perform important tasks and requiring documentation of experience and lessons learnt will mitigate any transitions that occur.

## 3.4 Supply chain systems

Strong supply chain systems that allow reliable quantification, timely procurement and appropriate storage and distribution of commodities for malaria interventions are essential for malaria elimination. For case management, all points of care must have

proper stocks of diagnostic and treatment commodities; for ACD surveys, commodities must be accurately quantified to ensure sufficient coverage of at-risk populations. In all cases, stocks must be adequate to adjust for changing dynamics of transmission and intervention coverage.

As the prevalence of malaria decreases, transmission becomes unstable, and countries are at increasing risk for epidemics. Epidemic preparedness plans are therefore necessary, with stockpiles of malaria commodities (diagnostic tests, anti-malarial medicines and insecticides and equipment for IRS) for epidemic response.

Even countries in which malaria transmission is very low must maintain a minimal stock of products at each level of the health care system, so that, if a case presents for care, it can be appropriately treated. In a successful elimination programme, some stock may never be used; however, expiration of unused medicines is the price to pay for ensuring that the health system is prepared for an unexpected outbreak of malaria.

## 3.5 Independent national malaria elimination advisory committee

It is recommended that an advisory committee be established to provide an external view of progress and gaps in a malaria elimination programme. The committee should be convened regularly to review epidemiological trends and operational progress. It should be clearly independent from the national malaria programme. It could comprise academics, health system experts, staff in other disease control programmes and representation from non-health sectors. Reports from the committee may be valuable documentation for eventual WHO certification. It should also be responsible for supporting audits of data to validate information and could play a role in verification of subnational elimination.

## 3.6 Creating an enabling environment

### 3.6.1 Political commitment

Leaders at the highest levels must make elimination a priority, especially as the malaria burden falls and other public health issues compete for resources and commitment. High-level political involvement is necessary to secure domestic funding, to ensure flexibility in programme decision-making and to demonstrate that the government is willing to do what it takes to ensure elimination and maintain it once it has been achieved. For subnational elimination, engagement with local political leaders is important. Verified malaria elimination should be of considerable interest for a provincial governor or a state prime minister in view of the benefits for the population and the health services, in addition to economic and political aspects.

### 3.6.2 Enact the necessary legislation and regulations

New legislation may be required to support elimination programmes in some contexts and programme requirements. For example, programmes should ensure compulsory notification of all confirmed cases of infection detected in both public and private health care facilities. Additionally, strengthened regulatory systems may be required for careful approval of products and tools and their use in the country; regulations can increase the availability and clarity of information and indicate the training that will be required for delivering the interventions (see also **section 6.3**).

### 3.6.3 Strategic partnerships across sectors

Malaria elimination is unlikely to be achieved only by the conventional health system: many parts of government and society will have to work together. In addition, success in one country depends on that of its neighbours: elimination is possible only with regional coordination and collaboration.

Once partners are identified, the national malaria programme should act as the central coordinator to ensure that there is no duplication of work and that the activities of partners are fully aligned with the national strategic plan. In planning multi-year and annual operations, the government should establish a common work plan with its partners and integrate their activities and milestones into the action plan. The ministry of health should meet all partners regularly to ensure that activities are aligned, do not duplicate each other and support the national strategic plan.

#### 3.6.3.1 Collaboration with other government sectors

Government partners that may be relevant for malaria elimination include the various departments of the ministry of health, including the national laboratory and central medical stores, and other ministries, such as those for education, the environment, public works, statistics, finance, agriculture and defence. Further considerations on collaborative responsibilities are discussed in a comprehensive review of disease eradication *(38)*.

#### 3.6.3.2 Collaboration with the private sector

Many entities in the private sector have roles to play in the various facets of elimination. The agricultural sector and extractive industries may rely on migrant labourers, who are sometimes at high risk for infection with malaria parasites, and agriculture, construction and mining may create breeding sites for certain mosquito vectors. Partnership with these sectors will help ensure a healthy, productive workforce. In some countries, the tourism industry has a strong incentive to invest in anti-malarial activities.

Private health facilities like hospitals and private clinics provide much of malaria treatment in many countries. If patients who receive malaria treatment in such locations are not reported in surveillance systems, the programme may miss areas of active or potential transmission. Finding ways to enforce notification and reporting from the private health care sector will ensure good case management of those who are treated and ensure complete coverage of surveillance.

### 3.6.4 Community engagement

Engaging the communities targeted for interventions is important for malaria elimination. The required level of coverage, particularly as malaria prevalence is reduced to very low levels, can be achieved and sustained only if communities are fully supportive. If communities feel that they "own" programmes and are actively involved in their implementation, activities will be easier to implement, and coverage targets will be more likely to be reached.

Community members should play meaningful, active roles in project development and decision-making. The objectives of community participation should include:

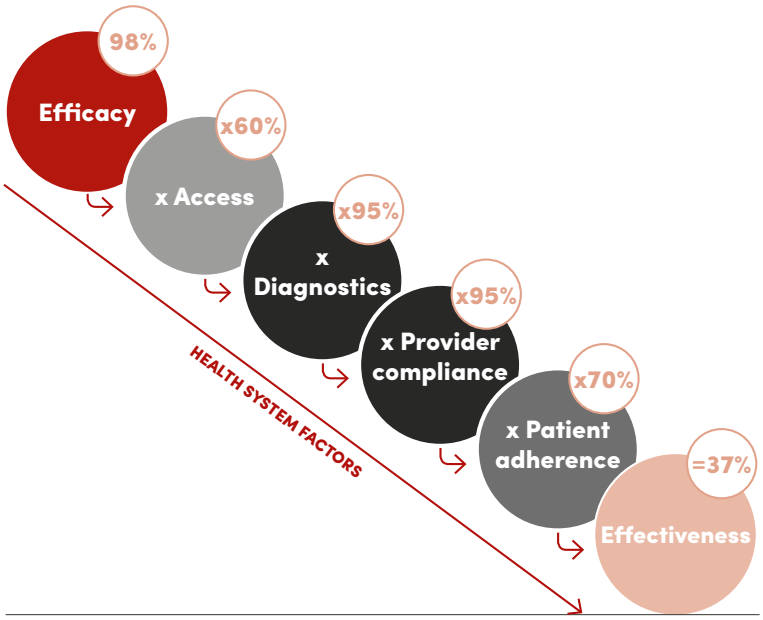
- encouraging appropriate health-seeking behaviour;
- strengthening community access to malaria testing, treatment and reporting;
- promoting acceptance and appropriate use of vector control tools;
- empowering communities to strengthen self-monitoring and decision-making about malaria;
- building community and local political support for eliminating malaria; and
- increasing active community participation in elimination activities, including a surveillance system linked to district and other systems up to national level.

Achieving these objectives may involve explaining the rationale of the strategies and their benefits to the community, offering training to permit active participation, explaining the indicators to be used to evaluate success and receiving feedback on the results of interventions or strategies.

### 3.6.5 Health system effectiveness

Malaria elimination depends on a high-performing health system that can deliver malaria interventions of good quality and coverage. Effective coverage depends not only on access to the intervention but also on provider compliance, patient adherence and individual benefit *(39)*. Thus, a highly effective intervention (as determined in controlled trials) can result in low overall programme effectiveness because of suboptimal access to the intervention, inadequate programme targeting due to supply shortages, incomplete provider compliance or poor patient adherence. **Fig. 7** shows an example of systematic decay of overall programme effectiveness even when the individual components appear to be of acceptable quality. For elimination programmes to succeed, health systems should be evaluated for their readiness to optimize novel programmes, systems or other interventions and for their continuing performance in all aspects *(40)*.

FIG. 7.
**Example of decay in overall programme effectiveness due to sequential imperfect delivery of individual components**



# 4. Prevention of re-establishment of malaria

The consequences of importation of malaria to malaria-free countries or areas are mainly clinical (uncomplicated to severe illness, death and disability) but also epidemiological (potentially resulting in introduced and indigenous cases) and economic (work days lost to the disease and costs of malaria control activities). Means for preventing the re-establishment of malaria are summarized in **Box 6**.

BOX 6.
**Prevention of the re-establishment of malaria: key points**

- Re-establishment of transmission is defined as the occurrence of three or more indigenous malaria cases of the same species per year in the same focus for three consecutive years.
- After malaria has been eliminated, a programme for the prevention of re-establishment should continue until malaria eradication, defined as complete interruption of transmission of all forms of human malaria throughout the world, is achieved.
- Preventing the re-establishment of malaria transmission requires proper management of **receptivity** (the ability of an ecosystem to allow transmission of malaria) and **vulnerability** (the probability of malaria parasite importation into a country or area).
- In order to manage the risk for re-establishment of malaria transmission effectively, a high-performing health system should be maintained to ensure early detection, mandatory notification and prompt treatment of all malaria cases; determination of the probable causes of re-establishment; immediate action in the event that local malaria transmission is detected; and measurement of the risk for malaria re-establishment by monitoring of receptivity and vulnerability.
- Once malaria has been eliminated from a country or area, political and financial commitment at national and subnational levels should be sustained.
- Once malaria elimination has been achieved, the malaria programme should be integrated into public health programmes in order to maintain the necessary technical expertise, even if the responsible staff no longer work solely on malaria.

