STRATIFICATION OF MALARIA BASED ON RISK OF TRANSMISSION AND ELIMINATION OF FOCI

Region of the Americas

February 2019
## Content

Glossary ................................................................. 4

Summary ....................................................................................... 6

1. Introduction .............................................................................. 7

   1.1. Background and objective of the manual ......................... 7

   1.2. Target audience ............................................................... 7

   1.3. Structure of the manual ..................................................... 7

2. Conceptual framework ............................................................ 9

   2.1. Elimination as a continuous process ................................. 9

   2.2. Diagnosis-Treatment-Investigation-Response Strategy .......... 9

   2.3. Principles for foci management ......................................... 11

   2.4. Organize operations around the biology of malaria ............ 12

3. Malaria risk stratification .......................................................... 15

   3.1. Receptivity and vulnerability ............................................ 15

   3.2. Stratification background ................................................ 16

   3.3. Current context of stratification ...................................... 16

   3.4. Prioritization .................................................................... 21

4. Micro-stratification and micro-planning ...................................... 22

   4.1. Micro-stratification: identification and classification of malarial foci ........................................... 23

      4.1.1. Micro-stratification: guiding principles ....................... 25

      4.1.2. Information recommended to conduct micro-stratification and micro-planning .................. 26

      4.1.3. Methodology .............................................................. 26

   4.2. Micro-planning ................................................................. 30

5. Management of malaria elimination based on transmission in foci ........................................ 31

   5.1. Organization of DTI-R actions in the micro-areas .............. 31

   5.2. DTI-R management cycle at municipal level ...................... 39

   5.3. Supporting elements for DTI-R strategy .......................... 39

   5.4. Monitoring and evaluation ............................................... 40

References .................................................................................... 41

Annexes ..................................................................................... 43

Annex 1. Other concepts .............................................................. 43

   Malaria focus ................................................................. 43

   Case investigation ............................................................ 45
Glossary

**Malaria risk stratification.** WHO defines *malaria risk stratification* as "classification of the geographical areas or localities according to factors that determine receptivity and vulnerability to malaria transmission" [1].

**Malaria stratification.** La OMS defines malaria as “classification of the geographical areas or localities according to epidemiological, ecological, social and economic determinants for the purpose of guiding malaria interventions” [1].

**Diagnostic, treatment, investigation and response (DTI-R) strategy.** Basic action for the elimination of malaria, triggered by the detection of a case or a conglomerate of cases, which prioritizes access to diagnosis, early treatment and the importance of an additional detection effort. The DTI-R seeks to operationalize in the Americas the concept of surveillance as an intervention promoted by the WHO in the Global Technical Strategy against Malaria.

**Malaria focus.** WHO defines *malaria focus* as a defined and circumscribed zone situated in an area that is or has been malarious and in which the necessary epidemiological and ecological factors are present for the transmission of malaria [2]. Foci are classified as active, residual non-active, and eliminated (Annex1).

**Focus investigation.** It means to “to identify the main features of a location (foci), including the population at risk, the rates of infection or disease, the distribution of vectors responsible for malaria transmission and the underlying conditions that support it” [3]. In this manual, reference is made to the "identification and characterization of foci" and to "micro stratification" as actions similar to the investigation of foci; and in order to simplify and facilitate operationalization, the three terms have been compared. It is clarified, however, that the concepts have certain different connotations. The focus investigation is designed especially for situations of low transmission, reintroduction or transmission concentrated in very few locations, and generally includes actions to establish the existence of vector transmission. The other two terms, widely used in this manual, apply to situations of greater dispersion of the endemic to the need to organize and monitor the operation of malaria (especially the diagnosis and treatment network) at a very local level, in sectors or operative units (micro-areas) that may include one or more foci.

**Micro-area.** Set of foci or conglomerates of localities that share the same transmission dynamics and are epidemiologically interconnected among them, mainly due to the movement of the population. The sectorization of the local health services and the logistics of operations are important elements in this exercise. Addressing these foci in a holistic approach is a key element towards the objective of transforming the active focus into cleared ones.

**Micro-stratification.** This manual defines *micro-stratification* as identification and characterization or micro-areas. This is an exercise of analysis at the local level with triangulation of information from different
sources. This manual uses the micro-stratification terminology to identify and characterize foci in order to plan a response.

**Micro-planning.** This manual defines micro-planning as the local exercise of organizing the DTI-R in a focus or micro-area. Far from wanting to promote ineffective local planning exercises, it is about define and implement very specific solutions to the local problems of detection, diagnosis, treatment, investigation and response, and establishing the necessary supervision processes. Micro-planning is the response to micro-stratification.
Summary

1. The present manual puts into practice the principles and concepts of the *Global Technical Malaria Strategy for Malaria* [4] and *A Framework for Malaria Elimination* [2] to provide guidance to the countries of the Americas on how to implement actions that will successfully eliminate malaria and prevent its reestablishment.

2. The first step to conduct activities against malaria is to stratify the territory based on the risk of malaria transmission to plan and prioritize interventions and identify target populations. The present manual presents a method to stratify a country in accordance with the interventions and objective of elimination.

3. For all strata, PAHO/WHO proposes integrated **Diagnosis, Treatment, Investigation and Response** (DTI-R) as the key strategy to eliminate malaria transmission and prevent its reestablishment. The DTI-R strategy, which emphasizes on the importance of ensuring prompt access to diagnosis and treatment at community level, seeks to put into practice the concept of surveillance as an intervention promoted by WHO in the Global Technical Strategy.

4. Elimination of transmission at the national level is the result of transforming active foci into eliminated foci and consolidating transmission-free areas. Therefore, foci identification, classification and management form part of an essential exercise in all malaria programs.

5. Foci identification and characterization starts with micro-analysis at the local level. In this manual, we define **micro-stratification** as identification and classification of foci or clusters of localities (micro-areas) that share the same transmission dynamic, are connected epidemiologically due to the movement of people (or less frequently, due to the movement of mosquitoes), and are therefore considered as a group for a local intervention called **micro-planning**. Micro-planning has the objective of identifying and correcting gaps in early detection and prompt access to diagnosis and treatment.

6. The DTI-R strategy, based on local-level organization of the basic malaria operation, depends on a programmatic approach from the national and intermediate level to ensure the existence of the necessary technical and regulatory platform. Organization of DTI-R in malaria foci requires actions at higher levels, from procurement and distribution of drugs and vector control products, to quality assured systems and the development of norms and processes for community health workers activities in disperse zones.
1. Introduction

1.1. Background and objective of the manual

All malaria-endemic countries in the Americas have taken on the challenge of eliminating the disease and launching actions to steer their health programs and strategies toward this objective. The Plan of Action for Malaria Elimination 2016–2020, approved by member states through Resolution CD55.R7, urges the countries to revise plans and set strategies to eliminate malaria and prevent reestablishment of transmission. The manual places emphasis on how to implement actions to achieve malaria elimination and prevent its reestablishment. Key actions for elimination have already begun to be implemented by the countries. However, it is essential to place greater emphasis on intensity and quality of actions, target efforts, prevent delays that favor transmission, and ensure solid monitoring that permits modifications to be made to the interventions.

The manual does not attempt to cover all factors related to management of malaria elimination programs. Nor is it a compendium or guidebook on malaria surveillance. WHO has developed materials to guide malaria elimination, which are used as references for this document. This manual seeks to translate two WHO publications (A Framework for Malaria Elimination; and Malaria surveillance, monitoring and evaluation: a reference manual) [2, 3] into more operative language. Consultations on specific aspects (such as diagnostic quality assurance, asymptomatic malaria, mass treatment, ultrasensitive rapid tests, or integrated vector control) should be directed at the global strategies, guidelines and technical notes prepared by WHO.

1.2. Target audience

The manual is for technicians involved in the malaria elimination efforts for planning, organizing, and supervising national / provincial / local actions against malaria. The material provides guidelines for each country to develop its own strategic technical tools to implement malaria operations in accordance with the country's own normative framework.

1.3. Structure of the manual

The manual is organized in five chapters.

The first chapter introduces the manual's objective and structure, and identifies its target audience.

The second chapter outlines the conceptual framework and introduces a series of basic principles and concepts on stratification and foci management.

The third chapter describes malaria risk stratification in a country: its background, stratification in the current context, and prioritization of interventions.

The fourth chapter examines micro-stratification and micro-planning and best methods to carry these out. It describes: (a) identification and characterization of foci or micro-areas; and (b) planning of response in
the micro-area based on ensuring an appropriate diagnosis-treatment-investigation-response (DTI-R) strategy at the local level.

The fifth (and final) chapter presents aspects of management to consider for the elimination of transmission in foci and the prevention of reestablishment.

Finally, the annexes present in-depth clarifications on different aspects related to malaria interventions, such as: malaria foci, case investigation, passive case detection, reactive case detection, proactive case detection and the DTI–R strategy. Some examples are presented to guide reactive case detection, suggested indicators for malaria programs, and a format for characterization and response to malaria foci.
2. Conceptual framework

2.1. Elimination as a continuous process
The new framework for malaria elimination [2] considers that regardless of the epidemiological situation, work toward elimination is a continuum. Terms such as control, consolidation and pre-elimination are no longer used.
The principles and strategies proposed are applicable to all countries where malaria is endemic or where efforts are being made to prevent its reestablishment. Each country will plan activities based on intensity of transmission and malaria risk stratification. Each national program may support zones with different risks of malaria transmission, differently (see Figure 1 below).

Figure 1. Illustration of the set of interventions and their intensities based on disease burden. WHO

2.2. Diagnosis-Treatment-Investigation-Response Strategy
For years, countries in the region have implemented diagnosis-treatment-investigation-response actions with greater or lesser intensity and quality. As we get closer to elimination, these actions should be sharpened to ensure that no infection escapes surveillance. Revisiting WHO's T3 initiative (Test, Treat, Track) [5] and China's 1,3,7 surveillance strategy [6] (notify same day of diagnosis, investigate each case within first 3 days, respond in the focus in first 7 days to prevent continuation of transmission), PAHO is
promoting the DTI-R strategy to ensure that diagnosis, treatment, investigation and response are promptly and systematically implemented, and with the necessary precision.

The DTI-R strategy is a group of activities to be implemented in the shortest time possible by the local team to eliminate malaria transmission and prevent its reestablishment. The strategy emphasizes on the importance of time, the concept of surveillance as an intervention, and the need to implement additional efforts for prompt detection of new cases in the community. The actions do not end after diagnosis and treatment of a case, but rather it continues detecting other possible additional cases related to each index case: diagnose and treat and detect more cases. The process of prompt diagnosis, treatment, investigation and response is applicable to different scenarios in all countries. However, how to do it and in which intensity, will depend on each context.

The DTI-R strategy has four components (see Figure 2 and Annex 1):

1. **Diagnosis:** All suspected malaria cases should be diagnosed by microscopy or rapid tests within the first 48 hours after onset of symptoms.

2. **Treatment:** All confirmed cases should start appropriate treatment according to national protocol on the same day of diagnosis.

3. **Investigation:** Each case should be investigated and classified to inform the response actions within the first 3 days after diagnosis.

4. **Response:** Each case or cluster of cases should trigger a basic action of prompt detection and treatment of other cases (reactive case detection) in the first 7 days after onset of symptoms of the diagnosed case. Vector control activities (mainly mosquito nets and indoor residual spraying) form part of the integrated response to the malaria focus when appropriate.

These components should be clearly established at the local care level. For large-scale implementation of DTI-R, the actions of diagnosis, treatment, investigation and response should be translated into concrete activities in the field that can be clearly understood by all health personnel in charge of diagnosing and treating cases. As such, the communication component is an essential part of the strategy.
2.3. Principles for foci management

1. Stratification according to risk helps identify and classify areas with active transmission and those with greater transmission potential for planning and prioritizing interventions.

2. Malaria transmission in a determined area is reduced by **eliminating transmission in each focus** (transforming active foci into residual foci and subsequently eliminated foci). Reduction in transmission in a country is the sum of the elimination in foci. If the intervention is not aiming at eliminating transmission in the foci, transmission will not be reduced in the national territory. Once transmission is eliminated, the objective is to prevent malaria reestablishment.

3. Heterogeneity in transmission and focalization is a characteristic of malaria epidemiology in areas of moderate and low transmission. In the district or municipality, malaria transmission is heterogeneous and based on receptivity, human activity \[2, 7\] and the quality of the health system.

