



DISEASE SURVEILLANCE FOR MALARIA ELIMINATION

AN OPERATIONAL MANUAL



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Foreword

Information on the number and distribution of malaria cases and deaths is critical for the design and implementation of malaria control programmes. It is needed to determine which areas or population groups are most affected by malaria, so that resources can be targeted to the populations most in need. Information on the incidence of disease in relation to past levels is needed to alert programmes about epidemics, so that control measures can be intensified. Data on changes in disease incidence and mortality are also needed in order to judge the success of a programme and to determine whether it is performing as expected or whether adjustments in the scale or blend of interventions are required.

The capacity of malaria surveillance systems to provide information on the distribution of and trends in malaria varies widely across the globe. The aim of this manual is to provide guidance to malaria-endemic countries in designing and managing surveillance systems for malaria control and elimination, so that malaria programmes can obtain more complete, and more accurate information on malaria incidence and mortality, which can be used to help plan and monitor the programme. The manual provides guidance on (i) the general principles that govern surveillance systems, including case definitions, procedures for case detection and investigation; (ii) data recording, reporting and analysis; and (iii) factors to be considered in establishing malaria surveillance systems.

Recent developments in diagnostic testing present new opportunities for malaria surveillance systems. The availability of inexpensive, quality-assured rapid diagnostic tests for malaria means that parasite-based diagnosis is now possible not only at peripheral health-care facilities but also at the community level. Thus, malaria surveillance can be based on confirmed rather than suspected cases at all levels of the health system. As malaria control measures expand and the proportion of fevers due to malaria falls rapidly, it becomes increasingly important to track confirmed malaria cases, rather than non-malarious fevers, so that resources can be targeted to areas where problems remain and progress in malaria control is accelerated.

This manual is one of three core WHO documents, along with *Universal Access to Malaria Diagnostic Testing and Guidelines for the Treatment of Malaria, Second Edition*, that form the basis for WHO's T3: Test, Treat, Track initiative (http://www.who.int/malaria/test_treat_track/en/index.html). The T3 initiative will support malaria endemic countries in their efforts to achieve universal coverage with diagnostic testing and antimalarial treatment, as well as to strengthen their malaria surveillance systems. The development of effective surveillance systems requires significant investments, both financial and human. A critical factor in the functioning and sustainability of monitoring systems is the availability of qualified, experienced personnel. Investment in data collection systems without a commensurate investment in human resources to analyse the data and use the information generated is unlikely to yield significant returns; ultimately, data should be used to influence decisions, and it is the quality of the decisions rather than the quality of the data that will accelerate the control of malaria.

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Abbreviations

ITN	insecticide-treated net
LLIN	long-lasting insecticidal net
PCR	polymerase chain reaction
RDT	rapid diagnostic test
WHO	World Health Organization

Acknowledgements

In 1994, a document from the WHO Regional Office for Africa described information systems for the evaluation of malaria programmes and included indicators for inpatient (severe) malaria cases and malaria deaths.¹ The 20th report of the WHO Expert Committee on Malaria (1998) included epidemiological indicators with standardized case definitions.² Malaria was one of 40 diseases included in the *WHO recommended surveillance standards*, published in 1999.³

In 2007–2008, WHO released three documents on malaria elimination that provided guidance on surveillance.^{4,5,6} Information on surveillance during the elimination phase is also available from the WHO Regional Office for Europe (in Russian). WHO published recommended indicators for monitoring malaria programmes in the *World malaria report* in 2008, 2009, 2010 and 2011.

In 2008, a document on disease surveillance and indicators for malaria control was prepared by the Global Malaria Programme at WHO. In April 2009, a WHO Global Malaria Programme Technical Advisory Group reviewed these draft disease surveillance guidelines and indicators for the control phase. The group recommended that WHO also prepare surveillance and indicator guidance for the elimination phase.

New versions of the manuals for disease surveillance for malaria control and elimination were produced in 2010 and revised in July 2011, before being reviewed by WHO regional offices and external partners, including members of the Roll Back Malaria (RBM) Monitoring and Evaluation References Group (MERG).

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¹ *Information systems for the evaluation of malaria programmes. A practical guide*. Brazzaville, WHO Regional Office for Africa, 1994 (AFRO/CTD/94.3). Available online at http://whqlibdoc.who.int/afro/1994-99/AFRO_CTD_MAL_94.3.pdf.

² *Expert Committee on Malaria: twentieth report*. Geneva, World Health Organization, 1998 (WHO Technical Report Series No. 892). Available online at http://whqlibdoc.who.int/trs/WHO_TRS_892.pdf.

³ Available online at <http://www.who.int/csr/resources/publications/surveillance/whocdscsr992.pdf>.

⁴ *Guidelines on the elimination of residual foci of malaria transmission*. Cairo, WHO Regional Office for the Eastern Mediterranean, 2007 (EMRO Technical Publications Series 33). Available online at <http://www.emro.who.int/dsaf/dsa742.pdf>.

⁵ *Malaria elimination: a field manual for low and moderate endemic countries*. Geneva, World Health Organization, 2007. Available online at http://whqlibdoc.who.int/publications/2007/9789241596084_eng.pdf.

⁶ *Global malaria control and elimination: report of a technical review*. Geneva, World Health Organization, 2008. Available online at http://whqlibdoc.who.int/publications/2008/9789241596756_eng.pdf.

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Glossary

Active case detection: The detection by health workers of malaria infections at community and household level in population groups that are considered to be at high risk. Active case detection can be conducted as fever screening followed by parasitological examination of all febrile patients or as parasitological examination of the target population without prior fever screening.

Annual blood examination rate: The number of patients receiving a parasitological test for malaria (blood slide for microscopy or malaria rapid diagnostic test) per 100 population per year.

Case-based surveillance: Every case is reported and investigated immediately (and also included in the weekly reporting system).

Case definition (control programmes)

Confirmed malaria: Suspected malaria case in which malaria parasites have been demonstrated in a patient's blood by microscopy or a rapid diagnostic test.

Presumed malaria: Suspected malaria case without a diagnostic test to confirm malaria but nevertheless treated presumptively as malaria.

Suspected malaria: Patient illness suspected by a health worker to be due to malaria. The criteria usually include fever. All patients with suspected malaria should receive a diagnostic test for malaria, by microscopy or a rapid diagnostic test.

Case definition (elimination programmes)

Autochthonous: A case locally-acquired by mosquito-borne transmission, i.e. an indigenous or introduced case (also called 'locally transmitted').

Imported: A case the origin of which can be traced to a known malarious area outside the country in which the case was diagnosed.

Indigenous: Any case contracted locally (i.e. within national boundaries), without strong evidence of a direct link to an imported case. These include delayed first attacks of *P. vivax* malaria due to locally acquired parasites with a long incubation period.

Induced: A case the origin of which can be traced to a blood transfusion or other form of parenteral inoculation but not to normal transmission by a mosquito.

Introduced: A case contracted locally, with strong epidemiological evidence linking it directly to a known imported case (first generation from an imported case, i.e. the mosquito was infected from a case classified as imported).

Locally transmitted: A case locally-acquired by mosquito-borne transmission, i.e. an indigenous or introduced case (also called 'autochthonous').

Malaria: Any case in which, regardless of the presence or absence of clinical symptoms, malaria parasites have been confirmed by quality-controlled laboratory diagnosis.

Case investigation: Collection of information to allow classification of a malaria case by origin of infection, i.e. whether it was imported, introduced, indigenous or induced. Case investigation includes administration of a standardized questionnaire to a person in whom a malaria infection is diagnosed.

Case management: Diagnosis, treatment, clinical care and follow-up of malaria cases.

Case notification: Compulsory reporting of detected cases of malaria by all medical units and medical practitioners, to either the health department or the malaria elimination service (as laid down by law or regulation).

Certification of malaria-free status: Granted by WHO after it has been proven beyond reasonable doubt that the chain of local human malaria transmission by *Anopheles* mosquitoes has been fully interrupted in an entire country for at least 3 consecutive years.

Control charts: Figures summarizing information on key malaria indicators collected by surveillance for regular, periodic review by malaria control programme personnel.

Discharge register: List of patients who leave inpatient hospital care. Discharge registers should contain the date of admission, patient's name, residence, age, sex, diagnosis, length of stay and reason for leaving (discharged, died, transferred, absconded). This information should be abstracted from the patient file by appropriately trained staff.

Elimination: Reduction to zero of the incidence of infection by human malaria parasites in a defined geographical area as a result of deliberate efforts. Continued measures to prevent re-establishment of transmission are required.

Endemic: Applied to malaria when there is an ongoing, measurable incidence of cases and mosquito-borne transmission in an area over a succession of years.

Epidemic: Occurrence of cases in excess of the number expected in a given place and time.

Eradication: Permanent reduction to zero of the worldwide incidence of infection caused by human malaria parasites as a result of deliberate efforts. Intervention measures are no longer needed once eradication has been achieved.

Evaluation: Attempts to determine as systematically and objectively as possible the relevance, effectiveness and impact of activities in relation to their objectives.

False negative (or false positive): A negative (or positive) result in a test when the opposite is true.

Focus: A defined, circumscribed locality situated in a currently or former malarious area containing the continuous or intermittent epidemiological factors necessary for malaria transmission. Foci can be classified as endemic, residual active, residual non-active, cleared up, new potential, new active or pseudo.

Gametocyte: The sexual reproductive stage of the malaria parasite present in the host's red blood cells.

Incubation period: The time between infection (by inoculation or otherwise) and the first appearance of clinical signs, of which fever is the commonest.

Intervention (public health): Activity undertaken to prevent or reduce the occurrence of a health condition in a population. Examples of interventions for malaria control include the distribution of insecticide-treated mosquito nets, indoor residual spraying with insecticides, provision of effective antimalarial therapy for prevention or curative treatment of clinical malaria.

Line list: Information on cases recorded in rows and columns, with data for each case in columns across one row. The information may include case identification number; demographic factors (patient's name, address, age, sex); clinical factors (date of attendance, type of test, test result, treatment received); intervention factors (house sprayed, insecticide-treated net ownership, preventive therapy).

Local mosquito-borne malaria transmission: Occurrence of human malaria cases acquired in a given area through the bite of infected *Anopheles* mosquitoes.

Malaria-free: An area in which there is no continuing local mosquito-borne malaria transmission, and the risk for acquiring malaria is limited to introduced cases only.

Malaria incidence: The number of newly diagnosed malaria cases during a specified time in a specified population.

Malaria prevalence: The number of malaria cases at any given time in a specified population, measured as positive laboratory test results.

Monitoring (of programmes): Periodic review of the implementation of an activity, seeking to ensure that inputs, deliveries, work schedules, targeted outputs and other required actions are proceeding according to plan.

National focus register: Centralized computerized database of all malaria foci in a country.

National malaria case register: Centralized computerized database of all malaria cases registered in a country, irrespective of where and how they were diagnosed and treated.

Outpatient register: List of patients seen in consultation in a health facility; the list may include the date of the consultation, patient's age, place of residence, presenting health complaint, test performed and diagnosis.

Parasite prevalence: Proportion of the population in whom *Plasmodium* infection is detected at a particular time with a diagnostic test (usually microscopy or a rapid diagnostic test).

Passive case detection: Detection of malaria cases among patients who on their own initiative went to a health post for treatment, usually for febrile disease.

Population at risk: Population living in a geographical area in which locally acquired malaria cases occurred in the current and/or previous years.

Rapid diagnostic test: An antigen-based stick, cassette or card test for malaria in which a coloured line indicates that plasmodial antigens have been detected.

Rapid diagnostic test positivity rate: Proportion of positive results in rapid diagnostic tests among all the tests performed.

Receptivity: Sufficient presence of anopheline vectors and existence of other ecological and climatic factors favouring malaria transmission.

Re-establishment of transmission: Renewed presence of a constant measurable incidence of cases and mosquito-borne transmission in an area over a succession of years. An indication of the possible re-establishment of transmission would be the occurrence of three or more introduced and/or indigenous malaria infections in the same geographical focus, for 2 consecutive years for *P. falciparum* and for 3 consecutive years for *P. vivax*.

Relapse (clinical): Renewed manifestation of an infection after temporary latency, arising from activation of hypnozoites; therefore limited to infections with *P. vivax* and *P. ovale*.

Sensitivity (of a test): Proportion of people with malaria infection (true positives) who have a positive test result.

Slide positivity rate: Proportion of microscopy slides found positive among the slides examined.

Specificity (of a test): Proportion of people without malaria infection (true negatives) who have a negative test result.