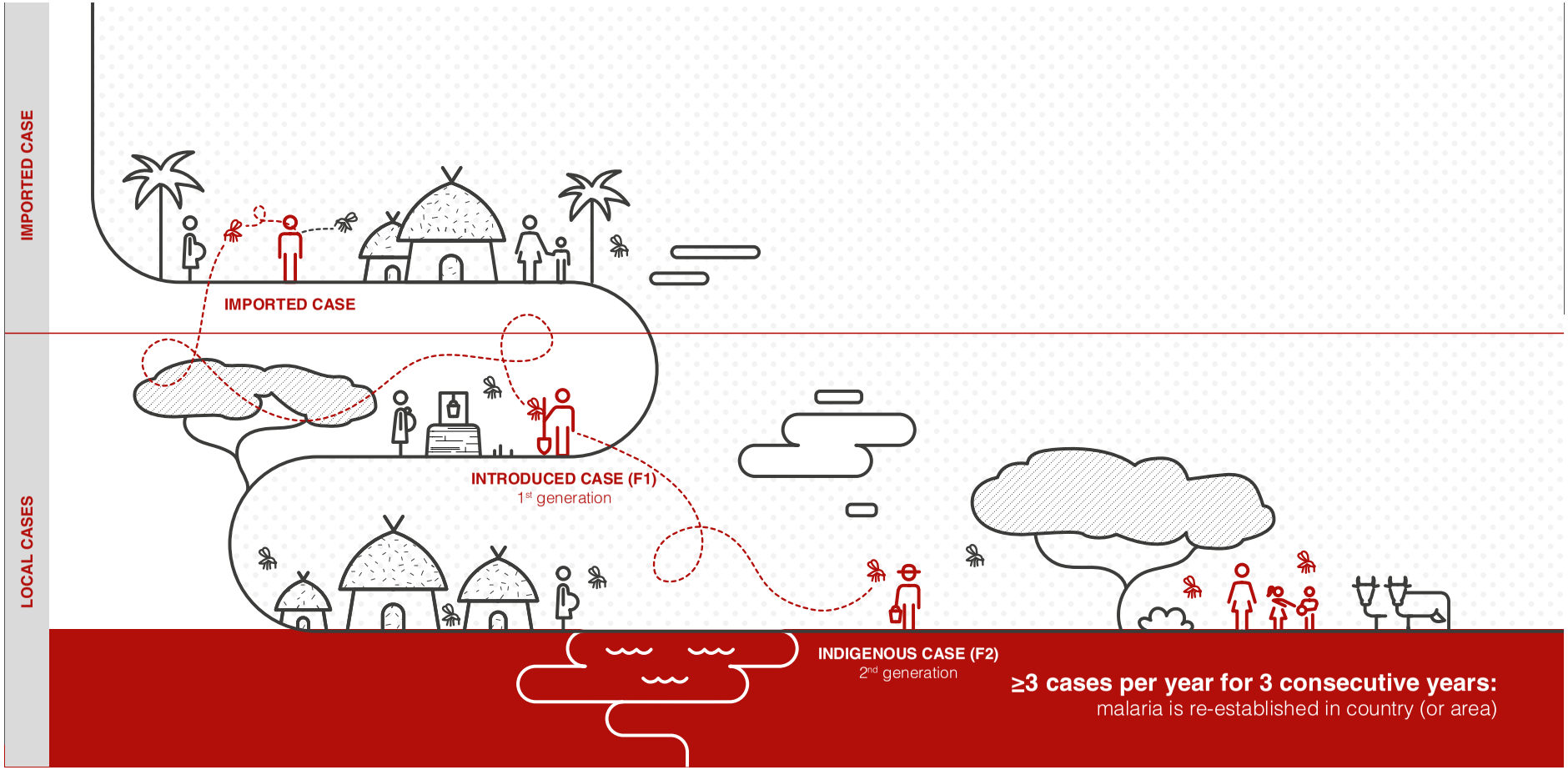
Countries or areas that have eliminated malaria should have a plan for preventing re-establishment of transmission when indigenous malaria cases are no longer observed but imported and introduced cases may continue to be reported. This is also important for countries and areas that are aiming for or have achieved WHO certification or subnational verification of malaria elimination, as described in **section 5**.

**Fig. 8** depicts the differences between imported, introduced and indigenous cases and the notion of re-establishment of transmission.

FIG. 8.

**Imported, introduced and indigenous cases and the notion of re-establishment of transmission**

This figure depicts a locality within a malaria-free area or country in which malaria is diagnosed in an individual who recently travelled to a malaria-endemic area or country (imported case). F1 and F2 are, respectively, introduced and indigenous cases (both by local transmission). While malaria reintroduction is the occurrence of introduced cases (cases of first-generation [F1] local transmission, epidemiologically linked to a confirmed imported case) in a previously malaria-free country or area, re-establishment of transmission is the occurrence of three or more indigenous malaria cases of the same species per year in the same focus for three consecutive years.



After malaria has been eliminated, prevention of re-establishment should continue until malaria eradication is achieved. As achieving malaria elimination relies on strong systems, it is expected that elimination will be durable or "sticky" *(41)*.

## 4.1 Risks for re-establishment of malaria

Malaria elimination is more likely to be sustained where vectorial capacity is naturally low or is decreased by improving socio-economic factors and in geographically isolated areas with limited cross-border population movement and importation of parasites. Therefore, preventing the re-establishment of malaria transmission relies on proper management of receptivity and vulnerability. "Receptivity" is defined as the ability of an ecosystem to allow transmission of malaria, while "vulnerability" refers to the probability that malaria parasites will be imported into a country or area (see also **section 2**).

### 4.1.1 Measuring the risks

An indication of the receptivity of an area may be derived from the history of malaria, in particular:

- the original endemicity, if data are available;
- the vectorial capacity before and after intensive vector control. In reality, there are very few data on vectorial capacity anywhere, in the past or recently. Data on the distribution and abundance of specific vectors and the entomological inoculation rate may give some idea of vectorial capacity. In most areas, data on malaria prevalence from cross-sectional surveys give an indication of the intensity of transmission.
- environmental changes resulting from development, which may affect the vector population; and
- the stability of or changes in health system responsiveness (e.g. to vector-borne diseases).

Although past information can help in assessing receptivity, it may no longer be relevant, so that vector surveillance is the basis for preventing re-establishment. Receptivity to malaria transmission depends on the presence of local vectors and environmental and climatic conditions favourable to malaria transmission. The major determinants of receptivity, as observed in vector surveillance, are the abundance of local vectors and their ecological requirements, their degree of anthropophily, the life expectancy of the mosquitoes and the time required for parasite development in the mosquito in the climatic conditions of the area.

An indication of the degree of vulnerability can be derived from traditional patterns of travel and population flow in the area and also from unexpected patterns that result from conflicts or a sudden influx of refugees or internally displaced people. These can be determined by epidemiological investigation of cases and foci, surveys from a department of immigration or tourism or from agencies that monitor refugees and internally displaced people. Malaria is imported by the arrival in a country or area of people infected with malaria parasites. This has become common in recent decades as a result of easier, more frequent international travel and increasing flows of immigrants and refugees. Malaria can also be imported when malaria parasites are brought into an area by mosquitoes that either fly across the border or are passively

transported, usually in aircraft or ships. Information on factors that can change vulnerability, such as the number of people arriving, travel history, categories of people arriving, local destination and length of stay, can be communicated promptly by mobile phone.

The combined effect of receptivity and vulnerability, and thus the risk for re-establishment of malaria transmission in a country, depends on ecological, climatic, socio-demographic, epidemiological, entomological, health system and other factors. Assessment of the risk, of its components and of the relations among them forms the basis for strategic and practical plans to prevent malaria re-establishment in the country. A detailed analysis of risk factors throughout the country could be used as the basis for stratifying the country, and designing surveillance activities appropriate for each stratum.

Receptivity and vulnerability are poorly or not correlated. Receptivity determines the possible onward transmission of malaria in a country after elimination of the disease, whereas vulnerability determines the risk for introduction of malaria parasites into a country or area in which they are not present. Juxtaposition of the two factors, however, makes it possible to identify where there is a risk for re-establishment of transmission and to simulate scenarios. If the value of one factor is 0, the possibility of malaria re-establishment is null even when the value of the other is high.

In order to maintain the malaria-free status of an area or country, the health system and the malaria programme should retain the ability to undertake one or more of the following activities:

- early detection, mandatory notification and prompt treatment of all malaria cases;
- determination of the probable causes of re-establishment of malaria transmission;
- immediate action in the event of detection of local malaria transmission; and
- determination of the risk for malaria re-establishment by regular monitoring of the receptivity and vulnerability of the area.

Maintaining capability requires funding, adequate human resources and sustained commitment at the highest level of the ministry of health.

### 4.1.2 Managing the risks

The programme should set detailed goals and use appropriate activities to assess the local situation and the corresponding receptivity and vulnerability.

#### 4.1.2.1 Reducing and mitigating receptivity

The suitability, effectiveness and quality of vector control activities should be determined from an entomological surveillance system that operates throughout the country to monitor populations of adult *Anopheles* mosquitoes (see also **section 2**) and changes in transmission risks. Vector larval sites should also be monitored, with estimates of the abundance of larval habitats and the density of larvae and adult mosquitoes (both indoors and outdoors), insecticide resistance and meteorological indicators such as the average daily temperature and rainfall. Entomological assessments should be a priority in vulnerable areas where the receptivity is not clear, to determine whether pre-emptive vector control is needed and, if so, the strategies to

be used either pre-emptively or reactively. To reduce receptivity, vector control should be maintained and adapted to local environmental conditions and vector behaviour. It should be coordinated with other programmes, local authorities and relevant services in neighbouring countries in order to reduce transmission and protect the local population on both sides of the border. Vector control should be targeted to high-risk foci, including the last ones to be cleared before elimination.

Depending on the vector, environmental management can reduce the oviposition sites of *Anopheles* mosquitoes and reduce malaria transmission by reducing the number and availability of larval habitats or rendering them less attractive to gravid anophelines.

In malaria-free receptive areas, individual and collective methods for protecting the population should be promoted.

#### 4.1.2.2 Reducing and mitigating vulnerability

In malaria-free countries or areas, malaria awareness should be maintained in the local population by various educational programmes or campaigns. Opportunities to include messages about malaria into communications in other vector-borne disease programmes or campaigns should be considered.

To limit the consequences of malaria importation, immigrants, travellers and other groups arriving from malaria-endemic areas should benefit from early detection, quality-assured diagnosis, effective treatment and follow-up, with detailed epidemiological investigation of malaria cases. People with malaria who are planning to stay for some time or live in area with high receptivity may be provided with preventive measures such as ITNs/LLINs.

Migrant workers and travellers exposed to malaria may receive diagnostic testing and treatment of symptoms at health centres, ideally free of charge. Likewise, prophylaxis should be distributed for free to local people travelling to endemic places, or, at the least, they should be informed of malaria prevention measures. At points of entry, immigrants from malaria-endemic countries or areas should be given printed materials on malaria, including information about what to do in case of suspected malaria.

## 4.2 Maintaining a strong health system

To manage the risk for re-establishment of malaria transmission effectively, a high-performing health system should be maintained, to:

- provide free diagnosis and treatment of malaria, with quality-assured microscopy and RDTs, in public health facilities;
- ensure that all suspected and confirmed malaria cases, whether treated in the public or the private sector, are notified;
- use a standard electronic form for early, mandatory notification to the ministry of health of all confirmed malaria cases in the public and private health sectors;
- investigate all confirmed cases and foci epidemiologically and entomologically; and
- establish an effective system for early detection of and response to malaria epidemics.

Once malaria has been eliminated from a country or area, the challenges are sustaining effective case management in order to maintain zero malaria deaths and ensuring continuous political and financial commitment at all national levels. These are prerequisites for adequate allocation of funds to the malaria programme to ensure continuing activities, including diagnostic, treatment and surveillance capacity. Funding will also ensure that the supply chain is fully operational and malaria commodities are available at all times, with proper management of safety stocks of essential medicines for diseases that occur at low incidence.