4. To reduce transmission in municipalities, the model should be based on a lower management level (in the focus or micro-area). Refinements of the operation should be determined in a more precise exercise and ongoing analysis and management at the micro-level. This element is related to the concept of "surveillance as intervention."

5. Transmission in each focus is eliminated by early **detection and treatment of the human reservoir**, and vector control activities (mainly long-lasting insecticide-treated mosquito nets and indoor residual spraying) sustained in time, with high coverage and quality.

6. The Annual Parasite Incidence (API) does not determine the strategy. The strategy is only one: diagnose and treat as quickly as possible, regardless of the number of cases. What may change is
the intensity of detection efforts (reactive case detection, case investigation) but not based on API but rather on the absolute number of cases at local level.

7. **Time is a key factor** in interrupting transmission, preventing the generation and dissemination of gametocytes from the first identified case (index case). Malaria elimination requires a surveillance system that can rapidly detect and respond to individual cases. WHO promotes prompt diagnosis and treatment in the first 24–48 hours after onset of symptoms [8, 9]. The new surveillance manual sets the target of notification of each case in the first 24 hours after diagnosis, investigation of the case in the first 3 days after diagnosis, and investigation of foci and response in the first 7 days after case notification.

8. **Suspected cases and diagnosis of malaria cases is an important bottleneck** in most Latin American countries. Without diagnosis, there is no treatment, no case investigation, no data for stratification, and no response.

9. **The core of the diagnostic operation is passive case detection.** The purpose of active case detection CANNOT be to fill gaps in passive case detection. With regards to malaria surveillance, the most important is to maintain a high suspicion of malaria in health units and to promptly provide quality-assured diagnosis, especially in vulnerable areas, without substituting passive for active case detection or by sentinel sites of fevers.

10. **Induce demand for diagnosis** Fostering demand should be a programmatic action linked to improvements in service provision (passive case detection) to ensure prompt diagnosis.

11. **Intervention in the focus does not end with treatment of malaria cases.** There should be an additional case detection activity (reactive case detection around the index case) associated with vector control to contain and interrupt transmission.

12. **The key operative change from control to elimination** is reflected in several elements to transform an active focus into an eliminated focus and to prevent the reestablishment of transmission: (i) 100% coverage of diagnosis and treatment and vector control activities; (ii) investigation of each confirmed case of malaria; (iii) early detection of other cases around the index case (beyond diagnosis and treatment, there should be an effort to detect additional cases); (iv) excellent quality of DTI-R with monitoring to continually adjust and improve the strategy; and (v) implement DTI-R to ensure recommended timelines are respected to effectively interrupt transmission.

2.4. **Organize operations around the biology of malaria**

The extrinsic incubation period refers to the parasite's cycle in the mosquito for development of the infectious sporozoites. This is also called sporogony. This period lasts a minimum of 7 days and average of
9–10 days. The intrinsic incubation period is measured from the inoculation of sporozoites to the onset of symptoms. It includes the hepatic and the erythrocytic phases. It lasts a minimum of 7 days and usually 9–17 days. In the case of \textit{P. vivax}, due to the presence of hypnozoites, it is possible to have delayed incubation periods and relapses at 3 and 18 months (rarely but sometimes up to 5 years). Identifying these incubation periods can help determine the origin of infection in each case.

Appearance of gametocytes in the blood occurs earlier with \textit{P. vivax} than with \textit{P. falciparum}: \textit{P. falciparum} gametocytes appear 7–15 days after onset of symptoms while \textit{P. vivax} gametocytes appear even before onset of fever and are already able to infect mosquitoes. So even though prompt diagnosis and treatment is important to reduce the severity of malaria by \textit{P. falciparum}, in the case of \textit{P. vivax}, there is an additional public health concern: that no more people become infected. Unlike in the case of infection from \textit{P. vivax}, chloroquine and artemisinin derivatives have little effect on \textit{P. falciparum}'s mature gametocytes, so if a dose of primaquine is not added (which has a gametocytocidal effect), these can remain in the blood for several weeks, maintaining transmission.

### Table 1. Duration of critical intervals for the two main species of human malaria

<table>
<thead>
<tr>
<th>Interval</th>
<th>\textit{P. falciparum}</th>
<th>\textit{P. vivax}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporogony (extrinsic incubation period)</td>
<td>7–10 days at 28°C</td>
<td>7–10 days at 28°C</td>
</tr>
<tr>
<td>Exoerythrocytic schizogony</td>
<td>2 – 7 days</td>
<td>6–8 days</td>
</tr>
<tr>
<td>Erythrocytic schizogony</td>
<td>2 days</td>
<td>2 days</td>
</tr>
<tr>
<td>Gametogenesis</td>
<td>days / weeks</td>
<td>Days</td>
</tr>
<tr>
<td>Prepatent (from inoculation to parasites identifiable by microscopy)</td>
<td>9–10 days</td>
<td>11–13 days</td>
</tr>
<tr>
<td>Non-immune incubation (intrinsic incubation period):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>\begin{itemize} \item Short (without hypnozoites) \item Long (caused by hypnozoites) \end{itemize}</td>
<td>\begin{itemize} \item 7–30 days \item Not applicable \end{itemize}</td>
<td>\begin{itemize} \item 8–30 days \item 3–18 months (in rare cases up to 5 years) \end{itemize}</td>
</tr>
<tr>
<td>Interval between appearance of asexual parasites and mature gametocytes</td>
<td>7–15 days</td>
<td>0 days</td>
</tr>
<tr>
<td>Time period until cleaning of gametocytes with treatment of effective blood schizonticide (without gametocide)</td>
<td>3–6 weeks</td>
<td>&lt; 1 day</td>
</tr>
<tr>
<td>Typical duration of untreated infection (if it does not result in death)</td>
<td>1–2 years (1 year or less in approximately 80% of cases)</td>
<td>1–2 years (rarely but occasionally up to 5 years)</td>
</tr>
</tbody>
</table>

\textbf{Source:} Bruce-Chwatt's Essential Malariology, Third Edition [10-12]

Relapses are a major challenge for elimination of \textit{P. vivax} in the Americas. Relapses can be a key factor in maintaining transmission in areas with residual malaria and also in the control of epidemics. The efficacy of radical cure treatment with primaquine recommended by WHO (0.25mg/kg for 14 days) is compromised by poor adherence or inadequate dosing. Some tropical strains, particularly in East Asia and Oceania,
require a higher dose of primaquine (0.5mg/kg for 14 days) because of development of a certain tolerance to the drug. In studies conducted in the Americas using 0.25mg/kg, there was an unweighted average of relapses of 9.74% (CI: 3.51%–18.47%) in 14 studies conducted up to 2010 [13-22]. The majority of these recurrences, when considered to be relapses, were attributed to lack of adherence to the prescribed treatment. However, not all relapses were due to lack of adherence: in controlled clinical studies, the average relapses were 12%. The problem of adherence to primaquine has been addressed in some countries with systematic actions of direct observed treatment, which, although they are sustainable under few conditions, can be too demanding in epidemic situations.

Other characteristic differences between *P. vivax* and *P. falciparum* [23] are presented in Table 2:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporogony of <em>P. vivax</em> produced at lower temperatures than <em>P. falciparum</em></td>
<td><em>P. vivax</em> has more extensive geographical distribution and transmission season</td>
</tr>
<tr>
<td>Shorter duration of sporogony of <em>P. vivax</em></td>
<td>Interventions to reduce lifespan of vector may be less effective in <em>P. vivax</em></td>
</tr>
<tr>
<td>In certain endemic zones with <em>P. vivax</em>, the vector (mosquitos) bite early and feed / rest in open air</td>
<td>Conventional preventive measures (LLIN and IRS) may provide less protection</td>
</tr>
<tr>
<td><em>P. vivax</em> has latent hypnozoite phase that can lead to multiple relapses after primary infection (undetectable with current diagnostic methods)</td>
<td>Malaria cases without additional bites by infected mosquitos Increase in the Ro transmission potential Potential source of reintroduction without an imported case</td>
</tr>
<tr>
<td><em>P. vivax</em> preferentially infects reticulocytes (young erythrocytes) in bone marrow</td>
<td>Repeated destruction of young erythrocytes causes chronic anemia Complicated culture of asexual parasites in the laboratory, making it difficult to discover new tools Infections in blood phase often progress with low parasitemia Traditional microcopy and RDTs cannot detect all infections, underestimating prevalence of malaria</td>
</tr>
<tr>
<td><em>P. vivax</em> gametocytes rapidly appear, prior to onset of symptoms</td>
<td>Increased risk of subsequent infections</td>
</tr>
</tbody>
</table>
3. Malaria risk stratification

WHO defines *malaria risk stratification* as “classification of geographical areas or localities according to factors that determine receptivity and vulnerability to malaria transmission” [1] and *malaria stratification* as “classification of geographical areas or localities according to epidemiological, ecological, social and economic determinants for the purpose of guiding malaria interventions” [1].

Stratification is thus understood as a tool to support decision-making and the first step in planning the malaria operation. Stratification helps orient resources and actions to areas with the highest disease burden and guide actions to prevent reestablishment of transmission in areas where transmission had been successfully interrupted. Stratification is a dynamic process that involves periodic analysis of information and helps establish differences in intervention for each stratum.

3.1. Receptivity and vulnerability

Receptivity is understood as the ecosystem's capacity to allow malaria transmission [2]. Vulnerability refers to risk of importation of the parasite [2]. When the receptivity or the risk of importation of the parasite in a zone is zero, there is no risk of reestablishment of transmission.

Receptivity level should be evaluated(mapped) based on entomological surveillance that enables identification of the most receptive areas. The historical information of malaria can be used as a proxy when the entomological information does not exist. Risk of importation of the parasite should be evaluated / mapped based on establishing surveillance that identifies populations at risk of imported cases and areas with higher risk of receiving imported cases. In certain contexts, the risk of transporting the infected mosquito to other areas should also be considered.

Factors affecting receptivity of malaria

Climatic changes (such as variations in rain and temperature patterns) and ecological changes (urbanization and economic development, changes in land use, modification of extensions of agriculture, deforestation, reservoirs, drainage, etc.) can affect distribution and density of *Anopheles* mosquitoes in one way or another.

Factors affecting risk of importation of the parasite in the Region of the Americas

Sociodemographic and socioeconomic changes that involve population movements from endemic zones favors a risk of importation of the parasite. For example, zones at risk of importation of the parasite are those that receive tourism or migrations from endemic zones for work in certain risky activities such as gold mining, farming (rice, chestnuts, banana, palm oil) and the harvesting of jellyfish. Illegal activities
present an additional complication since the population involved is not always easy to identify. In addition to these changes the population's general lack of knowledge about malaria and reluctance to seek health services, as well as health services' inadequacy in detecting and managing malaria.

3.2. Stratification background
All countries of America use or have used the annual parasite index (API) for stratification of areas (high, moderate and low risk)\(^1\) and for standard reporting to WHO. The API analysis and its trends have informed identification of priority areas; for example, areas with higher API or where API remains high despite interventions. With this same focus, since 2013, several Central American countries used API of the last 3 years to stratify (strata 1, 2 or 3)\(^2\) in the framework of the regional initiative *Elimination of Malaria in Mesoamerica and the Island of Hispaniola* (EMMIE). API-based stratification of municipalities was conducted as an intermediate step before stratifying lower (more local) levels (localities and foci), which is where we are now heading.

In the current epidemiology, the municipal API is not so useful in stratification in the Americas for the following reasons:

(i) In countries that have many areas where transmission has been interrupted or where case number is extremely low, the API value offers little guidance for stratification. The API does not help identify malaria-free areas with high transmission potential (receptive and vulnerable), an essential element for preventing reestablishment of transmission.

(ii) In many cases, the absolute number of cases by locality (or health unit) is a much more useful statistic than the API because this local information helps inform the local surveillance strategy as well as the municipal risk.\(^3\) Heterogeneity and focalization of malaria in remote parts of municipalities also make the municipal API less relevant in providing guidance to identify the localities that most contribute to transmission.

3.3. Current context of stratification
Stratification should be determined in terms of (i) intensity of transmission (number of cases); (ii) level of importation risk (importation of parasite); and (iii) level of receptivity [2] universal application throughout entire country. Stratification includes the foci but is not limited to them.