Surveillance (control programmes): Ongoing, systematic collection, analysis and interpretation of disease-specific data for use in planning, implementing and evaluating public health practice.

Surveillance (elimination programmes): That part of the programme designed for the identification, investigation and elimination of continuing transmission, the prevention and cure of infections and final substantiation of claimed elimination.

Transmission intensity: Rate at which people in a given area are inoculated with malaria parasites by mosquitoes. This is often expressed as the 'annual entomological inoculation rate', which is the number of inoculations with malaria parasites received by one person in 1 year.

Transmission season: Period of the year during which mosquito-borne transmission of malaria infection usually takes place.

Vector control: Measures of any kind against malaria-transmitting mosquitoes intended to limit their ability to transmit the disease.

Vector efficiency: Ability of a mosquito species, in comparison with another species in a similar climatic environment, to transmit malaria in nature.

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 conditions of non-immunity. Factors affecting vectorial capacity include: (i) the density of female anophelines relative to humans; (ii) their longevity, frequency of feeding and propensity to bite humans; and (iii) the length of the extrinsic cycle of the parasite.

Vigilance: A function of the public health service during a programme for prevention of re-introduction of transmission, consisting of watchfulness for any occurrence of malaria in an area in which it had not existed, or from which it had been eliminated, and application of the necessary measures against it.

Vulnerability: Either proximity to a malarious area or frequent influx of infected individuals or groups and/or infective anophelines.

1. Surveillance in different phases of malaria control

1.1 Introduction

A malaria surveillance system consists of the tools, procedures, people and structures that generate information on malaria cases and deaths, which can be used for planning, monitoring and evaluating malaria control programmes. An effective malaria surveillance system enables programme managers to:

- identify the areas or population groups most affected by malaria;
- identify trends in cases and deaths that require additional intervention, e.g. epidemics; and
- assess the impact of control measures.

With this information, programmes can direct resources to the populations most in need and respond to unusual trends, such as epidemics or the absence of a decrease in the number of cases despite widespread implementation of interventions. As a result, progress in malaria control can be accelerated and wastage of resources avoided.

The design of malaria surveillance systems depends on two factors: (i) the level of malaria transmission and (ii) the resources available to conduct surveillance. In the initial phase of control, there are often so many malaria cases that it is not possible to examine and react to each confirmed case individually: rather, analysis is based on aggregate numbers, and action is taken at a population level. As transmission is progressively reduced, it becomes increasingly possible, and necessary, to track and respond to individual cases. Table 1 illustrates the way in which malaria surveillance is undertaken in different transmission settings and phases of control.

The term ‘high transmission’ has usually been used to indicate hyper- and holoendemic malaria (parasite prevalence in children aged 2–9 years > 50%), ‘moderate transmission’ to indicate mesoendemic malaria (10–50% parasite prevalence) and ‘low transmission’ to indicate hypoendemic malaria (parasite prevalence < 10%).^{1,2} The threshold of 10% is used to characterize low transmission in this manual for consistency and to provide a general guide to the types of malaria surveillance possible at different levels of malaria endemicity. The thresholds are not, however, fixed, and surveillance strategies for low-transmission settings might sometimes be more appropriately undertaken when parasite prevalence is < 5% rather than < 10%.

¹ *Terminology of malaria and of malaria eradication. Report of a drafting committee.* Geneva, World Health Organization, 1963.

² Hay SI, Smith DL, Snow RW. Measuring malaria endemicity from intense to interrupted transmission. *Lancet Infectious Diseases*, 2008, 8:369–378.

Table 1 Malaria surveillance in different transmission settings and phases of control

	Control phase		Elimination phase
Transmission:	High & moderate	Low	Very low
Parasite prevalence (2-9 yrs):	>10%	<10%	
Incidence:	Cases and deaths common and concentrated in <5yrs Limited temporal variation Limited geographical variation	Cases and deaths less common distributed according to mosquito bite exposure Variable within and between years Risk of epidemics Geographical heterogeneity Concentrated in marginal populations	Cases sporadic Imported cases may be high proportion of total Focal distribution
Fevers:	Proportion of fevers due to malaria relatively large	Proportion of fevers due to malaria small	Proportion of fevers due to malaria very small (though may be high in certain foci)
Health facility attendance:	High proportion due to malaria	Low proportion due to malaria	
Vectors:	Efficient	Controlled efficient/ inefficient	Controlled efficient/ inefficient
Aims of programme:	Mortality & case reduction	Case reduction	Eliminate transmission
Surveillance system			
Resources:	Low expenditures per head Low quality and poor accessibility of services	Widespread availability of diagnostics and treatment	Resources to investigate each case
Data recording:	Aggregate numbers	Aggregate numbers Lists of inpatients and deaths → lists of all cases	Case details
Investigation:	Inpatient cases	Inpatient cases → all cases	Individual cases

1.2 Control phase: high- and moderate-transmission settings

High- and moderate-transmission settings are generally characterized by: (i) a concentration of malaria cases and deaths in children under 5 years of age, with pregnant women also susceptible to the effects of malaria; (ii) a high proportion of cases due to *Plasmodium falciparum*; (iii) suspected malaria comprising a high percentage (typically > 20%) of outpatient attendances, hospital inpatients and recorded deaths; (iv) a high proportion of fevers due to malaria (although generally < 30%); (v) high parasite prevalence rates in children (> 10%); (vi) efficient anopheline vectors; and (vii) a high frequency of malaria-related deaths.

High- and moderate-transmission settings are often found in low-income countries, which have low expenditures per person on health care services. This results in weak health systems that are not easily accessed by the population, lower staff to patient ratios, frequent interruptions of medical supplies and limited use of parasitological diagnosis. In such settings, the primary emphasis of malaria programmes has often been on reducing mortality (by prevention and appropriate management of severe cases) and the secondary emphasis on case reduction. The features of surveillance in high-transmission settings are shown in Box 1.1.

BOX 1.1.

Features of malaria surveillance systems in the control phase: high- and moderate-transmission settings

Registers of individual cases are maintained at health facilities, which allow recording of diagnostic tests performed and test results. Given the high frequency of malaria cases and the limited resources for maintaining an extensive recording and reporting system, malaria surveillance systems rely on the reporting and use of aggregate data by district and higher administrative levels. Malaria surveillance is frequently integrated into a broader system of health information or communicable disease surveillance.

At the health facility level, case-based surveillance of malaria inpatient cases and deaths is undertaken with the aim of responding to cases of severe disease and attaining a target of zero malaria deaths. Cases are graphed monthly to assess the extent to which control measures are reducing the incidence of malaria.

At district and national levels, cases and deaths are summarized monthly on five control charts, in order to assess the efficacy of malaria control interventions and identify trends that require an urgent response. The control charts cover: (i) malaria incidence and mortality rates; (ii) proportional malaria incidence and mortality rates; (iii) general patient attendance rates; (iv) diagnostic activity (annual blood examination rate); and (v) quality of diagnosis and health facility reporting. Analysis is also undertaken by health facility catchment area and by district in order to set priorities for malaria control activities.

1.3 Control phase: low-transmission settings

Low-transmission settings are characterized by (i) a lower incidence of confirmed malaria cases; (ii) a more uniform spread of cases by age or more concentrated in population groups with higher exposure; (iii) lower malaria mortality rates; (iv) a parasite prevalence in children aged 2–9 years < 10%; (v) generally more seasonal malaria, with a higher risk of epidemics;¹ (vi) a small proportion of fevers attributable to malaria, especially in the low-transmission season; (vii) malaria distribution more focal within districts; and (viii) imported cases comprising a significant proportion of all cases. In some temperate and subtropical areas, *P. vivax* may occur in higher proportions, particularly as *P. falciparum* disappears more quickly than *P. vivax* in response to control measures.

Health systems in low-transmission settings are usually stronger than in high-transmission settings, and there may be widespread availability of parasitological diagnosis and appropriate treatment. Malaria may, however, be concentrated in marginalized populations, such as those living in remote border areas, migrant workers and tribal populations, and innovative ways may have to be found to reach these groups. The features of malaria surveillance in low-transmission settings are shown in Box 1.2.

BOX 1.2.

Features of malaria surveillance systems in the control phase: low-transmission settings

Registers of individual malaria cases are maintained at health facilities, with records of the diagnostic tests performed and the results. As well as aggregate data being reported to district and higher administrative levels, line lists of inpatients and inpatient deaths are forwarded to district level, and, when case loads and district capacity permit (for example, < 150 patients per district per month), lists of all confirmed cases are submitted monthly.

At health facility level, case-based surveillance of malaria cases and deaths is undertaken, with the aim of identifying population groups with the highest malaria incidence and probable sources of infection. Cases are graphed daily or weekly to identify trends that require attention and are mapped by village to identify clusters of cases.

At the district level, malaria cases and deaths are summarized weekly or monthly on the same five control charts used in high-transmission settings, in order to assess the impact of malaria control interventions and identify trends that require urgent response. The control charts cover: (i) malaria incidence and mortality rates; (ii) proportional malaria incidence and mortality rates; (iii) general patient attendance rates; (iv) diagnostic activity (annual blood examination rate); and (v) quality of diagnosis and health facility reporting. Analysis is undertaken by health facility catchment area and by village in order to set priorities for activities. A register of severe cases and deaths is maintained and investigations undertaken to identify and address programme weaknesses.

At national level, cases and deaths are summarized monthly on the five control charts in order to assess the impact of malaria control interventions. Analysis is undertaken by district in order to set priorities for activities.

¹ The two types of setting with low transmission are (i) locations in transition from high or moderate transmission to low transmission and (ii) locations that have had low transmission for many years because of environmental factors or less efficient vectors. Epidemics may be more likely in areas in which malaria control has been successful and in which efficient anopheline vectors remain.

1.4 Elimination phase

In the elimination phase, cases occur sporadically or in distinct foci. Imported cases may comprise a significant proportion of all cases and may pose a risk for re-establishment of transmission in areas in which it had previously been interrupted. Countries have resources to investigate each case to ascertain whether it is imported or locally acquired and undertake appropriate control measures. Box 1.3 shows the features of surveillance in elimination settings.

BOX 1.3.

Features of malaria surveillance systems in the elimination phase

Case-based surveillance is performed. Each confirmed case is immediately notified to district, provincial and central levels. A full investigation of each case is undertaken to determine whether it was imported, acquired locally by mosquito-borne transmission (introduced, indigenous, relapsed) or induced. The national malaria reference laboratory reconfirms all positive test results and a sample of negative test results and organizes laboratory participation in a national quality assurance network.

Each new focus of transmission is investigated, including an entomological investigation, to ascertain risk factors and devise the optimal strategies for control. The focus is classified, and its status is updated continuously.

The malaria programme monitors the extent of surveillance, mainly by tracking blood examination rates by village and by month in high-risk foci and comparing the number of diagnostic tests done with the number expected.

Programme managers at district level keep: (i) malaria case investigation forms, patient records, focus investigation forms and a register of foci with changes in status; (ii) maps showing the distribution of cases by household, vector breeding places, possible sites of transmission and geographical features, such as hills, rivers and roads; and (iii) data on integrated vector control interventions.

Full documentation of programme activities and surveillance results is kept securely at national level in preparation for certification of malaria elimination.

There are no strict rules about when countries change their approach to surveillance. This depends on the level of malaria transmission and the capacity of the control programme to perform specific surveillance activities. Some countries in relatively high-transmission settings may adopt certain approaches used in low-transmission settings, and their control programmes would be expected to progress more rapidly as a result of better targeting of interventions. Many low-transmission countries may wish to adopt certain approaches used in the elimination phase. Different approaches may be used in different settings within a country, particularly when transmission intensity varies geographically.

This manual describes the general principles that govern surveillance systems in the elimination phase, including case definitions, procedures for case detection and investigation and focus investigation and classification. It also outlines recommended practices for recording, reporting and analysing data and presents factors to be considered when establishing surveillance systems in the elimination phase. The companion manual, entitled *Disease surveillance for malaria control*, covers similar topics in settings in which the programme is oriented towards malaria control.

2. Concepts of malaria surveillance in the elimination phase

2.1 Introduction

The aim of the elimination phase is to stop local transmission of malaria, in contrast to the control phase, in which the objective is to reduce the number of cases to low levels but not necessarily interrupt local transmission.