## 4.3 Integrating malaria activities into general health services

Once malaria elimination has been achieved, maintaining the necessary technical expertise to prevent re-establishment of transmission may be challenging. Programmes should consider integrating the malaria programme into public health programmes (see above and references in **section 3**); in such a transition, however, it is essential that expertise and functions remain operational, even if the responsible staff no longer work solely on malaria.

If a very low prevalence of malaria persists, most of the functions of what was previously a dedicated malaria programme will probably be integrated into the broader health system. Malaria will remain a notifiable disease in health reporting systems, and special studies should be integrated into the investigation systems for other emerging and epidemic vector-borne diseases. It will be important to maintain national expertise, coordinating function and capacity to react to reported malaria cases and to maintain skills in fields such as laboratory science, epidemiology, vector biology and control and informatics.

At the peripheral level, if possible, a staff member of the ministry of health with expertise in surveillance and response should be appointed as a malaria focal point. Staff who have expertise in malaria should be kept in the health system, their positions being moved to other departments. In order to keep staff motivated, all workers should be assured that elimination will not result in them losing their job.

Once elimination has been achieved, the central functions that must be maintained are limiting the consequences of malaria importation, with early detection, quality-assured diagnosis, effective treatment, epidemiological investigation of cases and foci and coordination of responses to prevent indigenous cases. A central reference laboratory with expertise in malaria diagnostics, including blood slide reading, should be maintained.

# 5. Certification and verification of malaria elimination

This section presents the prerequisites and process for WHO certification of national malaria elimination; it also describes the new concept of verifying subnational malaria elimination, a country-owned, step-wise process for documenting elimination of local transmission of malaria in a province, region, island or other subnational area. The latter undertaking is an option for large countries that have achieved interruption of local transmission in certain states, regions or provinces and will contribute to the detailed documentation required for WHO certification of national malaria elimination. Key points in the certification and verification of malaria elimination are listed in **Box 7**.

BOX 7.
**Certification and verification of malaria elimination**

- WHO certification of malaria elimination requires proof that:
    - local malaria transmission by *Anopheles* mosquitoes has been fully interrupted, resulting in zero incidence of indigenous cases for at least the past three consecutive years, and
    - an adequate surveillance and response system for preventing re-establishment of indigenous transmission is fully functional (in particular the curative and preventive services and the epidemiological service) throughout the territory of the country.
- Certification of malaria elimination involves:
    - preparation by the requesting country of a national elimination report with supporting documentation;
    - evaluation by an independent WHO malaria Certification Elimination Panel (CEP) of the national elimination report and documentation, and
    - submission by the CEP of a final report and recommendation to the WHO MPAC, which sends a summary report to the WHO GMP for submission to the WHO Director-General.
- Subnational verification of malaria elimination is an option for large countries that have achieved interruption of local transmission in certain parts of the country. This can be useful for countries with geographically isolated territories, such as islands.
- Documentation of elimination of local malaria transmission at subnational level will be "owned" and managed only by the national health authorities of the country concerned.
- Subnational targets for eliminating transmission are important internal milestones, which can enhance public and political goodwill and attract additional government and donor funding for national malaria elimination and certification.

Once elimination status is obtained, post-certification activities include annual reporting of cases to WHO and demonstration of continuous surveillance and response to imported cases.

## 5.1 WHO certification of malaria elimination – general

WHO certification of malaria elimination is official recognition of the elimination for all four human malaria parasite species (*P. vivax, P. falciparum, P. malariae* and *P. ovale*)[15] in the country as a whole. This achievement is of great importance for the international community and even more for the country concerned, as the political, social and economic impacts on sectors such as tourism and business are considerable. It is nevertheless the prerogative of national governments to decide to request certification of malaria elimination.

## 5.2 WHO certification of malaria elimination – procedure

The burden of proof of malaria-free status falls on the national authorities that are requesting WHO certification through their minister of health. The steps in certification of malaria elimination, managed by the WHO GMP applying standard operating procedures, are summarized in **Box 8**.

BOX 8.
**New steps in certification of malaria elimination**

1. The country, after reporting zero indigenous malaria cases for at least the past three years through a sensitive and robust national surveillance system, can submit an official request for certification to the WHO Director-General through the WHO Regional Director. The country should contact WHO about certification only when it believes it has eliminated mosquito transmission of all human malaria parasites within its borders.
2. The country, in consultation with the corresponding WHO regional office and the GMP, formulates a plan of action and timeline for the certification process. This takes place during an initial WHO assessment mission.
3. The country finalizes the required national elimination report and submits it to WHO.
4. A team of the independent Certification Elimination Panel (CEP), established by WHO, i) reviews the national elimination report and other key documents indicated in **Annex 5**, ii) conducts field visits to verify its findings, and iii) develops a final evaluation report.
5. The final evaluation report is reviewed and finalized by the CEP and submitted to the WHO MPAC with a recommendation to certify malaria elimination or to postpone certification with details on the extra evidence required to demonstrate that malaria elimination has been achieved.
6. The WHO MPAC makes a final recommendation on granting malaria-free status and provides a summary of the final evaluation report to the WHO GMP for subsequent submission to the WHO Director-General.
7. The WHO Director-General makes the final decision and officially informs the national government.

[15] *P. knowlesi* and other zoonotic parasites are not currently included among human malaria species, even though they can cause serious human disease. The list of species that should be excluded in order to obtain certification should be re-evaluated when there is proof of human-to-mosquito-to-human transmission of the zoonosis.

8. When granted, WHO publishes the certification in the *Weekly epidemiological record*, *International travel and health* and the *World malaria report* and the country is listed in the official WHO *Register of areas where malaria elimination has been achieved*.
9. The country continues its efforts to prevent the re-establishment of malaria transmission and reports annually to WHO in order to maintain its malaria-free status.

### 5.2.1 National elimination report

The country requesting certification provides proof of the absence of mosquito-borne malaria transmission and its ability to detect and respond to any malaria case in a national report. The report is a comprehensive summary of national documentation (for a detailed outline, see **Annex 6**), including the existence of an adequate surveillance system and a complete history of national malaria epidemiology and of the programme. It provides evidence that human malaria transmission has been interrupted in the country, indicates that the country has met the prerequisites for certification (see below) and includes a description of how the country plans to maintain its malaria-free status. The national report should be provided to WHO preferably in English or French; it may be provided in one of the other four official WHO languages.

The country also submits the database for the national elimination report, which includes:

- a national malaria case register, with individual case and focus investigation forms (see **Annexes 7 and 8**), for at least the previous five years, showing that no indigenous malaria infections were detected in the country during at least the past three years;
- annual malaria surveillance reports covering the previous 10 years;
- full information about active malaria foci in the five years before the last indigenous case;
- reports of quality assurance of diagnoses; and
- the existence of a central repository of information on entomological surveillance and application of selected vector control interventions in the five years before the last indigenous case.

### 5.2.2 Activities of the malaria Certification Elimination Panel

WHO arranges for members of the malaria CEP to review the national report and other relevant documentation and then to visit the country (the number of people is determined by the size of country) to gather any additional information required (see **Annex 4** for terms of reference, rules and composition of the CEP).

Members of the panel evaluate whether the following prerequisites have been satisfactorily fulfilled:

- a malaria surveillance system of high quality covering all the geographical areas of the country;
- evidence of no indigenous malaria cases for the past three years (based on comprehensive case investigation forms);

- an adequate system for early detection and effective treatment of malaria cases and for subsequent clinical and epidemiological monitoring, supported by continuing education on malaria for health workers, including in the private sector;
- laboratory services that provide prompt, quality-assured parasitological diagnosis of malaria throughout the country, including the most remote and inaccessible areas;
- prompt, thorough epidemiological investigation and classification of every malaria case and focus;
- immediate mandatory notification of all malaria cases by public and private health services;
- a central computerized database of malaria cases and foci, with a geographical information system for mapping, and a national register of cases; and
- a comprehensive national plan of action with continuing political and financial support for activities to prevent re-establishment of local transmission.

Special studies (for instance, molecular epidemiological studies by polymerase chain reaction techniques to map the distribution of sub-microscopic infections) may provide additional proof that malaria transmission has been interrupted.

The prerequisites for preventing re-establishment of malaria transmission are:

- an adequate system for early recognition and rapid response to malaria epidemics;
- inter-country information-sharing and functional border coordination, where relevant;
- an efficient malaria surveillance system (which may be integrated into systems for other communicable diseases);
- effective mechanisms for cooperation among all ministries and agencies involved in malaria prevention;
- a high-quality system for entomological surveillance, including monitoring of resistance of malaria vectors to insecticides, especially in areas with high receptivity; and
- services to raise awareness and provide practical advice on prevention and early detection of imported malaria (for nationals travelling to or returning from malaria-endemic countries).

During the field visit, CEP members review the quality and completeness of the database. The data are cross-checked against the information provided in the national elimination report. Attention is paid to the classification of individual cases and foci. CEP members pay particular attention to:

- coverage of populations by health services that provide access to malaria diagnosis and treatment, especially in former transmission foci and other entomologically receptive areas;
- the possible presence, in areas at risk for malaria, of treatment sites that do not always report cases to the surveillance system, including private pharmacies, private medical practitioners, drug vendors, public and private hospitals that were not included in the malaria surveillance system, military health services and services in neighbouring countries;

- documentation of surveillance at intermediate and primary levels, including case and focus registers, entomological surveillance reports and mapping of breeding sites in receptive foci;
- validation of surveillance reports against health facility records and anti-malarial drug supply figures;
- surveillance of populations at risk for malaria in time and space, based on a matrix showing the sizes of the smallest population units and the number of diagnostic tests (blood slides and/or RDTs) conducted in each of the units by month during the transmission season;
- the existence and performance of or requirement for special measures to ensure coverage of mobile populations, including temporary workers, illegal immigrants and refugees, whose presence and distribution in an administrative unit is variable or uncertain and who may not habitually use established health services;
- standard operating procedures for quality-assured diagnostic methods (RDTs and microscopy); an internationally certified, designated national central reference laboratory; and a national quality assurance system for malaria diagnosis reports;
- the timeliness of diagnosis and treatment specifically for malaria; and
- the timeliness of notification, epidemiological investigation of cases and foci and reporting.

CEP members also assess whether the systems and activities of the national programme can be considered adequate to monitor the potential for reintroduction of malaria into the country, to identify the areas that are receptive to resumption of transmission, to identify areas that are likely to become receptive, to identify areas vulnerable to parasitic importation and capture changes in vulnerability, and to take adequate measures to prevent reintroduction of transmission.