---
\(^1\) High risk: API ≥10, Moderate risk: 10>API≥1, Low risk: API<1. Some countries use other criteria not mentioned here; others use "Very high risk" as 4th level.
\(^2\) Stratum 1: 0 (zero) indigenous cases in last 3 years. Stratum 2: API ≤1 in last 3 years. Stratum 3: API >1 in last 3 years.
\(^3\) The number of cases at localities level, and not API, is the criterion that determines when a case investigation and response is needed for each case detected (strata with 3 or less cases per health unit per week) vs. an action aimed at the identification and analysis of clusters of cases (strata with higher transmission).
The proposed strata are:

- **Stratum 1.** Not receptive.
- **Stratum 2.** Receptive, no indigenous cases, without risk of importation of parasite. Includes eliminated foci, no imported cases, no migration from endemic areas.
- **Stratum 3.** Receptive, no indigenous cases but at risk of importation of the parasite. Includes eliminated foci, foci with imported cases or foci with immigration from endemic areas.
- **Stratum 4.** Receptive, presence of indigenous cases. Includes active foci and residual foci.

In countries with numerous areas with stable transmission (stratum 4), such areas should be stratified in turn according to the level of endemicity (based on the number of cases at the local level).4

Information required for stratification includes:

1. Indigenous malaria cases in the last years by place of infection (at locality level), enabling identification of past and current malarial zones.5 Four years of data enables us to differentiate localities that should be classified as Stratum 4 (active and residual foci) or Stratum 3 (foci eliminated).

2. Information on risk of importation of parasite: imported cases by locality and local knowledge of movement of population from endemic areas. Analysis of population movements from endemic areas and between localities in the area of interest is essential in orienting the local surveillance strategy, which aims at transforming active foci into eliminated foci or consolidating malaria-free areas.

3. Data on receptivity. In many countries, entomological data are very limited. In such situations, a proxy indicator for receptivity can be number of indigenous cases over last 10 years, since localities with malaria transmission are generally the most receptive areas. Equally, ecological zones similar to those where there has been transmission can be considered.

4. List of georeferenced geographic units6 at the level at which stratification will be conducted (municipality, canton, district, locality).

When the exercise is performed at the national level, especially in big countries, often the stratification is first made at the administrative unit level (ADM) 2 (municipality, district). Ideally, stratification at the

---

4 Number of cases per health unit and distribution of cases is what will determine the differences in basic surveillance operations (investigation of cases and reactive case detection) [3. World Health Organization, *Malaria surveillance, monitoring and evaluation: a reference manual*. 2018: Switzerland.]

5 Since most malaria cases in the Americas are due to *P. vivax*, where relapses contribute significantly to the disease burden and there is a large population movement, it might be difficult to identify the place of infection. Relapses do not always occur in the place of transmission. For example, in situations of seasonal work, people may spend a great part of the year in areas of transmission but reside in other areas.

6 The list of georeferenced geographical units can be obtained from country statistical departments if they are not available in the health system.
ADM2 level is the result of a previous stratification exercise on localities or sectors within the municipalities. In a country with many cases and various active-transmission foci, the exercise can begin by identifying and classifying foci that are in stratum 4 (micro-stratification -- section 4) and differentiating those foci that contain the highest endemic levels (number of cases per week) from those with more sporadic transmission. When this exercise has been completed, the areas corresponding to strata 3, 2, and 1 will continue to be identified. In small countries with low levels of transmission, the exercise can be performed directly, classifying the localities in the four strata. Either way, at the most local level, stratification should always be done at the level of localities or clusters of population (except for non-receptive or receptive non-vulnerable areas very homogeneous in terms of low risk) \(^7\).

To classify localities, the analysis should be conducted by local personnel who know the terrain and movement of population, epidemiologists who have access to the databases, the entomologists with the receptivity data and some informatic support for the mapping.

For example, a locality with transmission in the last year corresponds to stratum 4 (that locality would be part of an active focus or the locality alone would constitute an active focus); a locality that had transmission 2 years ago (residual-non active focus) would also qualify as stratum 4; a locality with no cases in more than three years (cleared focus) but considered to be vulnerable due to the arrival of imported cases or movement of population from endemic zones (for example, banana plantations that receive workers from endemic countries) would correspond to stratum 3; a locality with presence of malaria vectors (from entomological data or past malaria data) considered not-vulnerable would correspond to stratum 2; finally, a non-receptive locality (without vectors) according to entomological surveillance or because it does not present conditions for vectors to survive (altitude and temperature) or because it does not have a history as a malarial zone is considered to be stratum 1.

Stratification therefore involves a local exercise based on analysis of the magnitude of endemicity and the condition of risk of the geographic areas. It is a dynamic process that will depend on the quality of the surveillance of cases and the capacity to establish systematic processes for monitoring receptivity and vulnerability. Once the country has been stratified, interventions will be planned based on the strata. For example, if the risk of importation of the parasite is high in a receptive zone, passive surveillance should be assured and active case detection should be considered, as well as the need to protect populations with mosquito nets or indoor residual spraying to prevent reestablishment of transmission. In non-receptive areas with low risk of importation of the parasite, a prompt diagnosis based on passive case detection with case investigation and response should be enough. In the context of active transmission, the population at risk must be protected with bed nets or RRI. The number of cases (cases per week per health unit) determines

\(^7\) Once a locality is classified in a stratum, a comment should be included to justify why that decision was made. Since the stratification should be updated annually, these comments will help to recall the reason for the classification and to update it based on recent changes.
the need and feasibility of conducting individual investigation and response, and therefore determines the
differences in the operation. Table 3, Figure 3, and Table 4 show examples of stratification exercises, with
the maps produced and generic DTI-R interventions merited in function of the strata.

<table>
<thead>
<tr>
<th>Province</th>
<th>Canton</th>
<th>District</th>
<th>Locality</th>
<th>x coordinate</th>
<th>y coordinate</th>
<th>Stratum</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alajuela</td>
<td>San Carlos</td>
<td>Buena Vista</td>
<td>Buenavista</td>
<td>-84.4598</td>
<td>10.276</td>
<td>1</td>
<td>Located 875 m above sea level, not considered malarial area</td>
</tr>
<tr>
<td>Alajuela</td>
<td>Guatuso</td>
<td>San Rafael</td>
<td>Aguas Negras</td>
<td>-84.8379</td>
<td>10.68261</td>
<td>2</td>
<td>Presents favorable conditions to have the vector (below 600m above sea level); however, no recent cases and has migratory flow</td>
</tr>
<tr>
<td>Alajuela</td>
<td>Los Chiles</td>
<td>El Amparo</td>
<td>Alto Los Reyes</td>
<td>-84.6271</td>
<td>10.85105</td>
<td>3</td>
<td>High migratory flow and pineapple crops</td>
</tr>
<tr>
<td>Alajuela</td>
<td>San Carlos</td>
<td>Pocosol</td>
<td>Llano Verde</td>
<td>-84.382</td>
<td>10.8853</td>
<td>4</td>
<td>Reforestation, cattle, migrant population, sleeping area and active focus</td>
</tr>
</tbody>
</table>
Table 4. Generic activities of the diagnosis component of the DTI-R strategy by stratum

<table>
<thead>
<tr>
<th>Stratum 1 (non-receptive)</th>
<th>Stratum 2 (Receptive, not vulnerable)</th>
<th>Stratum 3 (Receptive and vulnerable)</th>
<th>Stratum 4 (Local transmission: active and residual foci)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive case detection with D available in municipal capitals</td>
<td>Passive case detection with D available in municipal capitals</td>
<td>Passive case detection with D available at local levels and in transit / migration zones</td>
<td>Passive case detection with D available at local levels and in accordance transmission dynamics</td>
</tr>
<tr>
<td>IEC to stimulate demand</td>
<td>IEC to stimulate demand</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal training of health workers</td>
<td>Personal training of health workers</td>
<td>Personal training of health workers</td>
<td>Personal training for health workers</td>
</tr>
<tr>
<td>Proactive case detection (mobile and migrant population). Fixed programmed actions (for example, once a month) or separate actions according to changes in vulnerability</td>
<td></td>
<td></td>
<td>Proactive case detection Periodicity: for example, 1-2/month</td>
</tr>
<tr>
<td>Weekly reading of slides acceptable if <em>P. vivax</em> in context of isolated communities without RDT</td>
<td>Weekly reading of slides acceptable if <em>P. vivax</em> in context of isolated communities without RDT</td>
<td>Weekly reading of slides acceptable if <em>P. vivax</em> in context of isolated communities without RDT</td>
<td>Reading of slides in less than 1 week</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Geo-referencing of cases. mapping of important characteristics of focus</td>
</tr>
</tbody>
</table>

Legend: D=diagnosis; IEC= information, education, communication.
3.4. Prioritization

Prioritization is an important element in the planning of anti-malarial activities and forms part of the exercise of stratification. It means selecting populations or geographical areas (municipalities, foci) that need more attention and effort for cost-effective management of resources and to meet set targets. Having classified the geographical units in strata, within a determined stratum it is necessary to prioritize certain units according to epidemiological importance.

There are various criteria to consider in prioritization: the malaria burden, the species of parasite, certain geographical contexts that involve a greater risk to public health, or areas of greater transmission potential. National malaria programs should consider the following factors in their prioritization:

1. Malaria transmission is concentrated in a limited number of municipalities, and within those municipalities, in turn, the disease burden is concentrated in foci or clusters of localities. Often, cases of malaria from these municipalities and foci get exported to areas with active transmission or malaria-free areas where they can reintroduce transmission. Municipalities that concentrate the highest disease burden in the countries should receive greater attention, with technical capacity, resources and the necessary political attention. Prioritization of the ADM-2 according to number of cases in the last year, or to average number of cases in recent years (depending on inter-annual variation), should be the first step in prioritization.

2. During a stratification exercise, use of a Pareto diagram\(^8\) with accumulated percentage of cases in the country or a determined region can be useful to identify the localities, foci or municipalities with higher disease burden. This exercise can help prioritize the stratum-4 areas with the highest disease burden. In the municipality, it is necessary to prioritize geographical units that have higher disease burden.

3. Elimination of malaria by *P. falciparum* is a priority due to the threat of appearance of resistance to treatment, more deaths compared with other *Plasmodium* species, in addition to being more feasible to elimination than *P. vivax* due to the later appearance of gametocytes and absence of relapses (see Table 2). Elimination of *P. falciparum* can thus be an intermediate goal in the elimination of malaria at the national level. Ensuring areas free of malaria by *P. falciparum* in many contexts can be another key element in prioritizing efforts and resources. The proportion of malaria by *P. falciparum* has been used by many countries in models that weigh different variables in the exercise of prioritization.

---

\(^8\) Pareto diagram: a graphic to organize data in bars in descending order to illustrate the Pareto Principle: that are many insignificant problems and only a few very important ones.
4. In low-transmission contexts, the greater prevalence of malaria by *P. falciparum* over *P. vivax* is in many cases a sign of deficiency in provision of diagnosis and treatment services. Identifying these areas where organized action can have high impact can be a criterion of prioritization.

5. The existence of urban transmission of malaria has also been used by the countries as another criterion for prioritized actions. In general, urban active foci have higher disease burden. Urban transmission defines a scenario where it should be easier to shorten the times between access to diagnosis and treatment, implement measures such as supervision of treatment for *P. vivax* and vector control actions (including larval control when indicated). The risk of exportation of malaria to rural areas is also an aspect to consider in favor of prioritization of urban active foci.

6. Preventing reestablishment of transmission, in many contexts, can also be an important element in prioritizing actions. In countries with active transmission, maintaining interruption of transmission in historically malarious areas can be as important as reducing transmission in active foci. The balance for management of priorities between municipalities with higher burden and municipalities at risk of reintroduction of malaria is dictated by each situation. The risk of importation of malaria from municipalities with transmission is always an element to underscore the importance of paying close attention to areas that continue to generate cases of malaria within the country.

7. Transmission-free areas (strata 1–3) in countries with active transmission, can be also prioritized according to risk of reestablishment of transmission based on historic behavior, analysis of receptivity and risk of importation of the parasite.

8. Even though the API in the current context of elimination, does not constitute the main element of stratification, it can be a useful variable to use, along with the Pareto diagram, for prioritizing localities within the stratum with active transmission (stratum 4). In this context, the API at the level of locality or focus can be useful to identify localities that, even if they are not top priority due to their disease burden, they are important due to the malaria risk for the population. We emphasize, however, the use of number of cases a criterion to more effectively impact disease burden.

4. **Micro-stratification and micro-planning**

Micro-stratification is a more local (micro) epidemiological analysis conducted in stratum 4 for identifying foci or micro-areas.