The objective of a malaria surveillance system in the elimination phase is to detect all malaria infections, whether symptomatic or not, and ensure that they are radically cured so early that they do not generate secondary cases.¹ In practice, countries accomplish this in two stages:

- The first stage is to identify all areas or *foci* with local transmission of malaria.² Foci are usually first identified from reports of confirmed malaria cases from public and private sector health facilities. Each malaria case is then investigated to determine whether it was locally acquired or imported and, if so, from where.
- Secondly, if a focus of local transmission is detected, the characteristics of transmission are documented by conducting a focus investigation. Control and surveillance activities are then intensified in the focus.

This two-step process targets symptomatic cases detected passively. Most malaria infections produce fever periodically in low transmission settings where people have no malaria immunity. Passive case detection should therefore lead to the detection of most malaria infections. The continuous presence of a health worker is required for good passive case detection in active transmission foci and is preferable to periodic visits by mobile teams.

Active case detection is a complementary strategy that involves the detection by health workers of malaria infections at community and household level in population groups that are considered to be at high risk. Active case detection is always used in epidemiological investigations of new cases and foci, among family members, neighbours, the population of the focus, people at the workplace of an index case, fellow exchange students, etc. Active case detection can be fever screening followed by parasitological examination of all febrile patients or parasitological examination of a target population without fever screening. Blood sampling of non-febrile persons by common methods (microscopy, rapid diagnostic tests) may still not result in detection of low-level asymptomatic infections or infections in the liver stage of development. Generally, mass parasitological screening could be considered for newly detected foci or for well-defined

¹ 'Cure': elimination of the symptoms and asexual blood stages of the malaria parasite that caused the patient or caregiver to seek treatment. 'Radical cure': in *P. vivax* and *P. ovale* infections only, this comprises cure as defined above plus prevention of relapses by killing hypnozoites.

² A malaria focus has been defined by Beklemishev in 1962 as "an integration of the populations of the parasite and populations of hosts and vectors that support its existence", in which populations are understood to be sets of interacting individuals of the same species that occupy the same territory (Beklemishev VN. Spatial and functional structure of foci of infections with special reference to malaria and tick-borne encephalitis In: *Biocenologicheskie osnovy sravnitel'noj parazitologii*. "Nauka", Moscow, 1970, 466–469 [in Russian]). In practical terms, a settlement with *Anopheles* breeding sites in the vicinity may be considered a malaria focus. Places frequented by its residents, especially at night, are also included. If the programme is successful, the number of active foci decreases and this makes it more feasible to thoroughly examine each focus.

high-risk populations, especially semi-immune migrants from endemic areas, but should not be a routine measure.

Although malaria may be focal in the elimination phase, surveillance systems must cover the entire country, with additional attention to areas with ongoing or a recent history of transmission. Surveillance in the elimination phase must be of a high standard:

- All suspected cases of malaria should receive a parasitological test.
- Diagnostic testing should be subject to quality control.
- Reporting should be immediate and complete.
- All cases and foci should be fully investigated.
- Records should be kept of all tests and investigations, to guide programme implementation, for future reference and to build the evidence base for eventual certification of the malaria-free status.

2.2 Case definition

Case of malaria (as defined in elimination programmes): a case in which, regardless of the presence or absence of clinical symptoms, malaria parasites have been confirmed by quality-controlled laboratory diagnosis.

In the elimination phase, all malaria infections are important, as they may lead to onward transmission. Therefore, all instances of detected parasitaemia (including gametocytaemia only) are considered a 'malaria case', regardless of the presence or absence of clinical symptoms.

Demonstration of malaria parasites in Giemsa-stained blood films by light microscopy is the usual means and gold standard of identifying malaria infection during the elimination phase. This method can provide the necessary information on the parasite species, stages and density, in addition to a permanent record for future reference and verification. The species of *Plasmodium* should be identified on thin films and the parasite stages detected and described. Even when rapid diagnostic tests are used for initial patient management, clinics should make a microscopy slide at the same time for subsequent confirmation of the diagnosis at a nearby reference laboratory. Cases with a positive rapid diagnostic test but no slide taken at the time of initial contact should be investigated in the same way as cases confirmed by microscopy.

Annex 1 describes the laboratory support required for effective malaria surveillance in the elimination phase. Further details are provided in the WHO *Malaria microscopy quality assurance manual*.¹

2.3 Case detection

In elimination programmes, potential transmission foci are identified from data reported by public and private sector health facilities (passive case detection). In areas where the population has limited access to facilities and in areas and situations of particularly high risk, cases may be sought in the community (active case detection). Cases detected passively and actively lead to immediate case notification (see section 3.2).

¹ *Malaria microscopy quality assurance manual*. Geneva, World Health Organization, 2009. Available online at http://www.who.int/malaria/publications/malaria_microscopy_QA_manual.pdf.

Passive case detection

Passive case detection: is the detection of malaria cases among people who went at their own initiative to a health facility or community health worker to get treatment, usually for febrile disease.

Criteria must be established in a malaria elimination programme to define which patients attending health facilities (whether public or private) should be given a parasitological test. Common criteria include:

- for residents of endemic areas and active transmission foci: patients with fever or a recent history of fever; and
- throughout the country: patients with unexplained fever and a history of travel to areas at risk of malaria, either within the country or abroad.

More specific categories include:

- all febrile patients from malaria foci, especially during the transmission season;
- patients with a history of malaria in the past 3 years and any increase in body temperature;
- patients who have fever within 1 year of having visited a malaria-endemic area (domestic or foreign), sometimes extended to 3 years for areas at risk of *P. vivax*;
- patients with fever, malaise and chills;
- patients with anaemia of unknown cause;
- patients with hepatomegaly and/or splenomegaly; and
- recipients of blood donations who have fever during the 3 months after the transfusion.

The established criteria should be disseminated to all health providers and the public, and the programme should provide periodic reminders.

Active case detection

Active case detection: is the detection by health workers of malaria infections at community and household level among population groups that are considered to be at high risk. Active case detection can be conducted as fever screening followed by parasitological examination of all febrile patients, or as parasitological examination of a target population without prior fever screening.

Active case detection is used to fill gaps in the passive case detection system and to detect malaria infections as early as possible in populations that may have a high risk of infection (e.g. febrile contacts of recent cases) or pre-existing immunity that would protect them from developing clinical symptoms (e.g. recent immigrants from highly endemic countries).

Active case detection is particularly useful for population groups that may be underserved by existing health services, such as migrant workers and tribal populations. This use of active case detection is sometimes referred to as 'proactive'. When possible, active case detection should be replaced by passive case detection, for instance by assigning a health worker to a focus where malaria transmission is occurring.

The distinction between active and passive case detection may not always be clear. Usually, active case detection is conducted outside health facilities (including village health posts), intermittently, by health workers visiting patients at their homes, workplaces, schools or other locations, such

as markets. Thus, monthly visits to mining camps by a health team would be considered active case detection, as there is no fixed facility and no regular service is provided between health worker visits. Most cases detected by community health workers are considered to be detected passively if patients visit a community health worker's home, but cases may be detected actively if a community health worker visits patients' homes regularly.

Active case detection is always conducted during epidemiological investigation of new cases and foci. Typically all household members (irrespective of fever status) and neighbours, those living in wider surroundings or work colleagues with a recent history of fever would receive a parasitological test. It usually involves a process of house-to-house visits. Active case detection may also involve parasitological examination of everyone in a targeted population (mass screening). Box 2.1 gives guidance on conducting active detection of malaria by regular fever screening during house-to-house visits in transmission foci.

BOX 2.1.

Organizing active case detection by regular house-to-house visits

1. Local health-care providers or mobile teams list the targeted population by household with the assistance of local authorities. There should be complete coverage of the target population. People from organizations associated with the target population should be included in the lists, e.g. transport workers, development project workers, the military. People living in outlying hamlets, who may not be recorded on existing household lists, should also be covered. All efforts should be made to include people living clandestinely in the target area, such as illegal immigrants.
2. A plan of visits should be prepared, and the targeted population should be informed of the dates and times they will be visited. Visits are usually made once every 2 weeks during the malaria season. They should be conducted when family members are most likely to be at home (before or after work or school).
3. During the visit, household members are asked about recent fever and chills. There is no fixed rule for the recall period: 14 days (nowadays used in standardized surveys for malaria control) is probably suitable in most settings. Body temperature can be recorded, but this is usually not essential.
4. In cases of current or recent fever, a blood slide should be taken and examined on the same or the following day at a local laboratory. If this is not possible, the slide should be sent to the nearest laboratory, and it is advisable also to use a rapid diagnostic test that is sensitive to the endemic parasite species. Any person in a clinically severe state must be assisted to obtain medical care, whether or not she or he has malaria. If the interval between blood sampling and examination is more than 1 day, care should be taken to avoid fixation of erythrocytes in the thick films (hot weather), for example by haemolysing them as soon as the film is completely dry or by keeping dried slides in a cool box. It is also important to protect thick blood films from flies.
5. A register of all people who had blood taken during active case detection should be completed. It should include the identification number of the household, the name of the head of the household, address, person's name, age and other risk factor information (e.g. occupation, insecticide-treated net ownership and use, indoor residual spraying in the past year), date blood taken, type of testing and results (species, stages, density, presence of gametocytes).

2.4 Case investigation

Each notified case of confirmed malaria leads to a case investigation in the field, ideally within 1–2 days.¹ The field investigation consists of:

- obtaining the details of the confirmed case;
- reviewing the details of cases reported previously in the same locality, obtaining information on potential malaria vectors from the vicinity of the case; and
- active case detection in populations thought likely to harbour parasites.

The aim of the field investigation is to determine whether an infection was acquired locally and therefore whether there is ongoing local malaria transmission. If a new case occurs outside a known active focus, the case and focus investigations (see section 2.6) are part of the same process. If the new case occurs in a known active focus, a focus investigation will have already been done, and the case will be used to update the focus record.

The investigating team consists of the intermediate or district-level malaria focal point (usually the head of the team), a skilled laboratory technician, an epidemiologist (often the same person as the malaria focal point), entomological staff from intermediate or central levels and local health facility personnel. The team leader should understand malaria epidemiology and have experience of malaria field investigations.

The team should assemble and review the following information:

- *Malaria case investigation form.* A case investigation form is completed for each confirmed malaria case (see example in Annex 2). This form is used to record patient demographic information and type of case detection, the presence of symptoms and a history of the current illness including diagnostic test results and treatment, as well as patient travel history, to ascertain where and how the infection might have been acquired and the possibility of onward transmission. It concludes with a section for classification of the case (to be filled in once the case investigation has been completed). It is essential to record the dates of all events in the travel and clinical history. A preliminary assessment of the likely locality and source of infection is recorded.
- *Epidemiological data from previous cases in the same village, locality or focus,* including age, sex, occupation, timing and species involved in previous cases and maps of the location of cases (by house and village).
- *Additional data from active case detection.* After a review of these data, active case detection is planned to help determine the origins of a case and to detect epidemiologically linked cases. The team leader must decide:
 - the subpopulations to be sampled: perhaps including family members, neighbours, village or local residents, co-workers, people in areas recently visited by the index case and populations living in the *Anopheles* flight range of certain vector breeding sites. The extent of active case detection will depend on the factors listed in Box 2.2.

¹ Labour-intensive case investigations (and thus the elimination phase itself) can in reality be done only when the total case burden in a country is low and adequate resources (especially skilled manpower at peripheral level) are available.

BOX 2.2.**Factors influencing the extent of active case detection undertaken as part of a field investigation**

Epidemiological situation. Index cases considered to be due to local transmission may trigger geographically more extensive active case detection. An apparently imported or relapsing case, especially in an area with low receptivity, might require more limited case detection; however, it is always better to err on the side of caution. If local transmission is at all possible, it is advisable to undertake active case detection at least in the surrounding cluster of households.

*Receptivity.*¹ Areas with increased receptivity should always be covered by active case detection.

*Type and degree of vulnerability.*² Vulnerability will guide both the type and the extent of active case detection in each area or subpopulation.

Type and extent of clustering. Local or national knowledge of the pattern of clustering of infection and local experience with the vectors, ecology and breeding sites might lead investigators to plan geographically wider or narrower active case detection.

Breeding sites. Knowledge of likely breeding sites in the area or locality may result in wider or more focused active case detection.

History of infection. History of infection in the area and the type of focus (endemic, new active, residual active, new potential, residual non-active, cleared-up; see section 2.6) will influence the type and extent of active case detection. When the index case is the first in a new active focus, less will be known about the focus and its population, and widescale active case detection of febrile and non-febrile, infected residents may be needed to investigate the situation thoroughly and to establish a baseline. If the index case is the 10th case in the same locality in the current transmission season in a well-known focus, active case detection can be more targeted, as the at-risk populations will already be known.