#### 5.2.2.1 Report from the malaria Certification Elimination Panel

CEP members prepare a comprehensive report of their findings and recommendations, to answer two fundamental questions.

- Is it proven beyond reasonable doubt that mosquito-borne local malaria transmission has been fully interrupted in the country, resulting in zero incidence of indigenous cases for at least the past three consecutive years, and, if so, on what evidence is this based?
- Can it be stated with full confidence that the national health system, as it is, will be able to prevent re-establishment of malaria transmission in the country, and, if so, on what evidence is this claim based?

#### 5.2.2.2 Granting malaria-free status

The report is reviewed by all CEP members. The country will be asked to clarify any technical issues or respond to questions. After any further clarification or supplementary information, the CEP submits its final evaluation report to the WHO MPAC with a recommendation to certify malaria elimination or to postpone it.

The WHO MPAC makes a final recommendation on granting malaria-free status in a summary report to the GMP which, in turn, informs the WHO Director-General, who makes the final decision and communicates it in an official letter to the national

government. When malaria-free status is granted, the WHO publishes the information in the *Weekly epidemiological record, International travel and health* and the *World malaria report*. In addition, the country is listed in the official WHO *Register of areas where malaria elimination has been achieved*, which was established at the request of Member States. As the Register is restricted to countries and territories that have eliminated malaria by specific measures, a supplementary list was opened in 1963 for areas in which malaria never existed or disappeared without specific measures *(42)*.

## 5.3 Follow-up of WHO certification

Certification confirms to the international community that an entire country has an adequate system for preventing re-establishment of local malaria transmission. It also demonstrates an accomplishment made possible by the necessary political will and vision, the required legislative and regulatory framework, adequate financial and administrative resources, personnel and technological capacity.

Reliable information on the global distribution of malaria is necessary to assess the risk of international travellers for exposure to malaria and the epidemiological risk of importation of malaria parasites into malaria-free areas that are receptive to transmission. Therefore, certified countries should continue to report to WHO annually on maintenance of their malaria-free status, providing information on reported malaria cases and their classification (for more information, see **Annex 9**).

A minimum indication of possible transmission re-establishment would be the occurrence of three or more indigenous malaria infections of the same species per year in the same focus for three consecutive years. Because certification represents recognition of a considerable operational achievement, a careful national investigation and consultation with WHO will be conducted before a country's malaria-free certification status is lost. As of November 2016, no certification had been withdrawn.

## 5.4 Subnational verification of malaria elimination

Subnational verification of malaria elimination is an option for large countries that have achieved interruption of local transmission in certain parts of their territory (states, regions or provinces). This option may be useful for countries that have geographically isolated territories, such as islands.

The documentation of elimination of local malaria transmission at subnational level should be as rigorous as that at national level but is managed only by the national health authorities of the country concerned. The outline of the subnational elimination report should be aligned with that of the national elimination report reviewed by WHO during certification.

### 5.4.1 General principles for interested countries

Use of the term "subnational certification" of malaria elimination should be avoided and the term "subnational verification" be used instead. Subnational verification is led by countries, which assess malaria elimination in subnational areas at their discretion.

WHO can provide technical assistance to Member States, as for other aspects of malaria control and elimination. In particular, WHO can provide advice on the approach to be used; however, WHO does not have the resources to participate in verification in all

countries. The processes and criteria for subnational verification should follow the WHO national certification scheme, as this will result in collection of essential information and establishment of the systems and structures required for certification of national elimination. Thus, the criteria and assessment procedures used in WHO certification of national malaria elimination are valid for subnational verification.

A clear distinction must be made between the role of national authorities, who verify, and that of local authorities in subnational areas, who are the objects of verification.

### 5.4.2 Suggested process for interested countries

Subnational verification of elimination of malaria transmission should be subjected to official regulations and/or administrative orders. A higher-level, experienced, independent national malaria elimination advisory committee should be established to monitor and verify the work of the national programme and help document it, including by publishing experiences and subnational verification milestones in the peer-reviewed literature. The advisory committee has a national political role in advocating for continuing work until the disease is eliminated.

It is recommended that subnational evaluations be conducted by independent national evaluation teams, including external international experts if possible, in order to increase their validity and credibility. The evaluation should include a review of documents on the malaria situation and the activities of the candidate administrative area, including validation of the absence of locally transmitted cases, resulting in zero incidence of indigenous cases for a statutory period (at least three consecutive years), related information and reports of field visits.

The criteria to be met to be confident that local malaria transmission has been interrupted in a given area should be defined in official regulations and should replicate WHO's criteria for national elimination as closely as possible.

The status of subnational verification of malaria elimination should be rescinded by national authorities if local transmission is re-established, i.e. the occurrence of three or more indigenous malaria cases of the same species linked in space and time, due to local mosquito-borne transmission in the same geographical focus in the same year for three or more years.

A central database on verification of subnational malaria elimination, with evaluation reports, should be created and maintained. High-quality surveillance and response should be sustained and remain efficient in the areas concerned until national certification is achieved.

Countries are encouraged to report annually to WHO on subnational verification of transmission elimination, so that this information can be included in the *WHO International travel and health* and the *World malaria report.*

# 6. Innovation and research for malaria elimination

Investment in basic science and product development must be sustained to create new tools and strategies for malaria elimination and its eventual global eradication. The operational feasibility, safety and cost-effectiveness of new tools and strategies should be evaluated by context-adapted operational research as a basis for reliable policy recommendations by national policy-makers and WHO. Efficient national regulatory processes (approval and registration) can substantially accelerate the introduction of new medicines, diagnostics, vector control tools and vaccines. Countries are therefore encouraged to:

- advocate for and/or contribute to continuous funding for basic science and product development;
- be actively involved in operational research to generate a reliable evidence base for policy recommendations and strategic planning; and
- streamline national and regional regulatory processes to avoid unnecessary delay in the uptake of new, high-quality tools and evidence-based strategies and ensure their safe use.

Key points related to innovation and research for malaria elimination are summarized in **Box 9**.

BOX 9.
**Innovation and research for malaria elimination**

- The research agenda for malaria elimination and eradication has been defined by consultative groups within the Malaria Eradication Research Agenda.
- Substantial research and development are currently under way on new medicines, diagnostics, vector control tools and vaccines for use against malaria.
- Country-driven operational research is essential for evaluating the operational feasibility, safety and cost-effectiveness of potential wide-scale use of new tools and strategies.
- To ensure efficient regulatory review of new tools and technologies, malaria elimination programmes should proactively evaluate the product development pipeline and define pathways for regulatory approval and registration, in close collaboration with the relevant regulatory authorities.

## 6.1 Research and development for malaria elimination and eradication

The research agenda for malaria elimination and eradication defined by consultative groups to the Malaria Eradication Research Agenda is available *(12)*, and an up-to date overview of the product development pipeline for medicines, diagnostics, vector control methods and vaccines can be found on the WHO Global Observatory on Health R&D at http://www.who.int/research-observatory/analyses/en/ (see malaria section).

### 6.1.1 Medicines

Substantial work is under way on new medicines to counter the resistance of vectors, to safely target hypnozoites (radical cure), to clear gametocytes and to prevent reinfection (prophylaxis). New formulations are being tested to increase patient adherence and to facilitate mass drug administration with a "single encounter radical cure and prophylactic" drug combination.

### 6.1.2 Diagnostics

Researchers are working on new assays for use at points of care to improve the sensitivity of diagnoses of both *P. falciparum* and *P. vivax* malaria and for quantitative measurement of G6PD deficiency. New assays are also being developed specifically for detecting gametocytes, identifying past infections (or the absence thereof) with serological markers, detecting resistant parasites with resistance markers and analysing parasite "connectivity" or importation by genetic "bar-coding".

### 6.1.3 Vector control

Current research and development are focused on new active ingredients for bednets and IRS that will overcome and prevent resistance to insecticides. New tools for residual (outdoor) transmission are being developed and field-tested. In collaboration with other mosquito-borne disease control programmes (e.g. for dengue and Zika virus disease), genetic modification of the mosquito population is being explored.

### 6.1.4 Vaccines

Research is under way to improve the efficacy and duration of the RTS,S vaccine and to develop a transmission blocking vaccine or new anti-infection vaccines. The results will further define the approach to vaccine use in elimination. More information can be found at http://www.malariavaccine.org/.

## 6.2 Operational research

National operational research is essential for evaluating the operational feasibility, safety and cost–effectiveness of potential wide-scale use of new tools and strategies. It will also be useful for evaluating specific aspects of the country's elimination strategy and exploring potential use of novel tools and approaches that are not formally recommended by WHO.

### 6.2.1 Operational feasibility

General recommendations often do not account for operational challenges in all contexts. For example, case investigation and reactive case detection around an

index case might be easy in settings with a very low case-load and a highly clustered population but more difficult in higher transmission foci with a scattered population distribution. Evaluation of operational feasibility in a few pilot areas before wide-scale implementation can indicate the appropriate strategies for the introduction and long-term sustainable use of interventions.

### 6.2.2 Safety

While certain tools might have been approved and recommended by stringent regulatory authorities, evaluation of their safety might still be warranted if they are to be used at scale or in asymptomatic populations. Recent examples include evaluation of the RTS,S vaccine (as per the WHO recommendation) and pharmacovigilance for the use of ACT in mass drug administration trials. Evaluations of safety should take into consideration the risks and benefits of the tool in the context of use (e.g. medicines for malaria treatment and for mass drug administration).

### 6.2.3 Cost and economic measures

The cost, budgeting, financial management and cost–effectiveness of prevention and treatment tools and strategies when the goal is elimination depend on the context and are often poorly understood. For example, surveillance strategies for finding and eliminating the asymptomatic parasite reservoir can vary from population-wide strategies to targeted case and focus investigation; and the cost and cost–effectiveness of each approach depends on the size and spatial distribution of programme activities. The cost–effectiveness of (novel) vector control measures also depends on the context. As costs may change dramatically after elimination but not be fully documented in advance, studies of the cost–effectiveness of a package of elimination interventions are fundamentally different from those of control scenarios, as they require assumptions of costs and cost reductions after elimination.

### 6.2.4 Other areas

Operational research can also address novel approaches that are still in the research phase, and the results can contribute to the evidence base required for national and global policy recommendations. The approaches include: (1) use of genetic epidemiology, which is being evaluated for distinguishing local from imported cases and defining the "connectivity" among parasite populations regionally; and (2) use of remote sensing satellite imagery and smart phone applications for disease mapping and reporting for malaria surveillance.