For the purpose of this manual, a micro-area is a set of localities or foci of malaria that are near each other, share similar eco-epidemiological conditions and malaria transmission dynamics. A micro-area can include several foci related to each other due to population mobility (for example, three separate banana plantations
where workers often move from one plantation to the other) or it can be a focus (a gold mine, for example, where transmission takes place, and another locality where the miners periodically rest). Certain countries use now the term focus or micro-area interchangeably. To simplify, in this manual micro-area are equated with foci. It should be clear, however, that the concepts are different. *Focus* is based on vector transmission. *Micro-area* considers epidemiological, social, population and operational criteria. It is based on connections between localities, movements of people, and social relations that determine whether the localities share the transmission dynamic and geographical access. In micro-stratification we consider the epidemiological concept of *focus*, but the concept of *micro-area* is more useful especially in situations where there are interconnected and interdependent foci that must be taken into account to plan an operation based on improving access to diagnosis and treatment.

Once the micro-stratification is completed and the micro-area has been characterised in terms of detection and treatment network, the response will be planned. Malaria elimination in the foci has two steps: micro-stratification and micro-planning (see Table 5 below).

**Table 5. Components for elimination of transmission in foci**

<table>
<thead>
<tr>
<th>Component</th>
<th>Elements</th>
<th>Objective</th>
</tr>
</thead>
</table>
| 1. Micro-stratification of malaria in municipality | • Identification of foci  
• Analysis of transmission dynamics in the foci  
• Characterization of health services (gaps, barriers, needs)  
• Determine ”hypothesis” on transmission, maintenance of transmission, social dynamics determining it and from there key actions to impact it | Generate inputs needed to organize diagnosis-treatment-investigation actions (micro-networks) and the response |
• Direct, orient, stimulate demand.  
• Coordination of the different stakeholders in the micro-network  
• Optimize active detection  
• Optimize vector control measures of adult mosquitos.  
• Dynamic exercise with weekly cycles of analysis and reorganization of actions.  
• Local supervisory model. | Implement local surveillance and treatment model that can successfully diagnose cases in <24 hours, treat same day as diagnosis satisfactorily |

4.1. Micro-stratification: identification and classification of malarial foci

The micro-stratification involves an exercise of epidemiological analysis at a local level and a characterization in terms of detection, diagnosis, investigation and response (Figure 5 and 6). Micro-stratification has five steps:

1. Knowledge of distribution of cases in the area, identifying localities with transmission and clusters of localities with transmission.
2. Identification of factors in the population that are affecting or can affect transmission: connections between communities, distances and transit routes, and other factors that affect transmission (for example, the arrival of imported cases in a locality, or if it is a close-knit community with ongoing
transmission; if the transmission is due to an economic activity, or if it is maintained due to relapses of *P. vivax*).

3. Group the different localities in micro-areas, according to factors deemed important in transmission: (i) localities that are close together in the same vector radius (<3 km); (ii) share transmission dynamics; (iii) there is a high level of contact between the populations; or (iv) they share the same health services network.

4. Characterize micro-areas in terms of organization of DTI-R. That is, analyze the conditions of the network: How many microscopy posts do they have? Are they appropriately located? Do they have rapid diagnostic tests? Where are the gaps? Are there delays between taking slide samples and examining them? Or delays for starting treatment? What are the causes of these gaps? What is the vector control coverage? etc.

5. Establish a first hypothesis of transmission, the perpetuation of transmission, the social dynamics that determines it, and thus the key actions to impact it.

![Figure 5. Demarcation of foci and micro-areas](image-url)
4.1.1. Micro-stratification: guiding principles

1. Start with the available information (although it might not be of optimal quality), without creating more data or expecting it to be in a standardized format. Use of existing information, making the best effort to analyze it, is an essential component of field epidemiology. Also, it shows health personnel the importance of data they have already collected and promotes the culture of data analysis and surveillance for action. The micro-stratification process depends on better and more specific data in order to understand transmission dynamics and organize the response or micro-plan. Obtaining more and better data should be a continuation of the initial micro-stratification exercise.

2. A locality or community is the minimum level of analysis. All data should be aggregated and analyzed at this level. When the number of cases is low, the cases should be identified on the map.

3. Absolute certainty is not always possible. Differentiation of transmission dynamics, especially in highly endemic zones, can be difficult. It is necessary to use the best evidence available and refine, confirm and adjust (if necessary) the analysis during visits to the locality.

4. There may be doubts in establishing the limit of a micro-area or in deciding in which micro-area a locality should be place. In these situations, one should think if the response or micro-plans will differ. If there are no differences, it is best to consider it a single micro-area instead of two.

To facilitate the organization of the health service provision and surveillance processes, and prevent fragmenting the response, it can be useful, in addition to epidemiological elements, that the micro-area
coincides with the area in charge of a local health team. When a malaria focus or micro-area corresponds to different health areas or municipalities, coordination between them will be essential to ensure a good foci characterization and adequate response.

4.1.2. Information recommended to conduct micro-stratification and micro-planning

1. Notification records of confirmed cases, with:
   a) Minimum information required: age, sex, place of residence, date of sample taken and type of species.
   b) Additional information desirable: probable location of infection, date of onset of symptoms, locality where sample was taken, date of diagnostic results, type of surveillance.

2. Number of cases by species and by epidemiological week or month in municipalities/localities with greater transmission.

3. Number of suspected cases by type of surveillance in each municipality and locality.

4. Map localities in the municipality.

5. Map of diagnostic posts (microscopy and RDT).

6. Map of accessibility of the localities to closest diagnostic posts.

7. Information on use of health services.

8. Information on distribution, vector dynamics/behavior in the municipality/locality (information of neighboring municipalities can also be useful).

9. Information on vector control activities in the last three years and their coverage in the municipality/locality.

10. Other contextual information on factors related to transmission in the zone (land use/mining, legal and illegal deforestation, illegal border crossings, presence of ethnic groups, reserves, etc.).

4.1.3. Methodology

Information recommended for micro-stratification is obtained through: (i) review of data in the regional health departments and health units; (ii) interviews with health workers of health units, community health workers, patients and neighbors in the community; and (iii) visits to main localities to understand key variables related to transmission dynamics, barriers in access to services, living conditions, and population dynamics.

The first four steps of micro-stratification, summarized in Table 6, are activities that normally take place in the health departments in the area where the planning of the malaria operation is taking place (region, municipality, district or national level in case of small countries). Step 5 takes place in the locality itself and is summarized in Table 7.
<table>
<thead>
<tr>
<th>Component</th>
<th>Information</th>
<th>Activities</th>
</tr>
</thead>
</table>
| Analysis of epidemiology of malaria and transmission dynamics in selected foci | Analyze epidemiological situation | • Malaria cases by localities.  
• Distribution of transmission.  
• Localities with continuous transmission.  
• Localities with sporadic transmission.  
• Key localities in maintaining the spread of transmission. | • Review cases register  
• Analyze maps and figures  
• Interview health team in charge  
• Review all available entomological information |
| Transmission dynamics | • Malaria transmission in localities.  
• Connection of transmission between localities.  
• Connection of transmission with another foci.  
• Connection of transmission with imported malaria.  
• Relation with occupational activities vs domestic transmission.  
• Economic activities and other aspects of the social and cultural dynamic related to transmission. | |
| Identify foci | • Identification of foci, localities that conform a focus.  
• Analysis of alternative for demarcation of foci. | |
| Transmission hypothesis | Formulation of hypothesis on dynamics of transmission | |
| Analysis of DTI-R | Diagnosis | • Location of microscopy posts.  
• Location of RDTs posts.  
• Number of microscopists and community health workers.  
• Access to localities to diagnostic posts.  
• Diagnostic process.  
• Community health workers, distribution, roles, supervisory strategy, access to localities.  
• Cultural aspects that can limit opportunity of diagnosis  
• Time interval between onset of symptoms and diagnosis. | • Interviews health team.  
• Analysis of maps with locations of health posts  
• Analysis of distances and routes to health posts  
• Review laboratory registers |
| Treatment | • Time between diagnosis and onset of treatment.  
• Availability of drugs.  
• Conditions of prescribing and dispensing drugs\(^9\).  
• Measures to ensure adherence.  
• Management of inventory consumables.  
• Cultural factors that can limit prompt high-quality treatment. | • Interview health team  
• Review treatment registers if possible  
• Review available drugs  
• Review registers of inventories |
| Investigation and response | • Reactive case detection: coverage, promptness.  
• Coverage of vector control interventions.  
• Cultural factors or other factors that limit access/use of vector control interventions. | • Interview health team  
• Review registers if possible |
| Expected result | • **Demarcation of malaria foci (or micro-areas)**  
• Identification of cultural aspects.  
• Preliminary transmission hypothesis to guide improvements in DTI-R strategy.  
• Preliminary identification of gaps in DTI-R strategy.  
• Preliminary identification of requirements to strengthen network (location of diagnostic posts, improvements in processes and routes for case detection, diagnosis, treatment, investigation and response). | |

\(^9\) It refers to the knowledge of treatment protocols, guidance to patients when prescribing medications-for example, the importance of adherence to primaquine-, calculation of doses by weight, delivery of medicines in appropriate containers, etc.)
1. First step is to analyze epidemiological situation in the municipality\(^\text{10}\). Once the area has been identified and explored (for example, having a map with the localities of the municipality) it is necessary to analyze trends in malaria transmission and its seasonal and spatial variations, locating the cases on the maps with localities. Different sources of available information will be used:
   a) Number of cases by locality (minimum 1 year of data but preferably last 3–4 years);
   b) Number of cases by species and by epidemiological week or month;
   c) Mapping of cases by locality.

Data analysis should provide information on:
   a) Affected localities;
   b) Distribution of transmission;
   c) Localities with continuous transmission, with sporadic transmission, and those key in dissemination of malaria identified to target efforts to interrupt transmission.

2. Second step is to begin to identify possible transmission links between localities (identify transmission dynamics). Different sources of available information will be used:
   a) Nominal database or case investigation records to know, for example, place of infection, the profile of cases (age, sex, etnia) and possible activities related to transmission in the different localities;
   b) Map of roads and communication routes between localities and diagnostic posts;
   c) Interviews with health team that knows the area, mobility of population and possibly the population's risky activities;
   d) Entomological data that provides guidance on the existence of vectors, their behavior, breeding sites and resistance to insecticides.

Analysis of these data should provide us with information on:
   a) Malaria transmission in the localities;
   b) Relation of transmission between the localities;
   c) Role of imported malaria in transmission;
   d) Transmission in occupational activities vs. domestic activities;
   e) Cultural and social factors that affect transmission.

3. The third step is the demarcation of micro-areas (clusters of localities) in the municipality based on transmission dynamics. The analysis conducted in points 1 and 2 will be used. The result of the exercise is that each municipality will have a map with its micro-areas identified.

\(^\text{10}\) It is operative to start the analysis at the municipality level. However, special attention must be paid to those foci that are on the boundary between municipalities. It is necessary to identify them and work in coordination with the neighboring municipalities to respond appropriately and interrupt the transmission.
4. The fourth step is to characterize micro-areas based on the diagnostic network's capacity and the actions to detect, diagnose, treat, investigate and respond. Different sources of available information will be used:
   a) Map of RDT and microscopy diagnostic posts (health units and community health workers);
   b) Number of suspected cases by type of surveillance;
   c) Interviews with health workers in health centers, health units and the community;
   d) Assessment of local capacity (municipal/canton) to diagnose, treat, investigate, and respond to detected cases.

This analysis will provide information on:
   a) Surveillance efforts by locality and by type of surveillance: number of suspected cases, detection efforts based on malaria risk, malaria suspicion from health personnel, activity of community health workers, behavior of population (including marginal groups) in health seeking behavior, etc.
   b) Access to diagnosis and treatment (in terms of geography, finance, culture and management of stocks).
   c) Delays in diagnosis / treatment / investigation / response and the causes.
   d) High-quality diagnosis, treatment, investigation and response (quality assurance, management of drugs, prescriptions, adherence, organization of BRC, acceptance of mosquito nets or indoor residual spraying).

5. The fifth step is to confirm and refine our transmission hypothesis and diagnosis of gaps in DTI-R
Once the micro-areas have been defined, visit them to continue refining the local-level analysis, prioritizing higher-transmission localities (Table 7 and Figure 7). The goal is to identify other factors to optimize processes and reduce delays between case detection, treatment, investigation, and response. To refine our hypothesis, different information sources will be used:
   a) Observations of the community to know housing type, living conditions and main points identified as larval habitats.
   b) Interviews with malaria patients or families of cases and other community members to identify risk factors and population health seeking behaviour.
   c) Interviews with community health workers to know their work dynamics and difficulties encountered.
   d) Interviews with personnel from health units in the micro-area to know constraints in diagnosis and treatment.