Current level of surveillance. The current level of surveillance will also determine the format and extent of active case detection. For example, if current disease surveillance has been at low-levels in the village of the case and in surrounding villages, active case detection covering both the case's and neighbouring villages is recommended.

Location of the infection. The hypothesized source of infection (work site versus residence) will influence the type and targeting of active case detection.

Resources. The amount of resources available will guide the type of active case detection, e.g. screening people with a recent symptomatic illness versus mass screening. The aim is to optimize use of the available resources and complete the investigations within a short time, for example 14 days.

¹ Presence of abundant anopheline vectors and other ecological and climatic factors that favour malaria transmission.

² Either proximity to a malarious area or frequent influx of infected individuals or groups and/or infective anophelines.

BOX 2.2. CONTINUED

Factors influencing the extent of active case detection undertaken as part of a field investigation

Sensitivity of the testing method. Active case detection involves not only finding additional cases of infection but also treating them to prevent onward transmission. As the current common methods of testing (microscopy, rapid diagnostic tests) cannot detect some cases of low-level asymptomatic infection, mass screening with current tools may not eliminate infection. Surveillance of malaria infections based on new methods of polymerase chain reaction (PCR) are being used for research and field studies, as they are more sensitive than light microscopy and rapid diagnostic tests for detecting submicroscopic infections, especially with rare species (*P. malariae*, *P. ovale* and *P. knowlesi*), mixed infections and low-density infections. In Cambodia, for example, in a national survey in 2007 in which the populations of 76 villages were screened, 13 more villages with malaria cases were identified with PCR than with microscopy.¹ During screening and treatment in Pailin, Cambodia, in 2008–2009, use of PCR with feedback and treatment of positive cases made it possible to treat 86 asymptomatic carriers (*P. vivax* in most cases) among the 928 people screened, instead of six when only RDTs were used (S. Hoyer, personal communication).

The relation between the incidence of symptomatic malaria and the prevalence of symptomatic infections in a population (called the ‘reservoir’) is not fully understood. It depends partly on the prevalence of low-density infections: the lower the overall parasite prevalence in a population, the more additional infections will be found by PCR than by microscopy.² It also depends on the speed at which malaria transmission decreases: when the decrease in transmission is more rapid than loss of immunity in a population, the reservoir of asymptomatic carriers can be significant, and mass screening is potentially appropriate. For example, in Cambodia, microscopy suggested a 3% prevalence, whereas PCR resulted in a prevalence of 7%. When transmission has decreased over many years, however, most people with parasitaemia are symptomatic because they have no immunity, and the reservoir is minimal; e.g. prevalence of 0% by microscopy, 0.5% by PCR for *P. falciparum* and 1.5% by PCR for *P. vivax* in the Brazilian mountains outside Amazonia;³ prevalence of 0% by PCR in two districts in Sri Lanka.⁴ In this situation, mass screening will probably not be cost-effective.

While PCR can be used to detect asymptomatic infections in some settings, the potential programme value of detecting low-density infections that are microscopy-negative but PCR-positive is unclear.

There are currently no methods to detect liver-stage malaria infections. Regularly repeated active case detection will increase case detection, as will education of the population to use the free services of the local clinic for parasitological examination in all cases of fever.

¹ *Parasitological confirmation of malaria diagnosis.* Geneva, World Health Organization, 2009.

² Okell LC et al. Submicroscopic infection in *Plasmodium falciparum*-endemic populations: a systematic review and meta-analysis. *Journal of Infectious Diseases*, 2009, 200:1509–1517.

³ Cerruti C Jr et al. Epidemiologic aspects of the malaria transmission cycle in an area of very low incidence in Brazil. *Malaria Journal*, 2007, 6:33.

⁴ Rajakaruna RS et al. Pre-elimination stage of malaria in Sri Lanka: assessing the level of hidden parasites in the population. *Malaria Journal*, 2010, 9:25.

- the type of sampling: people with fever in the past 2 weeks or entire population groups without regard to fever (mass parasitological screening). Generally, blood sampling of people with fever in the past 2 weeks is the preferred method, as this will mean that blood is taken from only 5–20% of the population, and larger populations can be covered for approximately the same cost. Sampling a large population (entire village or locality) is preferable, because other people with malaria might not live in the immediate vicinity of the index case, as the flight range of anophelines is typically 1–2 km. Different blood sampling strategies can be used for different populations. For example, mass screening might be undertaken for family members, neighbours or high-risk groups such as migrant workers, while screening of people with fever may be undertaken for other populations.

Once the case investigation is complete:

- The malaria focal point and the entomologist determine whether local transmission is occurring and decide on a final classification of the case and focus. The malaria focal point, in consultation with district and national experts, will prepare a response plan, according to the results of the field and focus investigation, including the entomological evaluation.
- Copies of the completed case form and the results of the investigation (including from active case detection) are distributed to the national malaria programme, the national malaria reference laboratory, the reporting district team and the reporting health facility.

2.5 Case classification

After a case has been investigated, it is classified into one of the following categories, which were first used in the context of the Global Malaria Eradication Programme in the 1960s:¹

Local: due to mosquito-borne transmission and acquired within the country (also called ‘autochthonous’ cases):

- *Indigenous:* any case contracted locally, without strong evidence of a direct link to an imported case
- *Introduced:* a case contracted locally, with strong epidemiological evidence linking it directly to a known imported case (first generation from an imported case, i.e. the mosquito was infected by a patient classified as an imported case).

The presence of indigenous and/or introduced cases indicates active transmission. In all such cases, it is useful to specify whether they originated within the focus in which they were detected or in another part of the country. The latter are also called ‘internally imported’. This information is recorded on the case investigation form (Annex 2). The extra category ‘internally imported’ is used especially in larger countries, and these cases are recorded for the administrative units they were imported from.

Imported: due to mosquito-borne transmission and acquired outside the country. The origin of imported cases can be traced to a known malarious area outside the country to which the case has travelled.

In areas with ongoing local transmission, elimination programmes should reserve the category ‘imported’ for ‘exotic’ parasite species and very recent arrivals from endemic countries (within the past 3 months). For all other cases occurring during the transmission season, it is prudent to assume a local origin of the infection.

¹ *Terminology of malaria and or malaria eradication, report of a drafting committee.* Geneva, World Health Organization, 1963. Available online at <http://whqlibdoc.who.int/publications/9241540141.pdf>.

Induced: not due to mosquito-borne transmission. Induced cases may arise from a congenital infection or by contamination with infected blood. Such cases are easy to classify if the person lives and works in an area with no known transmission for many years and has a history of blood transfusion or other exposure from blood that could have transmitted malaria. The incubation period (delay before onset of clinical symptoms) after contamination with infected blood from a needle-stick injury ranges from 4 to 17 days, with a median of 12 days. Induced cases never give rise to clinical relapses, as there are no liver-stage parasites.

Some non-endemic countries use an additional classification category, ‘cryptic’, indicating of unknown origin. In such cases, no plausible mode of infection is found after a complete epidemiological investigation. The cases have no history of travel to areas with known malaria transmission, and there are no known possibilities for transmission in the area of residence or work. This category should not be used in elimination programmes; local transmission should be assumed instead.

Uncertainty may arise in classifying cases as ‘imported’ rather than ‘introduced’ or ‘indigenous’ when the patient has a dubious travel history or suffers a relapse of a *P. vivax* or *P. ovale* infection acquired earlier that was not radically cured. If the evidence is unclear, the classification that reflects more local transmission should be assigned, e.g. cases should be classified as ‘introduced’ or ‘indigenous’ rather than ‘imported’. This conservative classification ensures that malaria elimination programmes are more responsive to possible renewed transmission within their national boundaries. Box 2.3 provides further indications for classifying cases. Often, the investigative skills of the lead epidemiologist are put to the test in determining where and when in the country an infection was acquired. Box 2.4 provides further information for deciding between classifications.

BOX 2.3.

Key for epidemiological classification of malaria cases¹

- | | |
|---|-------------------------|
| 1. How was the case contracted? | |
| • By blood | Induced case |
| • By mosquito | Go to 2 |
| 2. Where was the case contracted? | |
| • Outside the country | Imported case |
| • Inside the country | Go to 3 |
| 3. Which parasite caused the case? | |
| • <i>P. vivax</i> or <i>P. ovale</i> | Go to 4 |
| • <i>P. falciparum</i> or <i>P. malariae</i> | Go to 5 |
| 4. When was the case contracted? | |
| • Long ago (e.g. from 6 months to 3 years ago) ² | Relapsing case 3 |
| • Recently (e.g. up to last 6 months) ³ | Go to 5 |
| 5. From whom was the case contracted? | |
| • From an imported case | Introduced case |
| • From any other case | Indigenous case |

¹ Adapted from *Guidelines on the elimination of residual foci of malaria transmission*. Cairo, WHO Regional Office for the Eastern Mediterranean, 2007:24–28, 46 (EMRO Technical Publications Series, No. 33).

² The exact duration should be decided by the programme.

³ Relapsing cases cannot be distinguished from indigenous cases in areas with continuing local transmission and epidemiologically linked cases in the vicinity: recent infection or reinfection has to be assumed.

BOX 2.4.**Operational aspects of classification of cases**

In *high-transmission areas*, locally acquired cases often cannot be differentiated from other categories, but this information is not important if the cases occur in areas known to be endemic.

In *low-transmission areas*, it is almost impossible to distinguish between introduced and indigenous cases. In such instances, a simpler classification, with three categories—induced, imported and locally acquired—can be used.

Correct epidemiological classification of malaria cases is crucial in *malaria elimination* as it is the basis for classifying foci and for selecting surveillance and other control measures.

Distinguishing between ‘imported’ and local or autochthonous cases

The probability that a case was imported is associated with several factors to be weighed in the final assessment, including:

- The timing of travel to and from endemic areas:
 - The usual delay between an infectious bite and a primary clinical attack is 7–30 days. The minimal incubation period (time from inoculation to onset of symptoms) of malaria in humans is about 7 days for *P. falciparum* infection and 10 days for *P. vivax* infection; therefore, detection of malaria parasites within 0–5 days of initiating travel would indicate that the person was infected before travelling.
 - People who have lived in malaria-free areas for 2 or more years and have less immunity to malaria are highly likely to have clinical symptoms shortly after the usual incubation period.
 - As the time between returning from travel to an endemic area and detection of malaria infection increases beyond 6 months, the probability that the case is truly due to an imported infection starts to decline (and the probability that the case is due to local transmission increases).
 - Experience in many countries shows that approximately 50% of imported cases occur within 1 month of arrival back in the country of residence and up to 75% by 3 months.
- The parasite species:
 - *P. falciparum* infections can last for 18–24 months, but several febrile episodes would be expected during that period, as parasite density increases intermittently to cause fever or symptomatic illness. Predominantly asymptomatic long-term infections are unlikely to occur in people with little antimalarial immunity, but are possible.
 - *P. vivax* infections due to activation of hypnozoites can cause infections up to 5 years after the previous infection or clinical episode but are most likely within 3 years.
- The probability of local transmission in the area of residence and work of the patient:
 - if a person lives and works in a place in which there has been no local malaria transmission for many years, with adequate surveillance, and the person travelled to an area of known transmission within 6 months of documented infection, classification of the case as ‘imported’ is straightforward.

BOX 2.4. CONTINUED

Operational aspects of classification of cases

- If the area has had no malaria for more than 10 years, with reasonable surveillance, or has no known appropriate vectors, local transmission is unlikely.
- If the malaria patient lived in a focus with recent local transmission (classified as ‘residual non-active’ focus), there is less probability that the case is truly ‘imported’.
- Cases in areas with local transmission (classified as ‘residual active’ or ‘new active’ foci) should rarely (or never) be classified as ‘imported’.
- The extent of surveillance in the area in which the case was detected and the extent and quality of the field investigation around the home and work area of the case.
 - Consistently negative test results from strong pre-existing surveillance and extensive blood sampling during the field investigation decrease the probability of local transmission.

Deciding between different types of local or autochthonous transmission

There is little difference between introduced (first-generation local transmission) and indigenous (second or higher generation) cases. Both indicate local transmission, showing that malaria control was not strong enough. Indigenous transmission is more serious, as it indicates that neither prevention nor treatment contained the spread of malaria beyond the first generation. Prompt treatment may not prevent first-generation transmission from an imported case in all circumstances but should be able to prevent second-generation transmission by preventing progression of parasite development or destroying existing gametocytes. Introduced cases may be linked to foreign parasite carriers who have no symptoms or who may have stayed only one night in the area before moving on (e.g. long-distance lorry drivers): just enough time to infect local mosquitoes.