## 6.3 Regulatory environment for malaria elimination

The impact of new tools and technologies may be substantially reduced if uptake is slowed by regulatory processes and in-country registration. Malaria elimination programmes should proactively evaluate the product development pipeline and define the pathways necessary for regulatory approval and registration, in collaboration with national and regional regulatory authorities. It is therefore recommended that national regulatory authorities participate in the national malaria elimination advisory committee.

Certain countries require local trials of medicines for national registration, with evaluation in the epidemiological and demographic context of the country. In some cases, waivers or limited field trials can be used to ensure rapid uptake. Elimination programmes should work with national regulators to define the most appropriate, efficient pathway when local trials are required.

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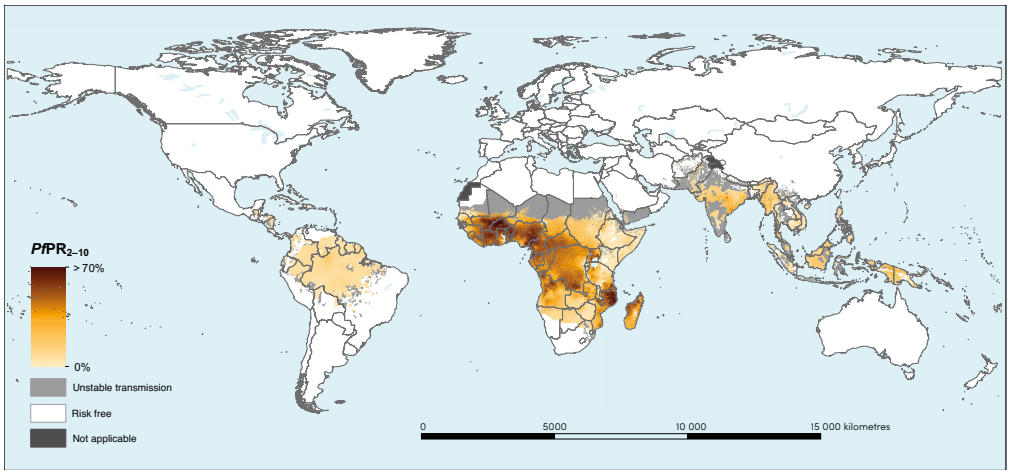
# Annex 1. Biology of malaria

## 1. Parasitological aspects

Malaria parasites are unicellular organisms belonging to the genus *Plasmodium*. Human malaria is due to four species that cause four types of malarial disease: *P. falciparum*, *P. malariae*, *P. ovale* and *P. vivax*. The four human malaria species are not evenly spread across the malaria-affected areas of the world, and their relative importance varies between and within areas, by zoo-geographical region (see **Fig. A1**). *P. falciparum* is the most common species and predominates in Africa south of the Sahara. *P. vivax* predominates in the subtropics and coexists with *P. falciparum* in tropical Asia, the tropical Americas and the Horn of Africa. *P. ovale* is found in Africa and sporadically in South-East Asia and the western Pacific. *P. malariae* has a similar geographical distribution to *P. falciparum*, but its incidence is lower and its distribution is patchy.

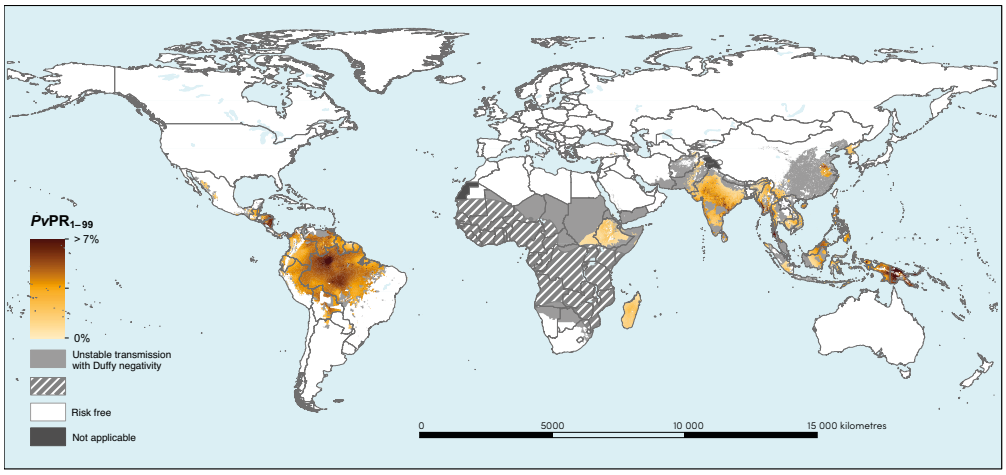
FIG. A1.
**Spatial distribution of *P. falciparum* and *P. vivax* (1)**

**(a)** Estimated annual mean *P. falciparum* parasite prevalence standardized to the 2–10-year age range, shown as a continuum of beige to brown with a range from 0% to > 70% *(2)*.




Source: Malaria Atlas Project.

**(b)** Estimated annual mean *P. vivax* parasite prevalence standardized across all ages, shown as a spectrum of beige to brown with a range from 0% to 7% *(3)*




Source: Malaria Atlas Project.

Note: Areas in which Duffy negative gene frequency is predicted to be > 90% are shown in hatching. Dark-grey areas are those with unstable transmission (annual number of reported cases < 0.1/1000 per year).

*P. vivax* and *P. falciparum* infections cause low birth weight in neonates and are associated with anaemia and splenomegaly, particularly in children and pregnant women. Unlike other *Plasmodium* species, *P. vivax* and *P. ovale* can remain dormant in the liver for up to several months or even years after inoculation and cause relapses. Forms of malaria due to *P. malariae* and *P. ovale* are less severe and are rarely life-threatening; unlike the other malaria parasites, *P. malariae* can remain undetected for decades and can lead to chronic immune-pathological sequelae.

The risk for contracting malaria is highly variable from country to country and even between areas in a country. The distribution of malaria in the world was widest in the late nineteenth century, since when, the area affected by malaria transmission has continued to contract.

During the past decade, cases of zoonotic *Plasmodium* infection, first and foremost with *P. knowlesi*, have been reported with increasing frequency in South-East Asia, especially in Malaysia. The natural reservoirs of this species are several macaque species found in forests in South-East Asia. The main vectors belong to the *Anopheles* leucosphyrus group, which is also associated with forest environments.

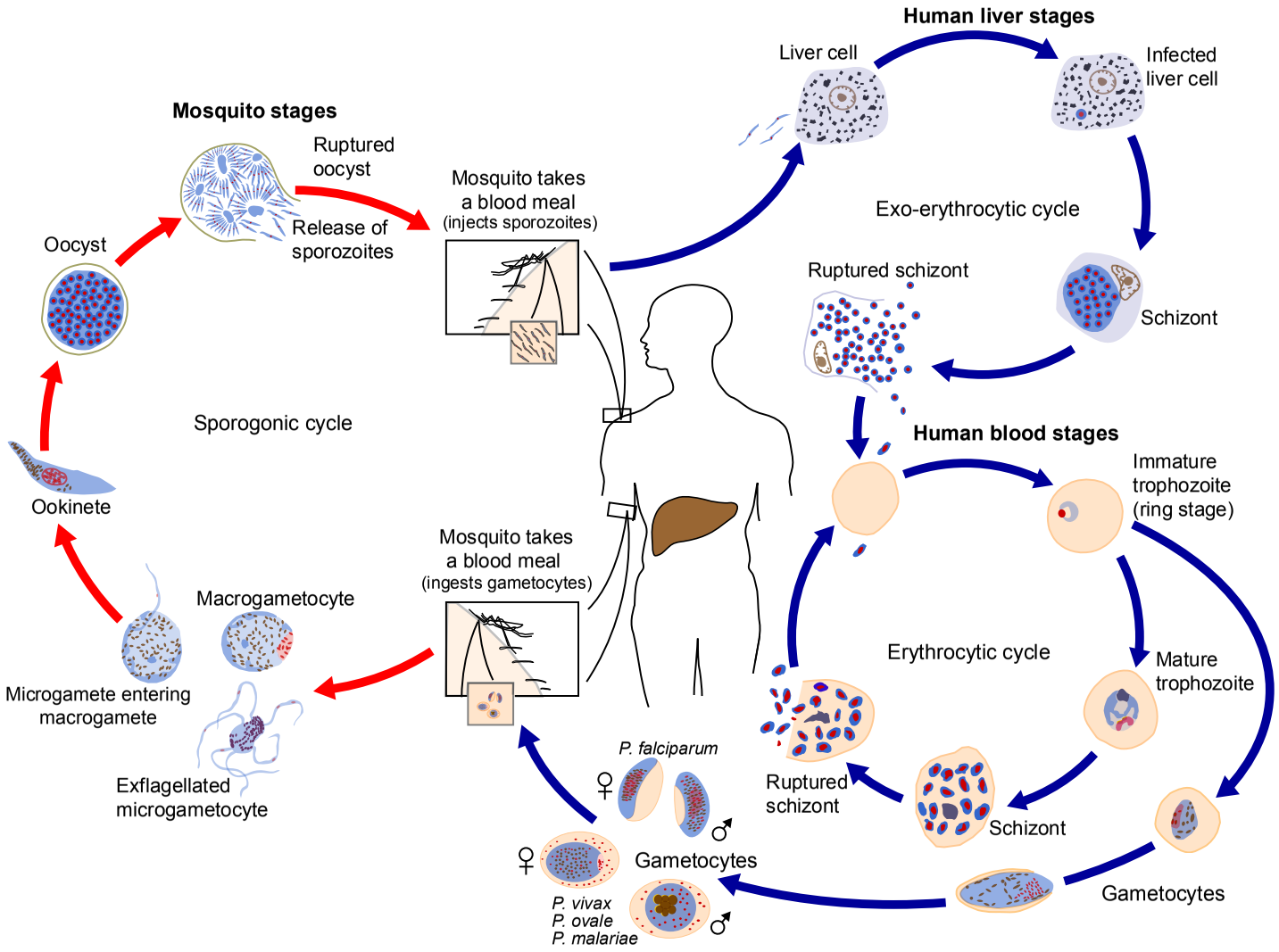
Malaria parasites are transmitted by female mosquitoes belonging to the genus *Anopheles*. The development of malaria parasites in the vector, called sporogony, includes a number of stages in different organs of the insect. Male and female gametocytes mate after being ingested by an anopheline mosquito during blood-feeding. The zygotes develop as ookinetes, which move across the mosquito stomach to form oocycsts, within which asexual multiplication leads to the production of up to thousands of sporozoites. The sporozoites migrate and accumulate in the salivary glands, from which they are injected when the infective mosquito bites a human or animal host for a blood-meal.