Analysis of information obtained should refine our previous information on:
e) The epidemiological situation (transmission in the localities, transmission links between localities, role of imported in transmission, transmission in occupational activities vs. domestic activities, cultural and social aspects that affect transmission).

f) Confirm the hypothesis of transmission in the micro-area.

g) Resolve the gaps identified in DTI-R.

Table 7. Identification and characterization of foci at the level of the locality

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Information</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis of malaria epidemiology and transmission dynamics in the locality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Epidemiological situation</td>
<td>• Distribution of cases in the locality&lt;br&gt;• Sectors with clusters of cases (&quot;hot spots&quot;)&lt;br&gt;• Key sectors in the locality in transmission dynamics</td>
<td>• Visit to sectors with higher incidence of cases (&quot;hot spots&quot;).&lt;br&gt;• Interview with cases or family members in sectors with higher number of cases (origin of cases, access to diagnosis).&lt;br&gt;• Interview with community agents (review of registers, tools, dynamic of transmission, times between onset of symptoms– diagnosis – treatment – investigation. Reactive case detection, active case detection (criteria).&lt;br&gt;• Visit to main points identified as breeding sites of Anopheles mosquitos.</td>
</tr>
<tr>
<td>2) Transmission dynamics</td>
<td>• Connection of transmission between localities.&lt;br&gt;• Connection of transmission with imported malaria.&lt;br&gt;• Connection with occupational activities vs domestic transmission.&lt;br&gt;• Connection of cases with breeding sites.</td>
<td></td>
</tr>
<tr>
<td>DTI-R</td>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Investigation and response</td>
<td></td>
</tr>
<tr>
<td>Expected outcomes</td>
<td></td>
<td>• Malaria transmission hypothesis in focus or micro-area.&lt;br&gt;• Gaps identified in detection / diagnosis / treatment / investigation processes.&lt;br&gt;• Proposals to improve health agents' performance.&lt;br&gt;• Proposals to optimize active case detection.&lt;br&gt;• Proposal for response intervention.&lt;br&gt;• Key cultural factors identified to be considered in DTI-R implementation in the communities</td>
</tr>
</tbody>
</table>

4.2. Micro-planning
Once the micro-areas are defined and characterized, a micro-planning or response plan will be drafted to reduce or eliminate transmission in each focus. A systematic detection-treatment-detection action, and the
vector control activities, should reduce the active foci until transmission is interrupted. The following steps are considered:

1. **Design the diagnosis-treatment-investigation-response network.** The diagnosis-treatment-investigation-response network shall be planned based on transmission dynamics and the gaps identified during the characterization of the micro-areas. Places where diagnostic services are needed for passive and active case detection should be identified and implemented: health posts with microscopy or RDT and community health workers with RDT (or trained staff to take blood smears when there are no RDT). The routes and processes between the blood smear taken and the nearest laboratory points (to examine the samples) should be well defined. The criteria for planning where to locate a diagnostic post is to ensure prompt diagnosis according to the time intervals established in all the localities.

2. **Implement diagnosis-treatment-investigation-response process and monitor results.** The parasitological diagnosis ideally should be conducted within the first 2 days from onset of symptoms. Treatment should commence within 24 hours of diagnosis; case investigation with reactive case detection in the first 7 days from onset of symptoms or within the first 3 days after diagnosis of index case. The follow-up of cases (when the number is low) should be done for 28 days to ensure adherence to treatment and to detect resistance. The vector control strategy should be clearly defined to help interrupt transmission and prevent reintroduction of cases. Supporting elements (training, management of drugs and inputs for diagnosis, quality assurance in diagnosis, information flows and analysis) should be guaranteed in order to enable the adequate implementation of the processes.

5. **Management of malaria elimination based on transmission in foci**

5.1. **Organization of DTI-R actions in the micro-areas**

Organization of DTI-R actions in micro-areas requires that each stakeholder's role and functions are clearly defined with good coordination between them. This is the starting point. In most American countries, malaria surveillance and control actions involve teams from malaria or Vector Borne Disease (VBD) programs, epidemiological surveillance departments and health services. The first step to ensuring a good response is to define the institutional roles of each.

a) **Organization of passive case detection**

Passive case detection has to be properly implemented in all strata in the country. Regardless of whether personnel from the malaria/vectors program are responsible for diagnosing malaria cases, health services should support and take part in passive case detection. The first step for effective passive case detection is to have a clear definition of a suspected case. The definition can vary based on transmission and on the health personnel involved (community health worker, nurse, physician, etc.) (see Table 8). Health personnel
should suspect malaria and diagnostic services should be available to the entire population. Health workers should know where diagnostic services are available and guide patients there without delay. In other words, the patients flow should be well defined and understood by health personnel. Once transmission is interrupted, the suspicion of malaria decreases rapidly among health personnel. For this reason, ongoing training is necessary: to interrupt transmission, to avoid its reestablishment (in countries or areas where it has been eliminated) and prevent complications or death from imported cases.

Table 8. Examples of definitions of suspected cases in different contexts

<table>
<thead>
<tr>
<th>CONTEXT</th>
<th>DEFINITION OF SUSPECTED CASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>High and moderate transmission</td>
<td>1. Any case of fever (current or recent)</td>
</tr>
<tr>
<td>(more than 3 cases per health unit per week)</td>
<td>2. Anemia, headache, splenomegaly or general malaise with no other cause established</td>
</tr>
<tr>
<td>Low transmission</td>
<td>1. Fever without cause established</td>
</tr>
<tr>
<td>(less than 3 cases per health unit per week)</td>
<td></td>
</tr>
<tr>
<td>Local transmission interrupted</td>
<td>1. Fever or history of fever, etiology undefined, with presence of at least one of the following epidemiological conditions:</td>
</tr>
<tr>
<td>(zero indigenous cases)</td>
<td>• Individual has traveled in last 1 year to a region with active malaria transmission (extend to 3 years in areas at risk for P. vivax);</td>
</tr>
<tr>
<td></td>
<td>• Personal history of having been infected with malaria in the last 3 years;</td>
</tr>
<tr>
<td></td>
<td>• Reside in or has visited receptive areas in a country.</td>
</tr>
<tr>
<td></td>
<td>2. Individual with anemia, hepatomegaly and/or splenomegaly of unknown cause (with or without fever) and has traveled to an area with malaria transmission.</td>
</tr>
<tr>
<td></td>
<td>3. Recipients of blood transfusion or transplant presenting fever of unknown etiology during the 3 months following transfusion or surgery.</td>
</tr>
<tr>
<td>Community health worker in any context</td>
<td>1. Any case of fever (current or recent)</td>
</tr>
<tr>
<td>any epidemiological context</td>
<td>2. Headache, general malaise.</td>
</tr>
</tbody>
</table>

b) Organize diagnostic services
To ensure prompt diagnosis, the diagnostic points need to be planned based on the different strata and transmission dynamics in the foci. For example, in areas where transmission has been eliminated and there is low receptivity and no risk for importation of the parasite, the diagnostic services in municipal capitals or districts may be enough. In areas with transmission, however, diagnostic services should be available in the communities in accordance with local transmission dynamics. At the local level, the processes for the diagnostic quality assurance established at the national level (direct control, indirect control and supervision) must be implemented.
Malaria programs can opt to have only microscopy diagnosis or also rapid diagnostic tests (RDT) in more remote areas or outside the work hours of microscopists (at night or on weekends). The flow for taking
samples, collecting the slides, examining them, and communicating the results must be well defined to avoid delays in diagnosis.

c) Actions to address and promote demand

In addition to improving diagnostic services, it is important to promote demand for health services. In situations of high incidence of cases or absence of cases, stimulating demand for early diagnosis should be a core element of the intervention. Individuals with malaria symptoms who do not seek care are the second step in the gaps cascade of the parasite’s human reservoir treatment [24] and should receive attention through improvements in services provision and the fostering of demand. Information, education and communication activities on malaria and on steps to follow in case of malaria symptoms when living in an endemic area or in the case of traveling to an endemic area must always be included in malaria programs in all strata in the country. This could prevent self-medication and delays in diagnosis that could otherwise lead to complications for the patient and to maintaining or introducing transmission in a specific area.

Inducing demand is not generally addressed as a programmatic activity. It is often limited to generic communication messages that take part of a communication package with several messages on other aspects of malaria. These actions are generally not designed to improve demand. Actions to induce demand should be completely attuned to the efforts to resolve the obstacles in access to diagnostic services. They should be specific messages about where to go for local health care services, with solutions to the obstacles identified.

d) Organization of treatment and follow-up of cases

In the same way that it is necessary to define where to locate a diagnosis according to the different strata and the dynamics of transmission in the foci, the same is true for treatment.

Where there are diagnostic services, treatment services should be available as well, particularly in public health facilities. Depending on the strata, a decision must be made on where and how much treatment should be placed and the quantity for treating simple and complicated malaria cases.

Direct observed treatment and follow up of cases should be conducted according to the context. In a municipality with few cases and where efforts for supervised treatment do not affect efforts for case detection, all cases (100%) should receive direct observed treatment. In a different setting with many cases, other ways to ensure treatment adherence should be explored (such as partial supervision or telephone use). Follow up of cases is important to ensure the infection is cured. At the very least, a blood smear should be collected in all malaria cases when treatment is completed and on day 28 or 42 (depending on the treatment

11 Examples of possible messages: "Free malaria tests available from 9am–3pm daily at A, B, C health centers;" "Community health workers have free malaria tests in your community 24-7, so don’t let your work schedule stop you -- get treated and cured;!” "Feeling punk? Have a fever? Come get your free malaria test at any health post."
combination used). In countries with few cases, since it will be difficult to conduct therapeutic efficacy studies, WHO recommends follow-up of cases on day 0, 3, 7, 14, 21, 28, 35, and 42 (and once a month for three months in cases of *P. vivax* or *P. ovale*, and even up to one year depending on the context) so that therapeutic surveillance is integrated into routine surveillance systems (besides being a component of case management to ensure the cure). If early or late therapeutic failures or late parasitological failure, the use of second-line drug treatment is recommended. WHO recommends changing first-line treatment protocols when therapeutic failures exceed 10% in in vivo studies [3].

e) Organize case and foci investigation

Countries should determine who is responsible for conducting case and foci investigation, including reactive case detection (RACD).

Case investigation should begin in the first three days after diagnosis to help plan the response. The local level should be able to conduct the investigation using a standard investigation form, even if higher levels review and confirm the investigation and its classification, especially in elimination phases. Records of case investigations are essential in the certification process to declare a country malaria-free.

Case investigation will be conducted in all scenarios. In a scenario 4 with significant transmission, it will start and finish at the moment of detection (i.e., in the health unit or in the community if found by active detection), attempting only to analyze the origin of transmission and the obstacles to accessing diagnosis. In this context, the quality of interrogation with the collection of key information that helps identify the place of residence and the origin of infection is essential. Weekly analysis of data can lead to the identification of clusters of cases by place of residence or possible place of infection that should trigger an investigation in the community with reactive case detection. The objective is to identify new cases of fever, encourage demand for care, and identify gaps in passive case detection. These organized and systematic actions to identify clusters of cases can be an important element for change in the current operations in areas with active transmission. When the number of cases decreases (three or fewer cases per health unit per week), it is more feasible to conduct visits to the community for a more detailed case investigation and at the same time to conduct reactive case detection around each case. Case investigation will start at the moment of detection and will finish in the community in order to understand the dynamics of transmission. Countries close to elimination need an expert committee to review all investigation forms to officially confirm the classification of each case. This will give the certification team more confidence in analyzing the progress toward elimination.

Foci investigation is frequently conducted at the same time as case investigation in new active foci. The local epidemiologist, malaria technicians and (ideally) an entomologist are responsible for conducting the foci investigation. The main purpose is to determine whether vectoral transmission has taken place. The
foci investigation includes the identification of affected localities, their boundaries, the population at risk, the vectors present, the larval habitats, and the risk factors contributing to transmission. When a case appears in a focus that has already been investigated and classified, another investigation should not be conducted; the focus' status will be updated periodically updated (every 6 months, for example). In addition, when an outbreak occurs in a known active focus or when a different parasite species is detected, it is necessary to update the focus investigation to detect new factors that are determining the transmission.

f) Organization of active detection

Passive, proactive and reactive case detection are defined in detail in Annex 1.