For cases to be classified as ‘introduced’, the index case and all other infections found during the field investigation of the index case can be linked to a single imported case. During the case and field investigation, investigators should estimate the possible transmission pathways and incubation period for all confirmed cases. If in doubt, cases should be classified as ‘indigenous’ (at least second generation).

The certainty of case classification is never 100%, because epidemiological information can rarely link transmission between two uninduced cases with 100% certainty. For example, when there are only two cases in a locality, one imported and another emerging after a sufficient time, the probability that the former is the source of infection for the latter is high but not 100%.

In some instances, local transmission can be linked to the hypothesis that migrant infected mosquitoes have crossed borders, because all other possible sources of infection have been excluded. ‘Airport malaria’, in which infected mosquitoes are imported by aircraft, is one example. Another example is infected mosquitoes crossing the river that separates Afghanistan and Turkmenistan. In even rarer instances, people can be infected by mosquitoes that were infected in laboratories.

BOX 2.4. CONTINUED

Operational aspects of classification of cases

Imported cases from within the country but outside the focus versus imported cases from outside the country

From an epidemiological point of view, it is important for programmes to establish whether the origin of new cases is within the foci of residence and work or outside them (but within the country). For international reporting purposes, however, ‘imported malaria’ indicates cases acquired outside the national territory. Consequently, all internal importation is considered to be autochthonous.

Misclassification of cases as imported from foreign countries

A common mistake is to assume that a case is imported because the patient had visited a country known to be endemic for the parasite species in question. In nearly all malaria-endemic countries, however, large areas have no risk of transmission and seasons during which no transmission takes place. It is essential to determine exactly where the patient stayed overnight and when and then conclude whether he or she could have been exposed to malaria transmission abroad. If such detailed information on the country visited is not in the public domain (for instance in the country list at <http://www.who.int/ith>), the national malaria programme can request the assistance of WHO to obtain it or contact its homologue in the country in question directly.

2.6 Focus investigation and classification

Focus: a defined, circumscribed locality situated in a currently or formerly malarious area with the continuous or intermittent epidemiological factors necessary for malaria transmission.

Once a case of locally acquired malaria has been detected, a focus investigation is carried out to describe the areas where malaria occurred and delineate the population at risk. During a focus investigation, the relevant form should be completed (see example in Annex 3). The district or intermediate-level malaria focal point is responsible for ensuring that all foci are investigated and that reports for all foci are available and kept up to date.^{1,2}

The focus investigation identifies the main features of the location, including the populations at greatest risk, the vectors responsible for transmission, where they are located and when transmission occurs. An entomologist should participate in the focus investigation to delineate areas of receptivity. An investigation of foci is likely to involve an assessment of potential *Anopheles* breeding sites, collection of adult mosquitoes to identify the species responsible for transmission, and assessment of the vector’s susceptibility to insecticides.

A map should be drawn, with standard, recognized keys, to show:

- geographical features relevant for malaria transmission (e.g. rivers, rice fields, dams, ponds, forests, roads, altitude);

¹ In some countries, these reports are called ‘foci passports’.

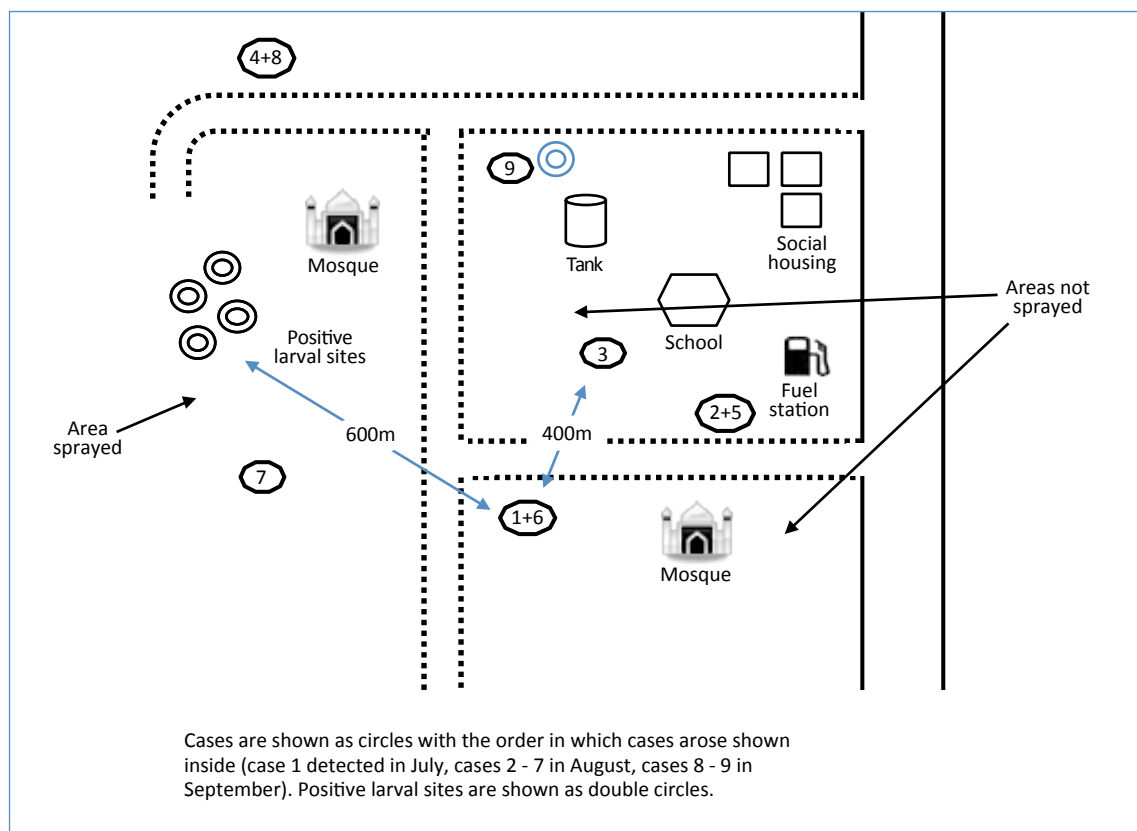
² If a focus crosses the boundary of two or more districts, provinces or even countries, collaboration will be needed to eliminate transmission. ‘Straddling foci’ are often the most puzzling for epidemiologists, as administrative boundaries may hide the sources of infection.

- the location of all households, highlighting those in which cases have been detected in the past 3 years (indicating the parasite species for each case);
- vector breeding places and possible sites of transmission;
- malaria control interventions, the location of test and treatment sites, including areas and households where active case detection has been undertaken; and
- vector control interventions.

Both paper and electronic maps can be used. Paper maps of villages or households can often be obtained from government departments with cartographic services, such as a mapping bureau or census office. Maps derived by satellite imaging, printed in large sizes, can be a starting-point. Programmes of cartographic services within a country or internationally, including web sites, can provide electronic maps showing altitude, hydrology (rivers and other water bodies), roads, settlements and other features. Additional features relevant to malaria transmission and control, such as the location of health facilities, might need to be added. The construction of electronic maps can be labour-intensive and require assistance from cartographic services, which may not be possible at district level. In many cases, the most practical approach is to use whatever suitable paper or printed electronic map is available and add important features by hand (Figure 2.1).

FIGURE 2.1.

Map showing location of cases and other features in Oman 2007-2008.¹



¹ Source: Department of Malaria Eradication, Ministry of Health, Oman

Focus investigations provide the necessary information for selecting the most appropriate combination of interventions for controlling and eliminating malaria in a specific locality. For example, vector breeding may depend on particular environmental factors (e.g. man-made breeding sites in arid areas), or exposure to vector biting may be linked to particular human behaviour (e.g. sleeping outdoors) or occupations (e.g. border guard or agricultural worker).

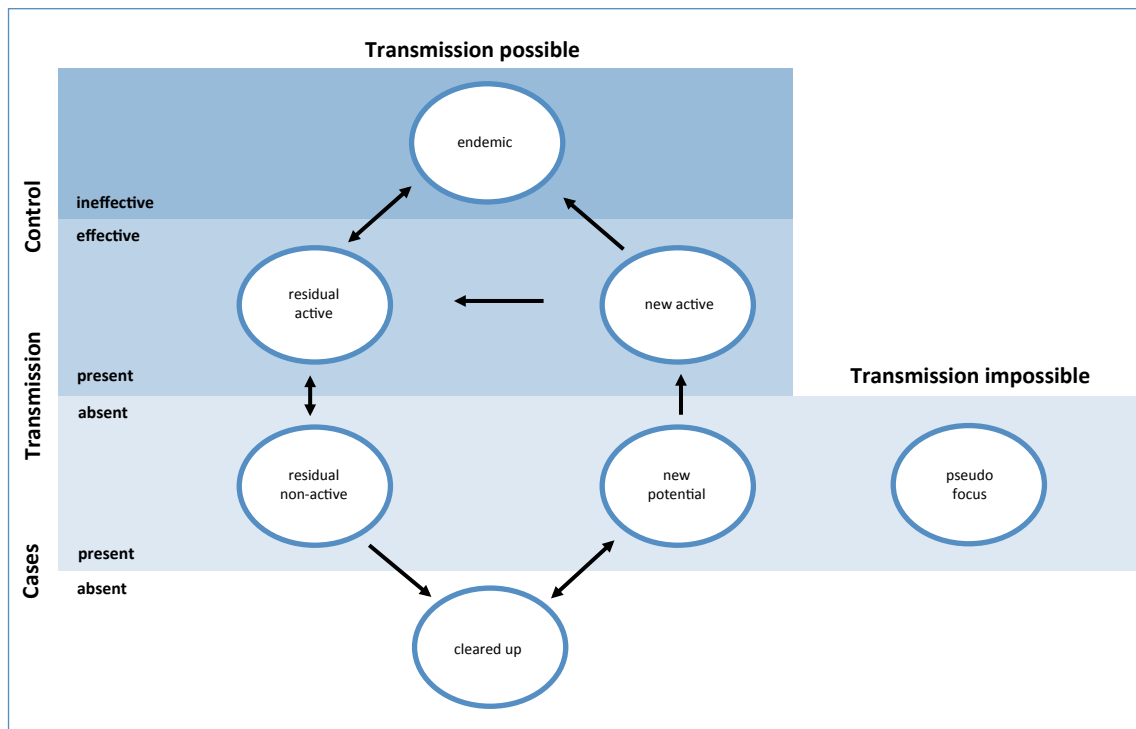
On the basis of the investigation, the focus can be classified into one of six types:¹

- **Endemic:** Transmission is occurring and is not effectively controlled; if malaria control interventions are being implemented, the effect has not yet been sufficient to reduce transmission to low levels.
- **Residual active:** Transmission is occurring in an area that has had transmission within the past 2 years (or past two transmission seasons); it is effectively controlled, with major reductions in malariological indicators after interventions.
- **New active:** Transmission is occurring in an area that has had transmission for less than 2 years or has never had local transmission. New active foci can be further subdivided into *first degree*, in which only the first generation of transmission has taken place (i.e. only introduced cases are present) and *second degree*, in which second- or later-generation malaria and indigenous cases are present.
- **New potential:** Isolated imported, induced or relapsing cases are occurring during the transmission season in a receptive area that had no transmission in the past 2 years or more. If there is no evidence of renewed local transmission after 1 year, these areas would cease to be new potential foci and would become 'cleared up'.
- **Residual non-active:** There is no local transmission in an area with a history of local transmission within the past 2 years. Relapses or delayed primary infections with *P. vivax* or a recrudescence (treatment failure) of an infection acquired before transmission ceased may occur.
- **Cleared-up:** No local transmission has been recorded during the past 2 years in an area with a history of malaria and conditions that are suitable for transmission.

Figure 2.2 shows these focus categories diagrammatically. Box 2.5 provides a key for classification of foci. The reference periods (two years, two transmission seasons) in the categories above can be adjusted according to local circumstances. The term 'pseudo-focus' is used for clusters of imported cases (from abroad or from a different area of the country) for which investigation has shown that there is no possibility of local transmission.

¹ *Guidelines on the elimination of residual foci of malaria transmission.* Cairo, World Health Organization Regional Office for the Eastern Mediterranean, 2007.

FIGURE 2.2.
Classification of malaria foci



BOX 2.5.