The speed of development of sporozoites depends on temperature and the parasite species. At the optimal temperature, 28 °C, the duration of sporogony is 9–10 days for *P. falciparum* and 8–10 days for *P. vivax*. The time from ingestion of gametocytes to release of sporozoites is the extrinsic incubation period (or duration of sporogony). Sporozoites injected by a mosquito enter the host's blood circulation; when they reach the liver, they invade hepatocytes. All *P. falciparum* sporozoites then undergo exo-erythrocytic schizogony, in which the parasite nucleus divides repeatedly over several days; at the end, the schizont bursts, giving rise to thousands of merozoites, which are released into the bloodstream. The duration of exo-erythrocytic schizogony is 5.5–7 days for *P. falciparum* and 6–8 days for *P. vivax*. In *P. vivax* malaria, some sporozoites, after invading hepatocytes, become dormant as hypnozoites for periods lasting from 3 to 18 months and very rarely up to 5 years.

The merozoites invade erythrocytes, where the great majority multiply asexually, undergoing repeated cycles of growth, rupture, release and reinvasion of fresh red cells. All clinical manifestations of malaria are due to this erythrocytic schizogony. The duration of each cycle of erythrocytic schizogony is about 48 h for both *P. falciparum* and *P. vivax*. Some merozoites grow and develop into male or female gametocytes within erythrocytes. When mature, they do not develop further, unless they are ingested by a mosquito vector. The immature gametocytes (stages 1–4) of *P. falciparum* are sequestered in the bone marrow and other deep tissues; only mature gametocytes (stage 5) circulate in the blood. In contrast, all stages of gametocytes of the three other species are present in the peripheral circulation.

The transmission cycle of malaria is represented in **Fig. A2**.

FIG. A2.
**Malaria transmission cycle**




Adapted, by permission of the publishers, from references *(4)* and *(5)*.

The duration of the biological processes mentioned above is not observed directly in clinical or public health practice. It is, however, possible to define a number of critical, observable intervals that depend on these elementary processes. For example, the clinical incubation period is equal to the duration of exo-erythrocytic schizogony plus the time required for a build-up of the parasite density above the pyrogenic threshold, which may take one or more cycles of erythrocytic schizogony. These observable intervals are of great importance for determining from a patient's history whether the case was imported or contracted locally and for how many days it may have been infective to vectors in a given area. The intervals are summarized in **Table A1** for *P. falciparum* and *P. vivax*. They should be taught during training of field staff and included in standard operating procedures for case and focus investigation.

TABLE A1.
**Duration of critical observable intervals for the two main species of human malaria parasite**

| INTERVAL | *P. FALCIPARUM* | *P. VIVAX* |
|---|---|---|
| Sporogony (extrinsic incubation period) at 28 °C | 9–10 days | 8–10 days |
| Pre-patency (from inoculation to appearance of microscope-detectable parasitaemia) | 9–10 days | 11–13 days |
| Incubation in non-immunes (from inoculation to appearance of symptoms):<br>• Short (not preceded by hypnozoites)<br>• Long (preceded by hypnozoites) | <br>9–14 days<br>Not applicable | <br>12–17 days<br>6–12 months |
| Time to appearance of mature gametocytes as observed by light microscopy after appearance of asexual parasitaemia | 7–15 days | 0 days |
| Time to disappearance of circulating gametocytes after treatment with effective blood schizonticides (without gametocytocide) | 3–6 weeks | < 1 day |
| Typical duration of untreated infection | 1–2 years (≤ 1 year in about 80% of cases) | 1–2 years (exceptionally ≤ 5 years) |

All values are from *(6)*, except times to appearance and disappearance of gametocytes, from *(7)*.

## 2. Entomological aspects

There are about 515 species of *Anopheles* mosquito in the world. Approximately 70 can transmit malaria, and, of these, 30–40 are vectors of major importance. Each species has a different pattern of behaviour. Most areas harbour multiple species of *Anopheles*, and different ones occur in different parts of the world.

The life cycle of the mosquito has four distinct stages: egg, larva, pupa and adult. The development periods of the various stages depend on the ambient temperature and nutritional factors and are shorter at higher temperatures. A blood-meal is necessary for maturation of the eggs.

**Vector efficiency** refers to how effective a given species is as a vector, irrespective of its density. This measure is determined mainly by the following properties of mosquitoes:

- vector competence: the ability of a mosquito species to transmit a given parasite species;
- longevity: expressed as the probability of a female mosquito surviving through one day (24 h);
- anthropophily: the proportion of a given vector's feed on humans, measured as the human blood index; and
- gonotrophic period: the interval between two oviposition cycles; the shorter the interval, the higher the biting frequency and hence vector efficiency.

**Vectorial capacity** is defined as the number of new malaria infections that the population of a given vector would cause per day at a given place and time, assuming that the human population is and remains fully susceptible. Vectorial capacity depends on inherent characteristics of vector species (biting time and host preference), density, human-biting rate and longevity, which are affected by the ambient temperature and relative humidity, as well as insecticides.

**Transmission intensity** can be considered a function of two main components: first, the mosquito-related factors that determine the vectorial capacity (probability of an infection being transmitted from an infectious person on any given day) and, second, the detection- and treatment-related factors that determine for how long an infection persists to contribute to transmission (gametocyte carriage rate). Of note, symptomatic infections (typically with higher parasite densities) are significantly more infectious to mosquitoes; thus, early detection of illness, testing and treatment may be critical in reducing transmission. Areas with higher vectorial capacity and low treatment rates will tend to have the highest transmission rates, as infections in these areas will remain untreated for a long time, resulting in a high probability of transmission to mosquitoes and humans throughout that time. Knowing whether transmission intensity is driven more by low treatment rates or by high vectorial capacity may suggest which interventions are likely to have the most impact (e.g. strengthening surveillance with treatment versus increasing coverage with vector control).

## References


1. Control and elimination of *Plasmodium vivax* malaria – a technical brief. Geneva: World Health Organization; 2015 (http://apps.who.int/iris/bitstream/10665/181162/1/9789241509244_eng.pdf?ua=1&ua=1, accessed 17 June 2016).
2. Gething PW, Patil AP, Smith DL, Guerra CA, Elyazar IR, Johnston GL, et al. A new world malaria map: *Plasmodium falciparum* endemicity in 2010. Malar J 2011;10:378.
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4. Life cycle of *Plasmodium* spp. Atlanta, GA: United States Centers for Disease Control and Prevention; 2004 (http://www.cdc.gov/dpdx/malaria/index.html, accessed 17 November 2016).
5. Sullivan S *P. vivax life cycle*. New York, NY: *vivax*malaria.com; 2006 (http://www.vivaxmalaria.com/images/vivax_lifecycle.jpg, accessed 17 November 2016).
6. Gilles HM, Warrell DA. Bruce-Chwatt's essential malariology. 3rd edition. London: Edward Arnold; 1993.
7. Bousema T, Drakeley C. Epidemiology and infectivity of *Plasmodium falciparum* and *Plasmodium vivax* gametocytes in relation to malaria control and elimination. Clin Microbiol Rev 2011;24:2377–2410.

# Annex 2. Diagnosis and treatment of *Plasmodium falciparum* and *P. vivax* malaria *(1)*

Even where malaria is eliminated or close to elimination, diagnostic capabilities, including quality assurance, should be maintained, and parasitological confirmation by microscopy (or by RDT) is recommended before treatment is administered. Where both malaria species coexist, bivalent RDTs should be used in order to differentiate *P. falciparum* from *P. vivax*. If microscopy is used, WHO standards for malaria microscopy training, certification and quality assurance should be in place.

The treatment of *P. falciparum* and *P. vivax* infections, however, differs (**Table A2**).

TABLE A2.
**Treatment of *P. falciparum* and *P. vivax* infections**

| *P. FALCIPARUM* | *P. VIVAX* |
|---|---|
| **TREATMENT OF BLOOD-STAGE INFECTIONS** | |
| ACT (except pregnant women in their first trimester) | In areas with chloroquine-susceptible infections, treat with either ACT (except pregnant women in first trimester) or chloroquine. Artesunate + sulfadoxine-pyrimethamine is not recommended for the treatment of *P. vivax* malaria because of its limited efficacy. |
| A single dose of 0.25 mg/kg body weight of primaquine on the first day of treatment, except to pregnant women, infants < 6 months of age and women breastfeeding infants < 6 months of age | Not applicable |
| In the first trimester of pregnancy, quinine should be used instead of ACT.[a] | Pregnant women should be treated with chloroquine (all trimesters) or quinine (first trimester) and ACT (second or third trimesters). |
| **TREATMENT OF LIVER-STAGE INFECTIONS** | |
| Not applicable | The G6PD status of patients should guide administration of primaquine for preventing relapses (for more information, see reference *(2)*). |
| | To achieve radical cure (cure and prevention of relapse), a 14-day course of primaquine at 0.2–0.5 mg/kg body weight per day is given, except to pregnant women, infants aged < 6 months, women breastfeeding infants aged < 6 months, women breastfeeding older infants unless they are known not to be G6PD deficient and people with G6PD deficiency. |
| | For G6PD-deficient patients, primaquine may be considered at a dose of 0.75 mg base/kg body weight once a week for 8 weeks, with close medical supervision for potential primaquine-induced haemolysis. |
| | If G6PD testing is not available, a decision to prescribe or withhold primaquine should be based on an assessment of the benefits of preventing relapse against the risks of primaquine-induced haemolytic anaemia. |
| **SEVERE MALARIA** | |
| Adults and children with severe malaria (including infants, pregnant women in all trimesters and lactating women) should be treated with intravenous or intramuscular artesunate for at least 24 h and until they can tolerate oral medication. | |
| After parenteral artesunate for at least 24 h, treatment can be completed with a full course of ACT. | After parenteral artesunate for at least 24 h, treatment can be completed with a full course of ACT or chloroquine (in countries where chloroquine is the treatment of choice for *vivax* malaria). Artesunate + sulfadoxine–pyrimethamine is not recommended for the treatment of *P. vivax* malaria because of its limited efficacy. |
| | A full course of radical treatment with primaquine should be given after recovery. |

[a] Treatment guidelines are updated regularly, and this recommendation is currently being re-evaluated.

## References


1. Control and elimination of *Plasmodium vivax* malaria – a technical brief. Geneva: World Health Organization; 2015 (http://apps.who.int/iris/bitstream/10665/181162/1/9789241509244_eng.pdf?ua=1&ua=1, accessed 3 May 2016).