Proactive case detection is basically directed at special and mobile populations who do not seek care. This detection (generally for individuals with fever) should be routinely planned in scenario 4, i.e., areas with active or residual foci, and in scenario 3, where there are vulnerable and receptive areas.

Reactive case detection forms part of the response to a case or cluster of cases. It involves additional case detection once an index case has been detected, due to the tendency for more cases to appear near a confirmed case. In addition to detecting more cases and thus playing a part in reducing the reservoir, reactive cased detection can help educate the population about the importance of seeking care when symptoms appear (induce demand) and using mosquito nets, and verify that the population has mosquito nets or that their houses have been sprayed. Reactive case detection is considered during the foci investigation to identify the at-risk population and extension of transmission.

The organization of reactive case detection will vary according to the burden of disease and receptivity. The recognition of the area around a case will help to identify the distribution and proximity of the houses, if there are vectors present and their possible breeding sites. This recognition should guide entomological investigations. If vectors are found, the investigation team must delimit the area with the risk of continuing the transmission. This delimited area determines the area where to apply vector control and reactive detection. Annex 2 presents several examples that countries have used to guide this search based on the scenario and burden of disease.

g) Weekly routine analysis and reorganization of operation

In the context of the Americas, routine data analysis should be conducted weekly at the local level to early detect changes in transmission and to respond appropriately (see Table 9). If both, malaria personnel and epidemiologists are available, they should jointly update the malaria situation at least once a month. Part of the appropriate response is informing health personnel in the micro-area (health units’ staff and community health workers) on the results of these analyses to ensure the necessary alerts. Routine analysis should include:

- Analysis of suspected cases by parasite species, passive and active case detection, locality, and diagnostic post. Such analysis will determine if proper surveillance is maintained and by whom
(malaria team in active case detections or health services in passive case detection) in order to make the appropriate modifications to improve the operation if necessary.

- Analysis of the slide positivity rate by type of detection (active, passive, reactive) will also indicate the quality of our surveillance and whether it should be intensified or not.
- Analysis of confirmed cases by place of residence and diagnosis. This analysis will allow to identify localities with cases, detect epidemics in time, and verify if our actions are producing results in terms of reducing the number of cases. This analysis should conclude with a more detailed study of the time intervals in diagnosis and response.
- Analysis of the time intervals in diagnosis and response. A routine analysis of the intervals (between onset of symptom and the diagnostic test, between the diagnostic test and its results, between the results and treatment, between the result and the reactive case detection) can help to identify weaknesses in the health system and to subsequently reorganize the operation to improve (shorten) these intervals.
- Follow-up of patients after treatment is critical to ensure that cases are cured and to issue alerts about problems related to the effectiveness of the treatment.

Table 9. Analysis of information at the sector level to improve detection and diagnosis

<table>
<thead>
<tr>
<th>Information</th>
<th>Findings</th>
<th>Decisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of new cases by place of residence, probable place of infection and place of diagnosis.</td>
<td>Cluster of cases and hot spots identified</td>
<td>Improve health seeking behavior from individuals with fever.</td>
</tr>
<tr>
<td>Number of individuals tested and positivity by neighborhood and by diagnostic point (microscopy or RDT) within the sector.</td>
<td>Low number of individuals with fever seeking health care (to health unit, community health workers, etc)</td>
<td>Relocate microscopy or RDT posts. RCD actions.</td>
</tr>
<tr>
<td>Number tested and positivity according to active vs. passive case detection.</td>
<td>High slide positivity rate in passive case detection</td>
<td>Communication to foster demand by individuals with fever.</td>
</tr>
<tr>
<td>Cases per species (detection of <em>P. falciparum</em> cases in situations with zero transmission).</td>
<td>Low number of cases examined through RCD with respect to new cases</td>
<td>Improve health seeking behavior from individuals with fever. ACD actions.</td>
</tr>
<tr>
<td>Parasitological examination follow-up with patients.</td>
<td>New cases in areas with surveillance gaps</td>
<td>Intensify RCD</td>
</tr>
<tr>
<td>Identification of clusters of cases or positive households</td>
<td><em>P. falciparum</em> cases after weeks without cases</td>
<td>ACD actions Reactivate PCD</td>
</tr>
<tr>
<td>Identification of clusters of cases or positive households</td>
<td>Therapeutic failures</td>
<td>RCD actions intensified</td>
</tr>
<tr>
<td>Identification of clusters of cases or positive households</td>
<td>Detection of pregnant women with malaria</td>
<td>Use of second-line treatment Molecular studies on resistance to antimalaria drugs.</td>
</tr>
</tbody>
</table>

Key: ACD= active case detection; PCD= passive case detection; RCD=reactive case detection; RDT= rapid diagnostic tests.
h) Local supervision

The local DTI-R supervision process should be well organized and systematized taking into consideration the different levels. The main supervisory activities include:

- Supervision of community health workers on their passive and active case detection activities, RDT use, the quality of the blood smear and its shipping to the laboratory. Community health workers, who play a critical role in increasing access to diagnosis and treatment, require additional efforts to ensure continuous supervision due to their situation as volunteers in remote areas. Limited transportation can hamper this supervision so health personnel will have to find creative solutions and coordinate with other programs to conduct supervision;

- Supervision of community health workers in observed treatment, patient follow-up, and outreach to the population on acceptance/use of mosquito nets and IRS;

- Supervision of health personnel in health facilities, which are key to ensure adequate passive case detection, to understand the degree of suspicion of malaria and the application of fever algorithms which must consider malaria as the differential diagnosis;

- Supervision of laboratory personnel to ensure that their competences remain adequate and there is proper implementation of the established processes for preparation of blood smears, staining, examining, and the shipping of slides for indirect and direct quality control;

- Supervision of different health agents in management of antimalarial drugs and other consumables such as RDTs; and

- Supervision of all health agents in information management.

i) Vector control activities

Vector control activities aim at interrupting transmission and preventing reestablishment. Among these activities, a distinction can be drawn between routine and reactive operations triggered by detection of a case or a cluster of cases in an area with low or zero transmission. These actions mainly refer to mass distribution of long-lasting insecticide-treated mosquito nets (LLIN) or indoor residual spraying (IRS).

The entire population living in active and residual foci (strata 4) should be routinely protected with LLIN or IRS (planned operations) based on the existence of local conditions favorable for their success. The decision whether to maintain vector control in strata 3 (receptive and with risk of importation) will depend on the degree of receptivity and vulnerability. For example, in a zone that is very receptive (due to the presence of a very competent vector such as *Anopheles darlingi*) and highly vulnerable (importation of parasites from endemic regions), coverage should be maintained in targeted and selective areas to optimize use of available resources. Strata 1 and 2 do not require use of vector control.

With regards to investigation and response activities to a new case, if the case occurs in an already-identified active or residual focus, the population should already be protected with vector control activities. In this
context, reactive case detection will provide a good opportunity to verify the last time the house was sprayed or whether mosquito nets are being used. If the case appears in a receptive area not protected by LLIN or IRS, the household where the malaria patient resides, and the surrounding area should be sprayed or protected with mosquito nets as part of the response in the first 7 days after diagnosis. As already mentioned, the recognition of the area around a case will help to identify the distribution of houses and breeding sites and will therefore guide entomological investigations to determine if necessary and where to apply vector control and reactive case detection.

Table 10 summarizes different treatment, investigation and response interventions for implementation according to the scenario.

Table 10. Generic activities of components for treatment, investigation and response of DTI-R according to strata

<table>
<thead>
<tr>
<th>Scenario 1 (Non-receptive)</th>
<th>Scenario 2 (Receptive, not vulnerable)</th>
<th>Scenario 3 (Receptive and vulnerable)</th>
<th>Scenario 4 (Local transmission: active and residual foci)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment available in municipal capitals</td>
<td>Treatment available in municipal capitals</td>
<td>Treatment available at local levels and in areas with transit / migration</td>
<td>Treatment available at local levels</td>
</tr>
<tr>
<td>Early treatment (treatment starts within 24 hours of diagnosis)</td>
<td>Early treatment (starts within 24 hours of diagnosis)</td>
<td>Early treatment (starts within 24 hours of diagnosis)</td>
<td>Early treatment (in first 48-72 hrs after symptom onset)</td>
</tr>
<tr>
<td>Follow-up provided in all cases</td>
<td>Follow-up provided in all cases</td>
<td>Follow-up provided in all cases</td>
<td>Follow-up on all cases (if there are many cases, adherence should be based on proper guidance and partial supervision)</td>
</tr>
<tr>
<td>Investigation of all cases</td>
<td>Investigation of all cases</td>
<td>Investigation of all cases</td>
<td>Investigation of all cases / foci</td>
</tr>
<tr>
<td>Entomological surveillance in sentinel sites(^{12})</td>
<td>Entomological surveillance in sentinel sites and in reaction to a case</td>
<td>Entomological surveillance in sentinel sites and in reaction to a case</td>
<td>Entomological surveillance in sentinel sites and in reaction to a case</td>
</tr>
<tr>
<td>Monitoring vulnerability (influx of people from endemic areas) and factors that influence receptivity (irrigation, deforestation, etc.)</td>
<td>Monitoring vulnerability (influx of people from endemic areas) and factors that influence receptivity (irrigation, deforestation, etc.)</td>
<td>Monitoring vulnerability (influx of people from endemic areas) and factors that influence receptivity (irrigation, deforestation, etc.)</td>
<td>Monitoring vulnerability (influx of people from endemic areas) and factors that influence receptivity (irrigation, deforestation, etc.)</td>
</tr>
<tr>
<td>Reactive case detection</td>
<td>Reactive case detection</td>
<td>Reactive case detection</td>
<td>Reactive case detection</td>
</tr>
<tr>
<td>Vector control (LLIN and IRS) as response to case (if vectors found)</td>
<td>Vector control (LLIN and IRS) as response to case (if vectors found)</td>
<td>Routine vector control (based on increased receptivity and vulnerability)</td>
<td>Routine vector control (LLIN and IRS) with high coverage among population at risk</td>
</tr>
</tbody>
</table>

\(^{12}\) Esta información debe incluir como mínimo: conocimiento sobre la o las especies de vectores presentes, tener una indicación de sus densidades, comportamiento de picadura, características y localización de los habitas larvarios y el estado de susceptibilidad a los insecticidas en uso.
5.2. DTI-R management cycle at municipal level
The planning of activities to eliminate malaria in the foci (DTI-R) requires monitoring and consequent adjustments to changes in the local transmission. In this sense, micro-stratification and micro-planning are not single actions, but rather a management cycle. With a preliminary analysis of the situation, a set of activities is proposed such that diagnosis, treatment, investigation and response are adequately implemented to lead a continuous reduction and subsequent interruption of transmission in the focus. The better the dynamics of infection are understood, the better the DTI-R activities will be planned. Each micro-area's situation should be updated regularly (every six months, for example) to ensure that the response plan is tailored appropriately based on updated data (see Figure 7).

![Figure 7. Management cycle in a micro-area](image)

5.3. Supporting elements for DTI-R strategy
Key to the DTI-R strategy's success is the organization and planning at the national level to support local surveillance and response processes based on prompt access to diagnosis, treatment and basic vector control interventions. The aim is to make the necessary changes to move from control to elimination in the country’s political and strategic level to support the response local-level to malaria and make it sustainable to prevent reestablishment of transmission. The components required for management of the national malaria program include:

- Political and normative framework to ensure universal access to malaria diagnosis, treatment and surveillance in the health services;
- Development of laboratory network and quality assurance for microscopy and RDT;
- Information systems and analysis at the different levels. Inclusion of malaria surveillance in the alert-response processes. Malaria information management;
• Procurement and distribution of drugs;
• Development of entomological surveillance network; and
• Procurement / distribution / monitoring strategy for use of LLIN / application and monitoring of IRS coverage and sensitivity to insecticides; vector control actions and entomological surveillance, entomological actions in foci characterization, LLIN, IRS, and larval control if appropriate.