Key for operational classification of malaria foci¹

1. Are the conditions suitable for transmission of malaria?
 - No, none throughout the year **Pseudo-focus**
 - Yes, for a period that is sufficient for maturation of sporozoites **Go to 2**
2. Is there a history of recent transmission (e.g. during the past two years)?²
 - No **Go to 3**
 - Yes (presence of introduced and/or indigenous cases) **Go to 7**
3. Are cases present?
 - Yes **Go to 4**
 - No **Cleared-up focus**
4. Is effective infection of mosquitoes possible?
 - Yes **Go to 5**
 - No (e.g. an imported case arrived during a seasonal break of transmission and received antigametocyte treatment before the onset of effective infectivity) **Cleared-up focus**
5. Which categories of cases are present?
 - Only induced, imported or relapsing cases **New potential focus**
 - Other categories also present (introduced or indigenous) **Go to 6**
6. Are indigenous cases present?
 - No **New active focus; only introduced cases present**
 - Yes **New active focus; indigenous cases present**
7. Are indigenous cases present?
 - No **Residual non-active focus**
 - Yes **Go to 8**
8. How effectively is transmission controlled?³
 - Transmission is effectively controlled **Residual active focus**
 - No effective control **Endemic focus**

¹ Adapted from *Guidelines on the elimination of residual foci of malaria transmission*. Cairo, WHO Regional Office for the Eastern Mediterranean, 2007:28–30, 47 (EMRO Technical Publications Series, No. 33).

² The exact duration of the period should be decided by the programme.

³ Criteria for the effectiveness of control should be specified by the programme.

The focus classification should be updated periodically. In countries with seasonal transmission, classifications of foci are often reviewed at the end of each malaria transmission season. The status of a focus should also be reviewed as new cases appear and field investigations are undertaken. The focus investigation results are maintained at district and national levels (comprising a focus “register”). In addition a summary of the status of foci is updated at least annually (Annex 4).

3. Data recording and reporting

3.1 Data recording

Health facility

Case detection: Health facilities should keep a register of each suspected malaria case among attendees. This should contain the identification number, date of attendance, patient's name, residence, work or daytime address, sex, age, whether the attendance is a new or a repeat visit for the same episode of illness, type of testing, test results and treatment given. Similar registers should be maintained in areas in which active case detection is undertaken to supplement passive case detection, noting also the location of the testing. Double-counting should be avoided, through the use of pre- and post-data entry cleaning and verification when electronic records are kept.

Field level

Case investigation: For each laboratory-confirmed case of malaria, a case investigation form should be completed (Annex 2). When active case detection is undertaken as part of a field investigation, the following elements should be recorded for each person examined: identification number, date of testing, address, sex, age, occupation or other potential risk factors, clinical indication (fever, other clinical sign or mass screening), type of test, test result.

Focus investigation: For each new focus identified, a focus investigation form should be completed (Annex 3). For each new malaria case identified in an existing focus, the focus information is updated.

District level

The malaria team at district or intermediate level should keep the following records:

- monthly reports of the numbers of patients tested for malaria and the numbers of confirmed cases from public sector and private health facilities and by active case detection in areas with inadequate passive case detection. The total number of people tested for malaria during passive and active case detection is used to calculate the annual blood examination rate;
- a register of malaria programme health structures and staff, including health facilities by type and personnel by specialty (parasitologists, epidemiologists, laboratory technicians, clinicians) and their professional qualifications. The register should be updated annually and include a list of all health facilities and laboratories undertaking malaria testing. A record of staff qualifications and participation in training should be included;
- malaria case notifications. All confirmed cases should be recorded, whether or not a field investigation has been undertaken. The initial registration of all positive cases becomes the denominator for cases that should have a field investigation;
- malaria case investigation forms, including the results of active case detection (Annex 2). Once completed, case investigation forms should be entered immediately into the district database;
- focus investigation forms (Annex 3);

- a list of foci with changes in status over time (Annex 4);
- an entomological database containing an inventory of *Anopheles* breeding sites, species, vector density and behaviour, seasonality and maps of the area;
- a vector control and intervention database containing information on larval control (biological and chemical larviciding), indoor residual spraying, number of long-lasting insecticidal nets distributed, environmental management activities, and behaviour change communication activities.

All periodic and annual reports and district analyses produced by staff during the past 5 years and submitted to higher levels should be filed and kept. Feedback and other information from higher levels should be also collected. The team should use statistical software to analyse aggregate and case-based data. Clear illustrative mapping, electronically or on paper, should be a routine.

Maps constructed during a focus investigation that show the distribution of cases by household should be kept up to date by plotting the location of each newly confirmed case and updating other information as necessary. Summary maps can be created, amalgamating information from different foci, showing the distribution of cases by village.

National level

Early in the shift to an elimination programme (during the pre-elimination phase), a database of malaria elimination should be established at central level. It serves two purposes: to aid the programme to make informed decisions, and as a national repository of all information related to malaria elimination. The main components of the database are:

Cases and foci:

- *National malaria case register*: a consolidated list of all malaria cases in the country, including unique identifiers (to allow tracking of subsequent infections in individuals), demographic information and location, a reference to the location of the original patient records, case investigation forms, laboratory forms;
- *Malaria focus investigation data*: all data from the malaria focus investigation forms (Annex 3);
- *List of foci with changes in status (Annex 4)*: The status (classification) of each focus is re-evaluated after each new confirmed case and at least at the end of each transmission season. Changes in focus classification status and the date of the change should be recorded. The list will be dynamic, as the status may change after each new case (change in focus classification or addition of new foci). All new foci (including 'new potential' foci) are immediately added to the list and become the denominator for new foci to be investigated.

Health services:

- *National malaria reference programme health structures and staff*: annual records of health facilities by district and type, personnel by specialty (parasitologists, epidemiologists, entomologists, laboratory technicians, clinicians) by administrative level; in particular, a register of health facilities and laboratories undertaking malaria testing;
- *National malaria reference laboratory quality assurance data*: monthly and annual external quality assurance reports for the reference laboratory, including information on the results of retesting (positive and negative slides) and of proficiency panels;
- *Reports of activities of specially assigned mobile teams*: Mobile teams often conduct active case detection or gather information on at-risk populations such as migrants and minority groups.

Vector surveillance and control:

- *Entomological surveillance data*: entomological data from district reports on *Anopheles* breeding sites, including *Anopheles* species, vector density and behaviour, seasonality and maps of the area;
- *Vector control activities and interventions*: district reports on vector control activities, including larva control operations, indoor residual spraying, long-lasting and other insecticide-treated nets distributed, environmental management activities, and behaviour change communication activities.

Surveillance reports:

- *Malaria surveillance reports and analyses sent by districts*: monthly reports of the numbers of tests performed and the numbers of confirmed cases from public sector and private health facilities and from active case detection in areas with inadequate passive case detection;
- *National annual malaria surveillance reports and analyses*: annual and other reports describing the epidemiology of malaria cases, the quality of surveillance, entomological activities and the national malaria laboratory system. An annual report is good epidemiological practice, as it provides a synthesis of data from all information systems. It also helps to maintain interest in malaria once the disease ceases to be a public health problem.

Other:

All periodic and annual reports and district analyses produced by the staff during the past 5 years should be filed and kept. Feedback and other information to lower levels should also be collected. The team should use statistical software to analyse aggregate and case-based data. Maps, at least by village, are required for each focus when there more than about five foci. When there are fewer foci, maps by household with geographical coordinates are feasible at national level. Information on intersectoral collaboration, cross-border collaboration, health education and mobilization of the population and reports of operational research will complement the elimination database. Although many different types of data must be actively managed and archived, the information system for malaria elimination is often of modest size because the databases are inherently small.

3.2 Reporting

There are three main types of data flow (immediate, monthly and annually) and three points to which data are reported (district or intermediate, the national malaria programme and the national malaria reference laboratory).

Immediately

Clinicians, surveillance agents and laboratories should immediately notify the district team and the national malaria programme of all confirmed cases of malaria by telephone, SMS or e-mail, including the patient's name, village or neighbourhood and district of residence, date of malaria testing, type of test and *Plasmodium* species. The national malaria programme should immediately alert the national malaria reference laboratory to trigger re-testing of specimens.

Once the initial case history is taken, the district malaria focal point should send the information immediately to national level, by telephone or e-mail, and again once the case investigation form is completed. The results of field and focus investigations should also be sent to the national (and sometimes provincial) level as soon as they are completed and, if necessary, while the investigation is taking place. Such information may be transferred electronically once the new case and field investigation data are entered into the database.

The national malaria reference laboratory should immediately send the results of confirmatory testing for initially confirmed cases to the national malaria programme and the district focal point. It should also immediately notify the national malaria programme and district about slides that were initially negative but found to be positive on retesting, so that the field investigation can commence.

If a case is obviously imported and occurred in an area that is not receptive, in settings where imported cases are quite common, it may sometimes be acceptable to relax the above rules on immediate reporting, but nationally defined standard operating procedures should be followed.

Monthly

Each month, all health facilities undertaking malaria testing (in both the public and the private sector) should report the number of malaria tests conducted and the number of confirmed cases. This information may be submitted within a national health information system or a malaria-specific information system. Similar information should be reported for each village and hamlet in which active case detection is undertaken. Active case detection should not necessarily be undertaken every month and may occur only during the transmission season.

Districts should send the following paper forms or databases to the national level monthly:

- number of people examined and number of positive test results from public and private facilities;
- number of people examined and number of positive test results from active case detection, where it is done; and
- updated focus numbers and classification.

The national malaria reference laboratory should provide all the results of retesting of both positive and negative slides to health facilities and districts monthly. The national malaria reference laboratory and the malaria programme should use the same case identification numbering system, to ensure that the two files can be linked with a common identifier.

3.3 Analysis

Health facilities

Health facility staff should monitor the extent of surveillance of the population living and staying overnight in the facility catchment area during the malaria season, with particular attention to residents of new active, residual active and residual non-active foci. Health staff in the focus should determine the number of malaria tests undertaken each month during passive or active case detection. If no tests are done in some villages or locations during the expected transmission season, enquiries should be made to determine the possible reasons and actions that could be undertaken, such as instituting active case detection.

Districts

Tables and charts should be readily available for the indicators listed in Box 3.1. The aim of this type of monitoring is to detect any ongoing local transmission of malaria. The indicators should be reviewed monthly for each focus. The information for some indicators may not change from month to month if no cases have been detected. Particular attention should be paid to monitoring the extent of surveillance by village, location or hamlet each month, targeting the people staying overnight in active transmission foci. The district focal point should determine in which villages, locations and hamlets no malaria tests have been conducted for 1–2 months and plan active case detection in those locations. The most important question is whether or not any malaria tests were performed in a month.

BOX 3.1.

Surveillance indicators in the elimination phase

Indicator	Target or norm	Data source
Impact		
Number and incidence rate of confirmed malaria cases by classification, sex, age group, risk group (e.g. schoolchildren, migrant workers)		Malaria case investigation database
Number of foci by classification (see Annex 4 for an example report format)		Malaria focus database
Quantity and quality of surveillance		
Annual blood examination rate by district and focus detected passively and actively ¹	Indicative target in endemic, residual active, new active and residual non-active foci: 8% of population in focus	District monthly and annual reports database
	Indicative target in cleared-up and new potential foci: 1–3% of population in focus	
Percentage of expected monthly reports received from health facilities and laboratories (with number of patients tested for malaria and number positive)	Target: 100%	District monthly reports database
Percentage of confirmed cases fully investigated (including case investigation form, focus investigation form and active case detection)	Target: 100%	Malaria case investigation database
Percentage of foci fully investigated (malaria focus investigation form completed, including data from an entomological investigation) and registered (on register, with maps of each focus)	Target: 100%	Malaria focus database
Time from first symptom (fever) to first contact with the health system	Norm: within 48 h	Malaria case investigation database
Time from first contact to testing	Norm: within 24 h	Malaria case investigation database
Time from positive test result to start of treatment	Norm: same day	Malaria case investigation database
Time from positive test result to notification of the national malaria programme (to district or intermediate level, with copy to central level)	Norm: same day	Malaria case investigation database
Percentage of malaria testing laboratories participating in quality management system (all positive slides and 10% of negatives sent for retesting and the blind proficiency test completed each year)	Target: 100%	External quality assurance database
Percentage of past 5 years with national annual malaria programme report	Target: 100%	

¹ The annual blood examination rate targets are for supervisors. The surveillance work of staff at the primary level should be seen as service provision and not be quota-driven. An operational emphasis on annual blood examination rate targets could obscure the main objective, which is to ensure that any ongoing local transmission of malaria is detected in a timely manner.