2. Testing for G6PD deficiency for safe use of primaquine in radical cure of *P. vivax* and *P. ovale* malaria – Policy brief. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/250297/1/WHO-HTM-GMP-2016.9-eng.pdf, accessed 3 February 2017).

# Annex 3. Monitoring and evaluation indicators for interventions in an elimination programme

The list in **Table A3** is largely restricted to indicators specific to elimination programmes. It is illustrative, and each programme should modify or complement it according to their priorities; process indicators should be aligned with strategic and operational plans.

Additional indicators for national monitoring are provided in WHO operational manuals for disease surveillance, entomology, vector control and drug resistance, which are regularly updated and posted on the WHO Global Malaria Programme website at http://www.who.int/malaria/publications/en/.

TABLE A3.
**Monitoring and evaluation indicators for interventions in an elimination programme**

| INDICATOR | NORM OR TARGET | DATA SOURCE |
|---|---|---|
| **IMPACT** | | |
| Number and incidence rate (per 1000 population) of malaria cases<br>• by species, classification, sex, age group;<br>• by source (e.g. imported, indigenous), by ACD and PCD, by sector | Target values to be projected by the programme year by year | Malaria case database |
| Number of foci by classification | Target values to be projected by the programme year by year | Malaria focus database |
| Number of people and percentage of population living in active foci | | Malaria focus database |
| Number of malaria deaths by species and by imported or locally acquired | | Malaria case database |
| **QUALITY AND PERFORMANCE OF SURVEILLANCE** | | |
| Annual blood examination rate by district and focus and by RDT or microscopy[a] | | Malaria case and case detection databases |
| Percentage of microscopy results cross-checked by national reference laboratory | 100% of positive results<br>10% of negative results | Reference laboratory database |
| Percentage of testing laboratories participating in WHO-recommended microscopy quality assurance assessments | 100% | Reference laboratory database |
| Percentage of expected monthly reports received from health facilities and other service providers (with number of patients tested for malaria and number positive) | 100% | Malaria case and case detection databases |
| Percentage of cases notified within 24 h of detection | 100% | Malaria case and case detection databases |
| Percentage of cases with completed case investigation form submitted within stipulated delay | 100% | Malaria case and case detection databases |
| Percentage of foci for which completed investigation form submitted within stipulated delay | 100% | Malaria focus database |

| INDICATOR | NORM OR TARGET | DATA SOURCE |
|---|---|---|
| **CASE MANAGEMENT** | | |
| Percentage of patients with suspected malaria who received a parasitological test | 100% | Malaria case and case detection databases |
| Percentage of patients with confirmed malaria who received first-line anti-malarial treatment according to national policy | 100% | Malaria case and case detection databases |
| **VECTOR CONTROL** | | |
| Percentage of active and residual non-active foci and percentage of population living in receptive areas covered by appropriate vector control (IRS and/or LLINs), by year | 100% of targeted population | Operations records |
| Percentage of active and residual non-active foci protected by IRS, by year | 100% of targeted foci | Independent focus surveys |
| Percentage of population living in active and residual non-active foci protected by IRS, by focus and year | 100% of targeted population | Independent focus surveys |
| Percentage of population in active foci and residual non-active foci with high receptivity and vulnerability protected by LLINs, by focus and year | 100% of targeted population | Independent focus surveys |
| Percentage of potential larval habitats in active and residual non-active foci in which environmental modification is implemented | As per national target, depending on vector species | Independent vector survey |
| Percentage of potential larval habitats in active and residual non-active foci treated with larvicides or insect growth regulators | As per national target based on identified key habitats | Independent survey |
| **PROGRAMME MILESTONES** | | |
| Malaria is a notifiable disease | | Policy documents |
| Standard operating procedures for all components of surveillance have been prepared, field tested and are in use | | Surveillance and routine information systems assessment surveys |
| There is a national reference laboratory for microscopy, with a slide bank and implementation of external quality assurance | | Surveillance and routine information systems assessment surveys |
| An independent national malaria elimination advisory committee has been set up | | Malaria programme reviews |
| A comprehensive report on the elimination programme is prepared annually and shared with all district health offices | | Malaria programme reviews |
| The national malaria elimination plan has been approved and endorsed by the minister of health | | Malaria programme reviews |
| There is functional inter-sectoral collaboration in all districts concerned | | Malaria programme reviews |
| There is an updated list of all public and private health facilities and community health workers who provide malaria diagnosis or treatment | | Surveillance and routine information systems assessment surveys |
| Each facility is registered to receive appropriate supervision[b] | | Surveillance and routine information systems assessment surveys |

[a] There should be some case detection activities in each focus and each highly receptive village, workplace or other site every month during the transmission season.

[b] The nature and frequency of "supervision" depend on the country.

# Annex 4. Terms of reference for the WHO malaria Certification Elimination Panel

The terms of reference of the CEP have been revised in accordance with an updated, more streamlined process of certification for elimination to include a greater role for independent national committees (such as national malaria elimination advisory committees) and the MPAC, in collaboration with dedicated teams of observers and certifiers who conduct country visits.

## Key roles and responsibilities

1. Review submitted country documentation and national elimination reports, and discuss their content by video conference, teleconference or face to face.
2. Conduct country assessments and field missions, with the following terms of reference:

    a. Review and assess how procedures and criteria proposed by WHO have been applied to document the elimination of malaria transmission, including evaluation of the performance of the surveillance system and high-quality case management.

    b. Verify that the data and information in country documentation and reports are accurate.

    c. Conduct field visits to verify elimination, in particular visit the last malaria foci in the country to ensure that they have been cleared.

    d. Review national guidelines and plans of action to ensure that the strategic technical components and guidelines are up to date.

    e. Collect and review any additional information required on the malaria situation in the country by meetings with key stakeholders, published and unpublished documents, journal publications, etc.

    f. Assess the capacity of the government to maintain its malaria-free status and prevent re-establishment of malaria transmission.

    g. Prepare a final evaluation report for country certification, and submit it to the WHO GMP.

3. Review the final evaluation report with all other members of the CEP for review and comments. If necessary, feedback may be incorporated for finalization of the report (with the support of the WHO Secretariat).
4. Report key findings from the final evaluation report to the WHO MPAC, and make a recommendation on whether malaria elimination can be certified or whether a decision should be postponed, with details of the additional evidence required to demonstrate that malaria has been eliminated.

## Rules and composition of the CEP (at least eight members, with a WHO-designated chairperson)

Members are appointed by WHO, in consultation with relevant WHO regional offices, for at least three years (with possible renewal).

Members should have knowledge about and experience in malaria elimination, and at least one should be an entomologist. Members may represent fields such as medical

parasitology, tropical medicine, laboratory science, epidemiology, vector biology and control, information systems and other specialized areas of public health such as programme management.

Members should provide independent opinions and have no conflict of interest.

Members conducting assessment or evaluation missions should not be citizens of the applicant country nor have recently supported the country in reviewing its malaria programme nor have been involved in preparing the national elimination report.

## Annex 5. Documents for the Certification Elimination Panel to be prepared from the elimination database by the national government

- national malaria elimination strategic and operational plan;
- annual malaria programme report;
- plan of action for the prevention of re-establishment of malaria;
- organizational structure of the malaria department and malaria activities in general health services, with detailed budget and staff information; description of health facilities and their functions and activities in malaria surveillance; plans for continued staff education; and guidelines and standard operating procedures for malaria surveillance;
- all available annual malaria surveillance reports for at least 10 years, three years of which show zero indigenous cases;
- full information about malaria foci in the five years before the last indigenous case, with supporting maps (database of malaria focus investigations; focus register and analytical tables and maps);
- national malaria case register with case investigation forms for at least the previous five years;
- for laboratory support, reports of quality-assurance activities for diagnosis; designation of a national reference laboratory; participation in an external quality assurance scheme; standard operating procedures for malaria diagnostics; participation in WHO assessment of malaria microscopy competence; annual reports on performance of laboratory services for malaria diagnostics;
- national anti-malarial treatment policy;
- annual report of entomological and vector control activities;
- reports of independent committees on malaria (such as the national malaria elimination advisory committee), the surveillance system and entomological and vector control activities;
- recent published and unpublished reports of studies on malaria epidemiology and malaria vectors;
- legislation or regulations related to malaria and vector control;
- reports of inter-sectoral collaboration;
- reports of border coordination activities, if relevant; and
- documentation of health education and community awareness-raising.

# Annex 6. Outline of content of a national elimination report

**Executive summary**

**1. General information**

- **1.1** Geography
- **1.2** Physiography
- **1.3** Climate and vegetation
- **1.4** Key cultural characteristics
- **1.5** Population
- **1.6** Administration
- **1.7** Economics
- **1.8** General health profile
- **1.9** Organization, planning, description of general health services
- **1.10** Public and private health care delivery system

**2. Malaria in the country**

- **2.1** History of malaria
- **2.2** Epidemiology of malaria in the past 10 years, including description of last cases and foci (to include recent published and unpublished research reports on malaria epidemiology in the country)
- **2.3** Entomological aspects (to include recent published/unpublished research reports)

**3. Main surveillance and interventions undertaken to achieve malaria elimination**

- **3.1** Main strategies and approaches applied
- **3.2** Legislation and regulations
- **3.3** Organizational structure and responsibilities of the malaria network
- **3.4** Surveillance
  - **3.4.1** Case detection and response
  - **3.4.2** System of laboratory diagnosis and external quality control assurance
  - **3.4.3** Case management in public and private health-care delivery systems and national treatment policies

# Annex 7. Example of individual case investigation form for a national malaria case register

*This form is to be completed for all laboratory-confirmed (microscopy or RDT) malaria cases.*

**Section 1. Characterization of the case**

1. Malaria case ID:
2. Is this case linked to a larger focus?
   - Yes O If so, indicate the ID number of the focus:
   - No O
3. Date:
4. Facility:
5. Information about the case patient
   - 5.1 Name
   - 5.2 Present home address, including contact details
   - 5.3 Permanent address if different from the above
   - 5.4 Age
   - 5.5 Gender
   - 5.6 Occupation or other aspects that may have influenced malaria risk
   - 5.7 Date of confirmation of malaria diagnosis
   - 5.8 Date of notification of malaria case
   - 5.9 *Plasmodium* species identified
   - 5.10 Recent travel history within the country, i.e. to other malaria-endemic settings (past two weeks, six months and for one year)
   - 5.11 Recent travel history outside the country to malaria-endemic settings (past two weeks, six months and for one year)
   - 5.12 Blood transfusion within past three months
   - 5.13 Possible origin of malaria infection (place where malaria infection is likely to have been acquired) with GPS coordinates, if possible
   - 5.14 Previous history of malaria, if any (when, where, parasite species, treatment given, etc.)
   - 5.15 Recent contact with known imported case(s); provide details
6. Case detection and treatment
   - 6.1 Method of diagnosis (passive case detection, active case detection, mobile malaria clinic, other)
   - 6.2 Main symptoms
   - 6.3 Date of onset of first symptoms
   - 6.4 Test used (microscopy or RDT)
   - 6.5 Parasite species (if microscopy is used: parasite density and presence of gametocytes reported)
   - 6.6 Treatment (drugs, dosage, dates)
   - 6.7 Treatment outcome (follow-up visits, confirmation of clearance, dates)