5.4. Monitoring and evaluation
Anti-malarial actions should be monitored and evaluated according to indicators, changes in transmission dynamics and identification of case clusters. The local model should constantly be adjusted based on the updated information.
Indicators in the malaria surveillance guide [3] should be used to monitor and evaluate malaria programs (Annex 2).
References

23. Organizacion Mundial de la Salud, Control y eliminacion del paludismo por Plasmodium Vivax. Informe tecnico. 2015.
Annexes
Annex 1. Other concepts
Malaria focus
A malaria focus is a “defined circumscribed area situated in a currently or formerly malarious area that contains the epidemiological and ecological factors necessary for malaria transmission” [2]. A focus includes all components needed for the life cycle of an infection or parasite without influence from external factors. It takes into account the larval habitat, feeding and resting sites of the vector, and places frequented by people in the course of their activities, especially at night. For the purpose of malaria surveillance, the term focus refers to a defined area in which transmission persists during the final phases of elimination [3]. At the operational level, and to avoid confusion in the countries, this document accepts the use of the term focus for a group of localities with malaria transmission that share the same transmission dynamics.

The aim of identify and characterize a foci is to implement interventions to interrupt transmission or prevent reestablishment of transmission. When a new active foci is identified, a local team should begin foci investigation activities within 7 days of diagnosis of a confirmed case of malaria. The investigation will collect data on the population at greatest risk (defined by active case detection, routine data, etc.), presence of vectors responsible for transmission, and other factors and conditions that help define transmission dynamics.

The new framework for malaria elimination simplifies the former classification of seven foci, and instead proposes three types of foci (see Figure A1):

- **Active**: indigenous cases detected during current calendar year;
- **Residual non-active**: last indigenous case detected 1–3 years ago; and
- **Cleared**: no indigenous cases for three or more years.

![Figure A1. Classification of malaria foci](image-url)
As a locality gets closer to elimination, it may only have a single case of *P. vivax* classified as indigenous. This can generate confusion as to whether the locality is still an active focus and transmission is taking place there. Sometimes such a case can be a relapse, even though it does not meet the definition used by the countries (either because the interval between first infection and relapse is longer than the country's definition, or the original *P. vivax* infection was never identified as malaria and was simply treated with antibiotics). Another hypothesis could be that it is an introduced case where the imported cases was not identified and where, given vector control actions in the area with an incompetent vector, transmission has been interrupted. The framework for malaria elimination establishes that a single indigenous case in an area with the eco-epidemiological factors needed for malaria transmission makes the area become an active focus. Such localities with isolated cases should be identified and registered in some way and kept under surveillance. These localities with isolated cases should be included in the foci register although the transmission source remains unclear.

Considerations when conducting a focus investigation:

1. If there are many cases, it is more useful to identify localities that share transmission and use the term of micro-areas instead of foci. In these situations, the entomological component is less important because we already assume that there is local transmission, although it can guide us on vector control measures. If there is an increase in number cases more important than expected (outbreak), we must revisit the focus to see what is happening.

2. If there are few cases, the concept of malarial focus has greater relevance; however, the concept of micro-areas can be useful if there is a close group of foci or localities that it is useful to address together to organize the DTI-R strategy. The focus can be a single isolated locality or several localities related to each other that must be addressed in coordination to each other. If there is an increase in number cases more important than expected (outbreak), we must revisit the focus to see what is happening.

3. If a case appears in an unknown area of transmission (new active focus), the entomological component is important for determining whether transmission can occur. Whether we call it outbreak or not, the actions are the same: there should be an alert as this is a transmission area.

Often, as we approach the elimination, we can observe localities with only one case of *P. vivax* classified as indigenous. This sometimes generates confusion about whether or not it should be called an active focus, and whether or not a transmission is actually taking place in that area. In some cases, these cases could be relapses even if they do not meet the operational definition used by countries (for example, because the period from first infection to relapse is greater than the one a country considers, or because that first *P. vivax* infection never has been identified as such and treated with antibiotics). Another hypothesis could be that we are faced with a case introduced where the imported case has not been identified and where, due to the vector control interventions in an area with a poorly competent vector, the transmission has been
interrupted. The malaria elimination framework establishes that a single indigenous case in an area where the epidemiological and ecological factors necessary for the transmission of malaria occurs makes the area an active focus. In addition, it is convenient that these localities with isolated cases are identified and registered in some way, and that they are subject to surveillance. Therefore, including these localities with isolated cases in the focus register can be convenient even if there are doubts about the transmission in these areas.

Case investigation
Case investigation is the “collection of information to allow classification of a malaria case by origin of infection, i.e. imported, indigenous, induced, introduced, relapsing or recrudescent” [2]. Knowing the origin of the infection (probable locality of infection) is especially important when countries are close to elimination and when they are preventing reestablishment of transmission.

Case investigation should begin within the first 3 days from notification of the confirmed case. It starts in the medical consultation and ends in the community (patient's house or workplace) when feasible (if few cases). During this process, the patient's personal information is collected; current illness, including date of onset of symptoms, information on diagnosis and treatment; history of previous illnesses; travel history; transfusions received; places where patient has spent the night; and other questions that help to: (i) determine how and where the patient could have contracted the infection; and (ii) inform response actions and transmission containment. Case classification is presented in Figure A2.
Figure A2. Classification of malaria cases

Passive, reactive and proactive case detection

Case detection is a surveillance activity involving a search in the community for malaria cases. There are several types of detection:

**Passive case detection**: The patient takes the initiative to visit a health center for diagnosis and treatment. This is the basis of malaria surveillance and requires health personnel to suspect or be aware of malaria. Passive case detection fails if people will not or cannot seek health services of their own, if health service coverage is very low, or if health personnel are not trained, do not suspect malaria, nor have access to diagnostic capacity.

**Active case detection**: The health staff / community health worker takes the initiative to find the patient in the community. It is an additional effort to the passive case detection. It is important to conduct in areas of elimination, to detect: (i) symptomatic cases not diagnosed by passive case detection, and (ii) asymptomatic cases existing in the community- in the context of focus investigation. In general, active case detection
cannot be conducted when there is a high burden of disease. Active case detection is divided into proactive and reactive case detection.

- **Proactive case detection**: Conducted in at-risk populations (mobile populations, indigenous communities that do not traditionally use health services, etc.), without being triggered by diagnosis of a confirmed case. Proactive case detection is conducted regularly, i.e., every 1–2 weeks, depending on health system capacities. It can be done with rapid diagnostic tests (RDT) or microscopy and scheduled during periods of greater transmission when relapses are more likely to occur. To be successful, it should be done at a time when the population is traceable.

- **Reactive case detection**: Conducted after notification of a case or cluster of cases. The principle of reactive detection is the recognition that when transmission decreases, there are cluster of cases (the probability of getting infected is 5 times higher for those living in the same household of a malaria case) [22, 23]. Reactive case detection should be conducted among cohabitants, in a radius around the index house (i.e., 200 meters in an urban area, 1–2 km in a rural area), or in the entire focus. Reactive case detection is also conducted during the foci investigation. If the focus is new, coverage of detection should be broader; if the focus is known, detection can be more targeted on the at-risk population. The purpose of reactive case detection is transmission containment and focus investigation. As previously mentioned, for reactive case detection to be successful, it must be conducted when the population is traceable.

**DTI-R components**

**DIAGNOSIS**

All suspected cases should be diagnosed using microscopy or RDT in the first 48 hours after onset of symptoms. The goal of prompt diagnosis and treatment is to reduce morbidity and mortality (especially from *P. falciparum*) and interrupt transmission (especially from *P. vivax*) [4, 11]. In the context of low transmission with few confirmed cases each year, the objective of diagnosis / treatment within the first 48 hours after onset of symptoms remains the objective. Universal access to prompt diagnosis must be ensured, regardless the number of cases the country is experiencing. Microscopy and RDT together can assure that a country reaches universal diagnostic coverage in remote areas and prevent excessive workload for laboratories (with the understanding that microscopy and not RDT’s continues to be the “gold standard”) [25].

To achieve adequate access to diagnosis and treatment, determinants of access to health services and of quality of care (coverage and effectiveness) are important. Universal coverage for diagnosis and treatment
means that the entire population, including the migrant population and other minority groups, must have access to the services they need without financial risk for the family [26]. The extension and improvement of quality health services should be promoted whenever possible. When institutional health services are not available, the support of community health workers, mobile health services and active case detection should be considered [2, 27].

Because malaria is a human disease, without proper diagnosis there is no treatment, no investigation, no information on malaria distribution, no way to stratify risks or identify foci, no guidance for vector control and no response. Surveillance and response follow an appropriate diagnostic network. Access to prompt diagnosis continues to be a challenge in malaria-endemic countries in the Americas.

**TREATMENT**

All positive malaria cases should receive appropriate treatment based on national protocols beginning the same day that laboratory results are received. Health personnel are responsible for providing proper treatment. When health service coverage does not reach the entire population, efforts should be made to extend the services network. Because this takes time, countries should consider authorizing community health workers to prescribe treatment in order to avoid delays that could cause complications and persistence of transmission [27,28].

**INVESTIGATION**

Case investigation should be conducted within the first 3 days after diagnosis. Processes should be established to conduct case investigation within the stipulated time. Details of case investigations and the team in charge will vary based on health service coverage and number of cases occurring in the community. When there are many cases, investigation starts and ends at the diagnostic point. If there are few cases, investigation ends in the community within the first 3 days after diagnosis. Reactive case detection (described in the response component below) also has an investigative component – focus investigation – to identify new cases that could be occurring in the community.

**RESPONSE**

**a) Reactive case detection**

All malaria cases or cluster of cases should lead to prompt detection and treatment of other possible cases. This action can begin with case investigation (in the first 3 days after diagnosis) and always before 7 days from onset of symptoms [3]. Local health services should be organized to respond in the stipulated time. As mentioned in the section above, reactive case detection has an investigative component (case detection
in the focus) and an intervention component (reducing number of individuals with parasites). Each malaria case should be investigated, reactive case should be conducted among the patient's contacts (first to cohabitants, then close contacts) and all positive cases should be treated. The epidemiological situation should dictate the level and extension of the reactive case detection. Regardless the case classification as indigenous or imported case, reactive case detection should be done at the very least with travelling companions (if the case is imported) or with cohabitants if the index case is local (or with work companions if transmission is believed to have occurred at the workplace) even if they are asymptomatic. The same person who diagnoses the index case and starts the investigation should conduct reactive case detection without waiting for arrival of a higher-level team. In contexts of numerous malaria cases at a health unit (more than 3 cases per health unit per week), the investigation and reactive search in response to each case loses epidemiological relevance and could impose a heavy operational burden which would be difficult to assume. In these contexts, the DTI-R concept (as a programmatic effort to detect more cases) is equally important but becomes a set of systematic actions to encourage demand (family members or cohabitants) and/or RACD operations triggered to identify clusters of cases (i.e., requests for patients to bring anyone they have had contact with who could have malaria to the health service, or include groups of cases in areas of greater importance for reactive case detection). Thus, RACD plays a role in malaria surveillance, understood as a systematic action to analyze transmission dynamics and recognize case clusters that could lead to identifying gaps in passive detection and other measures that together can reduce transmission.

Reactive case detection should be conducted using RDT or microscopy, although the use of RDT’s is advisable to provide treatment in the field as quickly as possible. In areas of low transmission, infections with low parasitemia are common and *P. vivax* tend to have lower parasitemia than those of *P. falciparum*. [26-28]. Although RDTs are typically less reliable for *P. vivax* than for *P. falciparum* in detecting low parasitemia, these have been improving and in round 7 of RDT performance [32], six tests indicated 100% performance in low parasitemia (200 parasites/µl) compared to microscopy.