At the end of each year, the malaria situation should be reviewed by comparing the results with those for previous years. This should include an analysis of numbers of cases and incidence by location, sex, age, occupation and other risk factors, as well as number of foci by location and classification. Surveillance and other interventions should also be analysed. The results should form the basis of annual malaria programme planning, in order to adjust the programmes to new trends.

National level

The analysis of surveillance at the national level is similar to that at district level.

Continuous evaluation of the national surveillance network for weak spots (geography and subpopulations) is required. The national malaria surveillance focal point should be alert to areas of weakness by examining the characteristics of new confirmed cases, for example late detection or cases occurring after two or three generations of local transmission. In addition, malaria epidemiologists should collaborate with entomologists to identify receptive and vulnerable areas that do not have adequate passive or active case detection.

The national malaria reference laboratory should share the laboratory quality assurance database and a short bulletin or report on the results of quality assurance with the national malaria programme each month.

Intensive monitoring of surveillance quality indicators (Box 3.1) will lead to better surveillance for elimination.

An annual evaluation of the impact and quality of the surveillance programme is conducted. Progress made and gaps identified are considered in preparing the plan of action for the following year. The national level should provide at least two products as regular feedback:

- a monthly bulletin to provide feedback to personnel at district level and in malaria foci; and
- an annual report.

4. Establishing surveillance systems in the elimination phase

Establishment of surveillance systems for elimination takes time, as it often involves updating legislation and policies, establishing new surveillance system components (case and focus investigations, active case detection, laboratory quality control), training of staff and educating the public.

4.1 Pre-elimination phase

The pre-elimination phase is the time to review old systems and plan a new or revised surveillance system. Countries interested in achieving malaria elimination may consider entering a pre-elimination phase if the slide positivity rate during the peak malaria season is $< 5\%$. A slide positivity rate of $< 5\%$ each month during the peak malaria season is more stringent than an annual slide positivity rate of $< 5\%$. An annual slide positivity rate of 5% and an annual blood examination rate of 10% would result in a rate of five cases of malaria per 1000 population. A slide positivity rate of $< 5\%$ during the peak season would result in an annual malaria case rate of two to four cases per 1000 population, or 20 000–40 000 cases in a population of 10 million. In most countries that are currently in a position to consider elimination, however, the populations at risk represent only a fraction of the total population, so that the figures are usually more manageable: often ≤ 1000 cases per country per year. Countries entering the pre-elimination phase should have already started line listings of confirmed cases at district level (both inpatients and outpatients) and mapping of cases by village, which constitute an elementary form of malaria focus delineation.

At the start of pre-elimination, current surveillance systems should be reviewed to identify areas that require strengthening, which may include:

Updating legislation. Public health legislation might have to be updated to:

- include malaria as a mandatory immediately notifiable disease and provide guidelines on recording and reporting malaria cases;
- ensure parasite-based diagnostic testing for malaria and quality assurance systems for testing;
- regulate participation of the private sector in all aspects of surveillance and treatment;
- regulate treatment and follow-up of confirmed cases of malaria; and
- regulate access to antimalarial medicines.

Staffing at national level. The national level is responsible for policy- and decision-making, coordination, supervision, monitoring and evaluation of programme management and progress. The staff should include epidemiologists, parasitologists, entomologists and data managers. The national reference laboratory provides support to the ministry of health in establishing quality management systems for diagnostic testing.

Staffing at intermediate or district level. Depending on the public health structure and size of the country, intermediate levels (provinces, regions, districts) may require:

- epidemiological and parasitological units staffed by epidemiologists, parasitologists, entomologists and data managers, particularly in areas with active foci, repeated imported cases and high vectorial capacity. The staff are responsible for all aspects of malaria surveillance and control, including data collection and analysis, monitoring and early recognition of outbreaks or changes in disease trends. This team also directs case and focus investigations.
- entomological units to assist in case and focus investigations, undertake entomological surveillance and help lead vector control activities.
- in countries in which the system for quality assurance of diagnostic testing is present at intermediate level, laboratories supervise the primary laboratories in the district.
- hospitals at the intermediate level undertake management of complicated malaria cases.

Establishing new public sector malaria testing and treatment posts in active foci. Health posts or health workers, including community agents, may have to be added in foci with persistent local malaria transmission. These malaria treatment posts would serve both surveillance and control functions.

Involving the private sector. The way in which the private sector is involved depends on the national situation. In all instances, the minimum requirement is that private providers ensure that every suspected case of malaria is tested before treatment, notify every diagnosed malaria infection immediately and facilitate case investigation and follow-up. All private sector laboratories should report the number of patients tested monthly to the district, in addition to immediate notification of people with a positive malaria test. Private pharmacies should refer all suspected malaria cases to laboratories certified to test for malaria. The national malaria programme should inform private pharmacies about the profile (suspected malaria case definition) of patients who should be referred for malaria testing. Private pharmacies should be prohibited from dispensing antimalarial medicines without a prescription.

Regulations and guidelines should be drawn up on how private sector providers are to be involved in treatment and follow-up of confirmed cases. In general, the public sector supervises the treatment of confirmed malaria cases, including directly observed therapy, and follow-up of all patients, including retesting.

Reorientation of staff. Passive case detection and reporting are the responsibility of all health facilities, both government and private, and of all health care professionals, regardless of their specialty (e.g. general practitioners, internists, paediatricians, specialists in infectious diseases, parasitologists). The criteria for giving a diagnostic test should be disseminated widely to all health care providers and the public. The criteria might be people with fever and no other obvious cause and people with fever and a history of travel to an endemic area (see section 2.3), and reminders of these criteria should be sent periodically. All health staff in a country should be trained to recognize the symptoms and signs of malaria in order not to miss cases and to give appropriate treatment immediately after diagnosis.

Laboratory support for surveillance and quality assurance. All laboratory diagnostic services should be free of charge to the patients at public and, if possible, also private facilities. All laboratories that conduct testing for malaria should be part of a quality management network. National and intermediate-level laboratories run the quality management system. Clinicians, facilities and laboratories that are not part of the quality management network should preferably not test for malaria (unless this is temporarily justified by local circumstances) and should refer those patients with suspected malaria to a laboratory that is part of the network. The quality management system should:

- reconfirm positive tests;
- retest a sample of negative specimens from intermediate-level and national reference laboratories; and
- organize testing panels for all participating laboratories;

A full outline of the structure of a laboratory network is given in Annex 1.

4.2 Certification of elimination

Countries that have had no locally transmitted malaria cases for 3 consecutive years and have the surveillance systems to prove it can apply to WHO for certification of achievement of malaria elimination. This involves a review of national documentation and field visits to recent transmission foci to establish that the evidence that there has been no malaria transmission is credible, that the national surveillance system would be able to detect local transmission should it occur and that a funded programme for prevention of reintroduction is in place. The complete list of documents required is given in the WHO manual *Malaria elimination: a field manual for low and moderate endemic countries*¹. The surveillance-related documents required are:

- complete information on cases and active malaria foci in the 5 years before the last indigenous case, with supporting maps;
- annual malaria surveillance reports for the past 10 years;
- reports of quality assurance activities for diagnostic methods; and
- detailed reports on entomological activities.

4.3 Surveillance in the prevention of reintroduction phase

Vigilance: a function of the public health service during the programme for prevention of reintroduction of transmission, consisting of watchfulness for any occurrence of malaria in an area in which it did not exist or from which it had been eliminated and application of the necessary measures against it.

During the phase of prevention of reintroduction, the intense surveillance operations required for eliminating transmission will be scaled down and will be replaced by vigilance. This phase places more emphasis on nationwide early detection of imported malaria cases that pose a risk for renewed transmission and on monitoring changes in the levels of receptivity and vulnerability in a country. Vulnerability reflects the likely inflow of malaria parasites, and receptivity the likelihood that malaria infections will result in secondary cases. The probability that malaria will become re-established will vary from area to area, depending on these two factors, as follows:

- When either the receptivity or vulnerability of an area is zero, there is no risk for renewed transmission.
- At low levels of receptivity and vulnerability, early case detection by a vigilant general health service, complemented by epidemiological investigation of every case and focus and appropriate curative and preventive measures, may be sufficient to prevent re-establishment of transmission.

¹ *Malaria elimination: a field manual for low and moderate endemic countries*. Geneva, World Health Organization, 2007.

- At increasing levels of receptivity and vulnerability, it may be necessary to supplement these activities by active case detection, which could be combined with other regular health activities involving house visits.
- In highly receptive, highly vulnerable localities, it may be necessary to reduce receptivity during the transmission season by the use of timely, targeted vector control measures, including indoor residual spraying and larviciding, on the basis of continually updated information on the local situation. In the longer term, interventions that durably reduce transmission risk in these areas without repeated application of chemicals are preferred.

Annexes



ANNEX 1.

Laboratory support for surveillance in the elimination phase

A1.1 Introduction

In the elimination phase, every case should be confirmed by laboratory examination. Early microscopic diagnosis that gives information on the *Plasmodium* species, parasite density, the presence or absence of gametocytes in *P. falciparum* cases allows timely and appropriate treatment, monitoring of transmission and achievement of planned malaria elimination outcomes. All laboratory diagnostic services should be free of charge at both public and private facilities.

In view of the importance of laboratory support for surveillance in malaria elimination, policy and legislation regarding the organization of the laboratory network involved in surveillance should be reviewed and revised if necessary. The technical capacity of the laboratory network, including standard tools and quality management mechanisms, should be strengthened.

A1.2 Laboratory network

Laboratory services are typically organized into three main levels:

Peripheral level

- diagnostic facilities at primary health care facilities;
- diagnostic laboratories at hospitals or health centres that serve both inpatients and outpatients; and
- private laboratories.

Blood sampling and malaria laboratory examinations are performed at this level. The facilities report to laboratories at higher levels and participate in the national quality assurance programme. Mobile health teams of the malaria elimination programme can also provide diagnostic services in areas of inadequate surveillance and during case and focus investigation.

Intermediate (regional, provincial or district) level

- laboratories at regional hospitals;
- laboratories at regional public health centres; and
- private laboratories.

The laboratories at this level are responsible for supervising and monitoring quality and training the staff of peripheral laboratories. They also participate in the national quality assurance programme.

National level

- the designated national malaria reference laboratory;
- laboratories at public and private facilities in the capital city; and
- laboratories in specialized services (e.g. university, army).

The national malaria reference laboratory plays a key role in assuring high-quality laboratory diagnosis of malaria in the country. It is generally nominated by the Ministry of Health. It might be based in a research institute, medical school or large hospital. The national malaria reference laboratory collaborates closely with the national malaria elimination programme. It should have the necessary laboratory space, equipment, reagents and consumables, as well as a sufficient number of expert microscopists. The national malaria reference laboratory should participate in an international external quality assessment programme for reference laboratories. WHO has established a proficiency testing programme for several diseases, including malaria, for national reference laboratories.¹

A1.3 Quality management system

An important component of malaria elimination is establishment of a national quality management system. It is a good practice to implement quality assurance and control procedures in all malaria diagnostic laboratories in the country. Quality assurance and quality control are described in detail in the *Malaria microscopy quality assurance manual*.² Several activities should be organized by the national malaria reference laboratory, first applied to sub-national reference laboratories and then delegated to them to be applied to peripheral laboratories, if feasible:

Standard operating procedures and job aids

A series of standard operating procedures and job aids should be created preferably at the national malaria reference laboratory. Examples of standard operating procedures and job aids are provided in *Universal access to malaria diagnostic testing*³ and *Bench Aids for Malaria Microscopy*⁴ which can be adapted to local contexts:

- use, care and maintenance of microscopes;
- preparation of Giemsa stain solution;
- thick and thin blood film preparation for malaria;
- blood film staining for malaria;
- routine examination of blood films and parasite density calculation;
- waste management of malaria tests; and
- proficiency testing (external quality assessment) for microscopy.

Supervision visits of laboratories

Laboratories at all levels should be monitored by on-site visits with a standard supervisory assessment tool (see annex 8 and section 4.4.1 of *Universal access to malaria diagnostic testing*⁵). During these visits, assessments should be made of microscopists' competence by direct observation during preparation and staining of blood slides and of the general quality of the blood

¹ *Policy and procedures of the WHO/NICD Microbiology External Quality Assessment Programme in Africa Years 1 to 4, 2002–2006*. Geneva, WHO/CDS/EPR/LYO/2007.3. Available online at: http://whqlibdoc.who.int/hq/2007/WHO_CDS_EPR_LYO_2007.3_eng.pdf.