**Section 2. Classification of the case**

7. The case is classified as:

7.1 Parasite species:

| | | | | | |
|---|---|---|---|---|---|
| *P. falciparum* | O | *P. vivax* | O | *P. malariae* | O |
| *P. ovale* | O | Mixed | O | (specify: | ) |
| Other | O | (specify: | ) | | |

7.2 Classification:

| | | | | | |
|---|---|---|---|---|---|
| Imported* | O | Introduced | O | Indigenous | O |
| Relapsing | O | Recrudescent | O | Induced | O |
| Other** | O | | | | |

Comment on evidence used for case classification:

* Outside the district/province, from other country (please specify)

**This may be poor compliance or failure to follow up.

**Section 3. Follow-up of the case, household and neighbourhood**

Date of investigation

8. Case household visit (done, dates, map):

8.1 Household location (GPS)

8.2 Household members listed, screened (e.g. fever), tested, results

9. Neighbourhood visit (done, dates, map)

9.1 Household locations (GPS)

9.2 Household members listed, screened (e.g. fever), tested, results

*Note: If additional infections are identified in the case or neighbouring households, continue to focus investigation protocols.*

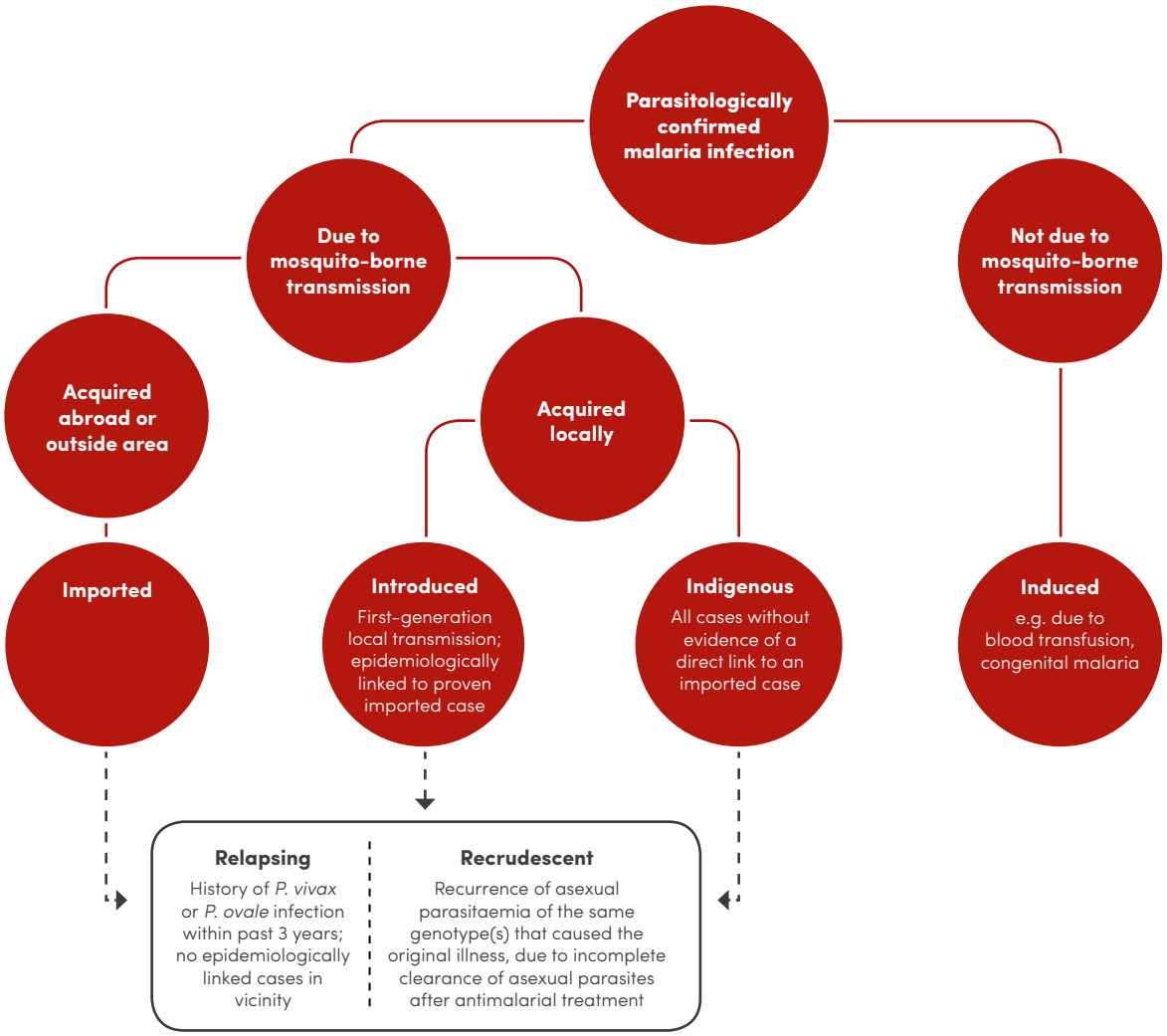
10. Vector control and preventive measures taken, if any

11. Follow-up measures taken, if any

12. Name and title of responsible officer who investigated the case

13. Reference to relevant case or focus investigation records and record numbers

## Reference


Parasitologically confirmed malaria infection
Due to mosquito-borne transmission
Not due to mosquito-borne transmission
Acquired abroad or outside area
Acquired locally
Imported
Introduced
First-generation local transmission; epidemiologically linked to proven imported case
Indigenous
All cases without evidence of a direct link to an imported case
Induced
e.g. due to blood transfusion, congenital malaria
Relapsing
History of P. vivax or P. ovale infection within past 3 years; no epidemiologically linked cases in vicinity
Recrudescent
Recurrence of asexual parasitaemia of the same genotype(s) that caused the original illness, due to incomplete clearance of asexual parasites after antimalarial treatment

# Annex 8. Example of individual focus investigation form for a national malaria case register

*This form is to be completed for all confirmed malaria foci.*

**Section 1. Characterization of the focus**

1. Malaria focus ID:
2. List all case ID numbers that are part of this focus ID:

3. Date of this report: Date of focus identification:
4. District and health facility catchment area:
5. Information about the focus
   - 5.1 Geographical map of focus and its limits
   - 5.2 Size of population, number of houses
   - 5.3 Administrative map of houses, heath facilities and other important structures, as well as access routes within the focus
   - 5.4 Distribution of parasites (species, number and location of infections identified)
   - 5.5 Distribution of vector species within the focus (principal and secondary malaria vectors and their behaviour, including breeding sites with presence or absence of larvae)
   - 5.6 Type of environment in relation to receptivity (urban or rural population, altitude, main geographical features, environmental changes as a result of development, original and current endemicity, etc.) and vulnerability (close proximity to endemic areas within the country or across international border, refugees, etc.) within the focus
   - 5.7 Population characteristics in relation to vulnerability (migration patterns, presence and numbers of temporary workers, typical travel histories, etc.) within the focus
6. Focus history
   - 6.1 Total number of malaria cases by species reported within the focus during the past five years
   - 6.2 Results of malaria surveys, including active case detection within the focus during the past five years
   - 6.3 Dynamics of the focus status during the past five years (active foci versus residual non-active foci versus cleared foci)
   - 6.4 Types and dates of vector control and other preventive measures applied within the focus during the past five years (provide details)

**Section 2. Classification of the focus**

7. Focus classification

   Focus classified as:

   7.1 Parasite species:

| | | | | | |
|---|---|---|---|---|---|
| *P. falciparum* | O | *P. vivax* | O | *P. malariae* | O |
| *P. ovale* | O | Mixed | O | (specify: | ) |
| Other | O | (specify: | ) | | |

7.2 Classification at time of detection (date: ):

| | | | |
|---|---|---|---|
| Active | O | Residual non-active | O |
| Cleared | O | Other | O |

Comment on evidence used for focus classification:

7.3 Classification at time of specified follow up (date ):

| | | | |
|---|---|---|---|
| Active | O | Residual non-active | O |
| Cleared | O | Other | O |

Comment on evidence used for re-classification of focus:

7.4 Relation of the focus to the malaria case that prompted focus investigation (in time, space and circumstance, e.g. the person in residence, work, etc.)

7.5 Location and total number of households with inhabitants where malaria cases were registered within the focus

**Section 3. Follow-up of the focus households and neighbourhoods, and response**

*Measures taken to clear infections and stop transmission within the focus and prevent possible onward spread of the current malaria infections from the focus, if any (provide details)*

8. Follow-up actions taken (provide details)

   For example:

   8.1 Neighbourhood visits (done, dates, map)

   Household locations (GPS)

   Household members listed, screened (e.g. fever), tested, results

   Household members treated (case management, prevention)

   8.2 Vector control and preventive measures taken, if any

   8.3 Other follow-up measures taken, if any

9. Reference numbers to relevant focus investigation records and case investigation records

10. Name, title and signature of responsible officer who investigated the focus and completed the form

**Reference**

| TYPE OF FOCUS | DEFINITION | OPERATIONAL CRITERIA |
|---|---|---|
| Active | A focus with ongoing transmission | Locally acquired case(s) have been detected within the current calendar year. |
| Residual non-active | Transmission interrupted recently (1–3 years ago) | The last locally acquired case(s) was detected in the previous calendar year or up to 3 years earlier. |
| Cleared | A focus with no local transmission for more than 3 years | There has been no locally acquired case for more than 3 years, and only imported or/and relapsing or/and recrudescent or/and induced cases may occur during the current calendar year. |

## Annex 9. Information to be included in annual report for follow-up of WHO certification

1. Confirmed malaria cases detected in the country during the reporting period, by species, case classification and origin
2. Brief histories of all reported introduced or indigenous cases, if any
3. Brief histories of all reported malaria deaths and other unusual events, including cases of congenital malaria and induced malaria
4. Measures used to prevent re-establishment of malaria transmission

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