² *Malaria microscopy quality assurance manual*, version 1. Geneva, World Health Organization, 2009. Available online at http://www.who.int/malaria/publications/malaria_microscopy_QA_manual.pdf.

³ *Universal access to malaria diagnostic testing*. Geneva, World Health Organization, 2011. Available online at: http://whqlibdoc.who.int/publications/2011/9789241502092_eng.pdf.

⁴ *Bench Aids for Malaria Microscopy*. Geneva, World Health Organization, 2010. Available online at: <http://apps.who.int/bookorders/anglais/detart1.jsp?sesslan=1&codlan=1&codcol=15&codcch=3294>.

⁵ *Universal access to malaria diagnostic testing*. Geneva, World Health Organization, 2011. Available online at: http://whqlibdoc.who.int/publications/2011/9789241502092_eng.pdf.

slides at the testing site (see annex 9 and section 4.4.3 of *Universal access to malaria diagnostic testing*¹).

Slide proficiency testing (reference blood slide reading at the testing site)

This activity (also called ‘panel testing’) consists of distributing pre-prepared stained blood films in a blinded manner to laboratories performing malaria microscopy for examination. This allows monitoring of the competence of a microscopist or laboratory to detect, identify and quantify malaria parasites on a well-prepared, stained blood film. It is not a measure of the performance of malaria microscopy in routine practice. This activity might be focused in priority testing sites (e.g. sub-national reference laboratories), as it requires a large number of standardized slide sets and is complex and time-consuming. On-site visits to these sub-national reference laboratories are a good opportunity to distribute the reference blood slides and, on a subsequent visit, to collect the results of their reading. A standard form should be used to report reading accuracy to laboratories and take necessary remedial action in cases of suboptimal performance.

Validation of routine blood slide results (cross-checking)

The national malaria reference laboratory can set-up a system to perform a second reading (cross-checking) of a sample of routine blood slides prepared at sub-national reference laboratories (see *Universal access to malaria diagnostic testing*¹ section 4.4.3). Once the results of cross-checking show that the expected level of competence has been reached at sub-national level, a similar system can be put in place between the sub-national reference laboratories and peripheral laboratories.

Some countries have plans to modify this system to include a third reading of peripheral slides by expert microscopists at the national malaria reference laboratory (either a random sample or focussing on slides with discrepant results after cross-checking), in addition to the second reading at sub-national level. A third reading of the same slide complicates reliable calculation of the percentage of agreement and prolongs feedback to the peripheral laboratories. The competence of microscopists at sub-national level can be evaluated by the national malaria reference laboratory only on the basis of slides prepared at the sub-national laboratory itself and not from their reading of blood slides prepared by others (peripheral laboratories). For more discussion on different approaches for slide validation, see section 4.4.3 of *Universal access to malaria diagnostic testing*¹.

Accreditation of microscopists

Accreditation of the competence of microscopists can significantly improve the accuracy of malaria diagnosis by microscopy and raise the confidence of the microscopist. It is recommended that national programmes:

- establish a national malaria microscopy accreditation system;
- give formal recognition to the skills of individual microscopists;
- set up a training programme linked with the accreditation system to improve the competence of microscopists working at each level of the laboratory network;
- monitor and record their competence continuously; and
- provide a career path for certified microscopists.

It is recommended that accreditation be time-limited and, for the best-performing microscopists, should be valid for no more than 3 years. Earlier reassessment should be available for those who are not performing well.

¹ *Universal access to malaria diagnostic testing*. Geneva, World Health Organization, 2011. Available online at: http://whqlibdoc.who.int/publications/2011/9789241502092_eng.pdf.

Certification of reference laboratories

Certification is recognition of the performance of a laboratory. It is usually voluntary and complements mandatory licensing or registration. For example, ISO 15189:2007 accreditation has been established for laboratories that meet internationally recognized standards. Inter-country initiatives exist or are being set up in some regions. A training toolkit for learning how to implement a quality management system in a laboratory on the basis of internationally recognized standards is available on the WHO website¹. Certification is, however, expensive to do and to maintain.

Monitoring the quality management system

Performance indicators should be chosen on the basis of data collected by health facilities and reported through the national health information management system or, possibly, during on-site supervisory visits. In addition to routine data, problems reported from peripheral health facilities should prompt additional on-site quality monitoring. To monitor improvements over time, it is essential to collect performance indicator data regularly over a long period. The main problems identified during supervisory visits should also be reported at secondary or central levels.

¹ *Laboratory Quality Management System Training toolkit*. Geneva, World Health Organization/ Clinical and Laboratory Standards Institute/ Centers for Disease Control and Prevention, 2009, Trainer's guide and handbook. Available at: http://www.who.int/ihr/training/laboratory_quality/en/

ANNEX 2.

Sample malaria case investigation form

Malaria case investigation form	
Case number:	
Case history	
Date history taken:	Location history taken:
History provided by:	Relation to patient:
Name of patient:	
Sex:	Age:
Current nationality:	
Full present home address:	
Home GPS coordinates:	
WHEN did the infection take place?	
Reason for diagnostic test	
Passive case detection <input type="checkbox"/>	Active case detection <input type="checkbox"/>
Contact survey <input type="checkbox"/>	Population-based survey <input type="checkbox"/>
Symptoms:	
Date of onset of first symptoms of current clinical episode:	
Blood sample	
Sample taken by:	
Name of health facility:	Clinician name:
Rapid diagnostic test	
Performed by:	Date:
Result:	
Manufacturer of test:	Batch number:
Microscopic examination	
Performed by:	Date:
Laboratory name:	Location:
Staining method:	
<i>Plasmodium</i> species:	Parasite density:
Gametocytes present (<i>P. falciparum</i> only)	Yes <input type="checkbox"/> No <input type="checkbox"/>
Molecular testing and polymerase chain reaction results	
Performed by:	Date:
Laboratory name:	Location:
Geographical origin of infection:	
Link to previous attacks:	

Malaria case investigation form		
Antimalarial treatment		
Type of medicine:	Doses:	Dates:
Treatment outcome:		
Previous clinical episodes		
Date:	Locality:	
Symptoms:		
Laboratory test results:		
Antimalarial treatment		
Type of medicine:	Doses:	Dates:
Treatment outcomes:		
WHERE, HOW, and FROM WHOM did the infection possibly take place?		
Length of residence at present home address:		
If residence at present home is less than one year: previous home addresses within past year, including dates:		
Current occupation:	Place of work:	
Recent travel history to known endemic area (including residual active or new active foci) in the country, in as far as this included possible dusk-dawn exposure to mosquito bites:		
Recent contact with known imported malaria cases (provide details):		
Travel to foreign endemic country		
• Within the past year (for <i>P. falciparum</i> infection)	Yes <input type="checkbox"/>	No <input type="checkbox"/>
• Within the past three years (for <i>P. vivax</i> infection)	Yes <input type="checkbox"/>	No <input type="checkbox"/>
Type of preventive measures taken during the above-mentioned travel to endemic areas/countries:		
If chemoprophylaxis taken - drug name, dose and duration:		
Blood transfusion within past three months:	Yes <input type="checkbox"/>	No <input type="checkbox"/>
Preliminary conclusion		
Malaria infection likely acquired at (specify locality and source):		

Malaria case investigation form	
Possible onward transmission	
Did patient travel overnight away from home since the onset of the current clinical episode and before completion of treatment: Yes <input type="checkbox"/> No <input type="checkbox"/>	
(If yes, provide exact places visited, dates):	
House of patient (type of construction, indoor residual spraying):	
Entomological studies carried out: Yes <input type="checkbox"/> No <input type="checkbox"/>	
Carried out by:	
Remarks:	
Case classification	
Date onset of symptoms:	Plasmodium species:
Case classification:	
Classified by:	Position:
Reviewed by:	Position:
Follow-up actions	
Actions taken:	
Investigation undertaken by:	Position:
Signature:	Date:

ANNEX 3.

Sample malaria focus investigation form¹

Malaria focus investigation form and register
Basic information
Name of the focus settlement (town, village, hamlet):
District:
Province:
Description of the locality
Type of environment in relation to possible receptivity (eg. urban/ rural, altitude, main geographical features) and vulnerability (e.g. close to endemic area across international border):
Type of population in relation to possible vulnerability(e.g. migration patterns, presence of large numbers of temporary workers, typical travel histories):
Mapping
Should include location of: <ul style="list-style-type: none"> • Focus and its geographical limits • Households with malaria cases in past three years • Health facilities • Breeding sites • Access routes • Other important features

1

¹ Local adaption may be needed based on local malaria epidemiology and control interventions.

Epidemiological information (for the last 5 years)

Table 1 Malaria cases in the focus by month

Years	Popu- lation	Number of cases by month												
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total

Table 2 Malaria cases in the focus by *Plasmodium* species

Years	Total cases	Number of cases by <i>Plasmodium</i> species				
		<i>P. vivax</i>	<i>P. falciparum</i>	<i>P. ovale</i>	<i>P. malariae</i>	Mixed

Table 3 Malaria cases in the focus by age

Years	Total cases	Number of cases by age in years					
		0-1	2-4	5-9	10-14	15-19	>19

Table 4 Malaria cases in the focus by sex

Years	Males		Females		Total
	Number	%	Number	%	

Table 5 Malaria cases in the focus by social and high risk group

Years	Total cases	Number of malaria cases by category							
		Small children attending day nurseries/ kinder-gartens	Small children at home	School children	Agricultural workers	Labourers	Office workers	House-wives	Other

Table 6 Number of blood samples taken in the focus and examined

Years	January		February		March		April		May		June	
	ACD	PCD	ACD	PCD	ACD	PCD	ACD	PCD	ACD	PCD	ACD	PCD

Table 6 (continued) Number of blood samples taken in the focus and examined

Years	July		August		September		October		November		December		Total	
	ACD	PCD	ACD	PCD	ACD	PCD	ACD	PCD	ACD	PCD	ACD	PCD	ACD	PCD

Table 7 Active and passive case detection in the focus

Years	Number of cases detected by:		
	ACD	PCD	Total

Table 8 Timeliness of care-seeking (time from first symptoms (e.g. fever) to first contact with the health system)

Years	Number of cases by number of days before contact with health system:					
	1	2	3-5	6-10	11-30	>30

Table 9 Timeliness of case detection (time from first symptoms (e.g. fever) to parasite detection)

Years	Number of cases by number of days before detection:					
	1	2	3-5	6-10	11-30	>30

Table 10 Timeliness of malaria parasite-based testing (time from first contact to testing)

Years	No. cases by no. hours between contact and testing			
	Same day	Next day	≤72 hrs	>72 hrs

Table 11 Timeliness of malaria treatment (time from malaria diagnosis to treatment starting)

Years	Number of cases by number of hours between diagnosis and treatment:					
	<2 hrs	2-5 hrs	6-12 hrs	13-24 hrs	25- 72 hrs	> 72 hrs

Table 12 Vector control activities - IRS						
Years	Insecticide applied – name and dosage	IRS dates	Number of house-holds	Number of house-holds sprayed	Coverage (%) of house-holds	Coverage in m ²

Table 13 Vector control activities - number of mosquito breeding sites in the focus and within a radius of 3 km and larval control activities									
Years	Number of breeding sites by type			Total area in hectares			Number of breeding sites with <i>Gambusia</i> distributed		
	Stationary	Temporary	Rice fields	Stationary	Temporary	Rice fields	Stationary	Temporary	Rice fields

Table 13 (continued) Vector control activities - number of mosquito breeding sites in the focus and within a radius of 3 km and larval control activities									
Years	Total area in hectares with <i>Gambusia</i> distributed			Number of breeding sites treated with chemicals			Total area in hectares treated with chemicals		
	Stationary	Temporary	Rice fields	Stationary	Temporary	Rice fields	Stationary	Temporary	Rice fields

Table 14 Management of the environment									
Years	Breeding sites of non economical value						Irrigation system		
	Primarily existing		Eliminated				Area requiring cleaning (ha)	Area cleaned (ha)	%
	Number	Area (ha)	Number	%	Area (ha)	%			

Table 15 ITN/LLIN distributed

Years	Number of households	Population	Coverage by ITN			
			Number of households	%	Population	%

ANNEX 4.

Sample form for updating focus classification

ANNEX
4

Years	Number of foci classified as:					
	New potential	New active	Residual active	Residual non-active	Cleared up	Endemic

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