When there are only a few malaria cases, case investigation, focus investigation and response should be carried out more intensely with greater precision. Several weekly rounds of RACD for individuals with or without fever could be planned with diagnosis of the index case to detect cases in the same generation, or of the second, third and possible late incubation periods in the case of *P. vivax*. If there are many cases, a single round of RACD for individuals with fever could be enough (Table A1). In reactive case detection, health personnel should use the opportunity to educate on malaria prevention and use of LLIN and IRS.
Table A1. Guidance on how to conduct reactive case detection

<table>
<thead>
<tr>
<th>Context</th>
<th>Trigger</th>
<th>Where</th>
<th>For whom</th>
<th>How many times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many cases</td>
<td>Cluster of cases. High positivity rate in passive case detection</td>
<td>Group of houses identified</td>
<td>Individuals with fever</td>
<td>Once (if there is diagnostic capacity)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>For whom</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>How many times</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Few cases (close to elimination)</td>
<td>Each case (if 1–3 per health unit per week)</td>
<td>House of confirmed case and neighboring houses. Fellow workers / travel companions</td>
<td>Individuals with fever and other mild symptoms. Individuals without fever in certain contexts</td>
<td>Once for each case. Weekly for 30–60 days after case clearing (based on context)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preventing reestablishment</td>
<td>Index case</td>
<td>Entire locality if area is receptive. Only travel companions if area is not receptive</td>
<td>Individuals with fever and other mild symptoms, individuals without fever</td>
<td>Weekly for 30–60 days after case clearing (based on context)</td>
</tr>
</tbody>
</table>

b) Vector control actions

In addition to reactive case detection, vector control activities are a key component in the response to a malaria focus. According to *A framework for malaria elimination* (2), optimum coverage of LLIN / IRS should be guaranteed and maintained in receptive and vulnerable areas. Malaria programs should ensure appropriate coverage of LLIN or IRS, which should be maintained to prevent a resurgence in malaria transmission. **In conditions of active transmission, vector control actions (IRS or LLIN) should have already been planned and localities already protected from the moment of the “response” operation in the event of a case or cluster of cases.** This means it is not expected that vector control actions in priority localities will be triggered as a “response” operation for occurrences of cases. In situations where the affected population is not covered and analysis of the situation determines the need for vector control actions as part of the “response,” vector control actions should be properly organized. Reactive case detection should not be delayed based on organization of the vector control operation. Persons responsible for carrying out these two responses can be different and may work at different levels. To avoid delays in response, the reactive case detection can begin immediately upon confirmation of the index case while awaiting arrival of the team responsible for provision of LLIN and IRS to ensure that the population living in the malaria focus is adequately protected.

To accomplish high LLIN and IRS coverage, malaria programs need to have the tools necessary to conduct proper planning of the needs (in receptive and vulnerable areas), appropriate selection of the product taking into account information about susceptibility to insecticides, adequate procurement and distribution processes in the communities, promotion of their use, as well as of monitoring and evaluation of the intervention. Tables A2 and A3 summarize DTI-R components and their operationalization according to context.
### Table A2. Components of DTIR strategy

<table>
<thead>
<tr>
<th>Component</th>
<th>Action</th>
<th>Rationale</th>
</tr>
</thead>
</table>
| **Diagnosis:** within first 2 days after onset of symptoms | Diagnosis of suspected cases by microscopy or RDT | 1. Reduction of complications and deaths from severe malaria, particularly by *P. falciparum*.  
2. Interruption of malaria transmission, especially due to *P. vivax*. *P. falciparum* gametocytes appear in the first 7–4 days of first asexual cycle, generally several days after onset of symptoms. *P. vivax* gametocytes appear 1–2 days after first asexual cycle, usually shortly after onset of symptoms. [8]  
3. Administer a single dose of primaquine for any infection by *P. falciparum* to reduce transmissibility. |
| **Treatment:** begins same day as diagnosis | Start treatment including primaquine | 1. Indigenous and introduced cases show active local transmission. Classification of a case as locally acquired (indigenous and introduced) or imported will guide the response.  
2. Case classification taking more than 72 hours could lead to a delay in response, permitting other undiagnosed cases to complete the incubation period and create gametocytes or enable extrinsic incubation period of mosquitos to be finalized. |
| **Case investigation:** within first 3 days after diagnosis | Case is investigated and classified as indigenous, introduced or imported | 1. Evidence of case clusters, especially in areas of low transmission. [29, 30]  
2. Reduce reservoir rapidly, especially in low-transmission context where health team does not always suspect malaria.  
2. WHO’s “Malaria Surveillance, Monitoring and Evaluation: A Reference Manual” emphasizes that active case detection is always carried out during epidemiological investigation of new cases and foci.  
3. To prevent infection from mosquitos of the same generation of cases as case index, perpetuating transmission. These cases could already be symptomatic in the community or in the incubation period.  
4. To prevent second generation of cases from index case. Once the mosquito took the patient's gametocytes, a minimum of 7 days is necessary for this mosquito to be infective, that is, to have sporozoites in its salivary glands (extrinsic period). Once this infective mosquito bites a susceptible person, a minimum of 7 more days is needed to complete the incubation period in the person (intrinsic period) and be part of the second generation of cases [9].  
5. If a case is classified as imported, the aim is to find other imported cases that share origin of infection with index case. Introduced cases are not found until a minimum extrinsic period of 7 days and intrinsic period of 7 days is completed and up to around 120 days (2 transmission cycles). |
| **Reactive case detection:** within first 7 days after onset of symptoms | Reactive case detection for family members / neighbors of index case | 1. LLIN and IRS are cost-effective interventions [33]  
2. LLIN and IRS have a greater impact on reducing vector capacity than other vector control interventions because they reduce the number of female *Anopheles* mosquitos, number of human bites per mosquito, and mosquitos' survival rate.  
3. The new vector control guidelines [31] consider LLIN and IRS as priority vector control actions, larval control as complementary, and do not recommend spatial spraying.  
4. Countries' experiences indicated a resurgence of transmission when these interventions were interrupted. |
| **Vector control** | All households in foci and areas of high malaria transmission potential should be protected with LLIN or IRS | 1. LLIN and IRS are cost-effective interventions [33]  
2. LLIN and IRS have a greater impact on reducing vector capacity than other vector control interventions because they reduce the number of female *Anopheles* mosquitos, number of human bites per mosquito, and mosquitos' survival rate.  
3. The new vector control guidelines [31] consider LLIN and IRS as priority vector control actions, larval control as complementary, and do not recommend spatial spraying.  
4. Countries' experiences indicated a resurgence of transmission when these interventions were interrupted. |
<table>
<thead>
<tr>
<th>WHAT</th>
<th>WHEN</th>
<th>HOW</th>
<th>WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Few and many cases</td>
<td>Within 2 days of onset of symptoms</td>
<td>Microscopy or RDT in health units, community agents, volunteer collaborators at mobile points or during active searches.</td>
</tr>
<tr>
<td></td>
<td>Microscopy or RDT diagnosis of individuals with fever or with atypical symptoms.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Few or many cases</td>
<td>Same day as diagnosis</td>
<td>Treatment prescribed according to national protocols.</td>
</tr>
<tr>
<td></td>
<td>Begin treatment.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Case investigation</strong></td>
<td>Case classification</td>
<td>Within 3 days of diagnosis</td>
<td>Few cases</td>
</tr>
<tr>
<td></td>
<td>Few cases</td>
<td>Begin with diagnosis, end with house visit.</td>
<td>Begin with diagnostic team and end with epidemiology team.</td>
</tr>
<tr>
<td></td>
<td>Detailed case investigation.</td>
<td>Many cases</td>
<td>Many cases</td>
</tr>
<tr>
<td></td>
<td>Many cases</td>
<td>Classification of cases as imported or locally acquired (specifying probable place of infection).</td>
<td></td>
</tr>
<tr>
<td><strong>Reactive case detection</strong></td>
<td>Detection of individuals with fever (and asymptomatic individuals according to context) around index case. Consider work companions.</td>
<td>Few cases</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Several weekly rounds starting as soon as possible, ideally in first 7 days after onset of symptoms in index case.</td>
<td>Begin in first 7 days after onset of symptoms in index case.</td>
<td>Response team: health unit personnel, microscopists, community agents, or volunteer collaborators, vector control team.</td>
</tr>
<tr>
<td></td>
<td>Many cases, without epidemic</td>
<td>Continue weekly for 30 days after clearance of cases.</td>
<td>Many cases, without epidemic</td>
</tr>
<tr>
<td></td>
<td>A round in first 7 days from onset of symptoms in index case</td>
<td>Consider monthly rounds until sixth month if <em>P. Vivax</em> [32].</td>
<td>Many cases, with epidemic</td>
</tr>
<tr>
<td></td>
<td>Many cases, epidemic</td>
<td>A round in first 7 days from onset of symptoms in index case</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A round in first 7 days from onset of symptoms in index case. Repeat rounds weekly according to resources.</td>
<td>Many cases, with epidemic</td>
<td></td>
</tr>
<tr>
<td><strong>Vector control</strong></td>
<td>Protect population in active and residual foci and in areas of high transmission potential with LLIN or IRS.</td>
<td>Routinely in active and residual foci and in areas of high transmission potential.</td>
<td>2–3 cycles according to insecticide used.</td>
</tr>
<tr>
<td></td>
<td>As response to one case (if area is receptive and not including routine activities).</td>
<td>Ensure population is protected with LLIN or IRS during case and foci investigation.</td>
<td></td>
</tr>
</tbody>
</table>

*Exceptional [2].
Annex 2. Operational changes to reduce transmission

In many contexts in which malaria transmission remains constant or reduction has stalled, a change in operations and work routines is needed to accomplish elimination. Health teams need to ask: What could be done differently? Ten operational modifications (summarized in Table A4) are proposed to revitalize the fight against malaria:

1. Move the response organization from the municipality to the most local scenario (focus, group of foci). Given the heterogeneity of malaria transmission in moderate to low transmission contexts (as is the case in the Americas), a detailed approach at the level of the foci where malaria is concentrated. The tools for analysis, technical capacity and supervision should be installed at the local level. This requires:
   a. Define micro-areas and prioritize foci even if in the more distant parts of the municipalities.
   b. Organize a management model in which the basic team (health unit, endemic agents, primary care agents) implements the response and incorporates routine analysis of the situation. The municipal team should provide support processes to the foci management model.

2. The purpose of local operations is to transform active foci into eliminated foci. Elimination in the municipality will be the result of interrupting transmission in each one of the active foci and preventing re-establishment once the foci is eliminated.

3. Strengthen detection / diagnosis / treatment capacity (especially in passive case detection). Diagnosis is the first priority. Without proper diagnosis, there is no proper treatment, no investigation, no information on the distribution of malaria, no way to stratify risk, no way to identify foci, no relevant local information for vector control, no response.

4. Involve other stakeholders (private providers, the community, stakeholders involved in key economic activities that can propel malaria) in the local municipality to determine specific solutions to improve detection / diagnosis / treatment / LLIN use.

5. When a case is detected, the response does not end with treatment. Each malaria case or group of cases should trigger additional detection efforts and the related cases should be diagnosed and treated. The timing and scope of the detection efforts will be dictated by the epidemiological situation.

6. Active case detection cannot replace the gaps in passive case detection, especially in the context of continuous transmission.

7. Prioritize early case detection above other actions that use operational capacity (such as case monitoring or direct supervision of treatment) in high-transmission areas.

8. Plan (and monitor) locally adapted actions to foster the community's seeking of health care (demand for malaria diagnostic care). Tune into / understand the culture, social dynamics / networks, and design effective communication strategies with concrete messages on ways to get diagnosed / treated and the improved diagnostic services in the health centers.
9. Apply an effective integrated sustainable strategy to reduce relapses from *P. vivax*. Toward this end, the countries should at least register the relapses, ensure that primaquine is administered according to weight, and provide observed or semi-observed treatment.

10. Maintain strong LLIN or IRS coverage in key localities, i.e., those with high transmission potential.

Table A4. Operational modifications to malaria elimination in foci from a context of control to one of elimination

<table>
<thead>
<tr>
<th>Control</th>
<th>Elimination</th>
</tr>
</thead>
<tbody>
<tr>
<td>The region is stratified according to API, but the regional API (municipality) does not determine differences in malaria epidemiology at the foci level, so cannot determine differences in malaria operations at the local level.</td>
<td>Intervention differences at the local level are determined by the endemicity level (number of cases) of active foci, analysis of receptivity and risk of importation in contexts with no transmission.</td>
</tr>
<tr>
<td>Municipal operations do not target active foci (to transform them to eliminated foci). In the best of cases, they are directed at rapid diagnosis / treatment (but not at eliminating transmission in foci).</td>
<td>The operation should be directed to transmission interruption in the foci.</td>
</tr>
<tr>
<td>The municipal operation does not target the foci. It aims to provide diagnosis and treatment in the localities, but does not require an understanding of transmission dynamics (such as malaria foci).</td>
<td>The diagnostic / surveillance operation is based on analysis of the cluster of localities as an epidemiological / operative unit within which transmission must be interrupted.</td>
</tr>
<tr>
<td>Work in operative sectors is conducted without an understanding of transmission</td>
<td>Work in operative sectors is conducted but intervening integrally with all localities that form a focus</td>
</tr>
<tr>
<td>The care process ends with treatment of case and follow-up</td>
<td>Detection of other cases around the index case is a key action.</td>
</tr>
</tbody>
</table>

Annex 3. Examples to guide reactive case detection and vector control triggered by a case

- **In the context of scenario 4 with active foci and a large number of cases** (more than 3 per health unit per week), it will be difficult to organize reactive case detection (RACD) for each confirmed case. In addition, in the case of areas of known transmission, where there is already active and passive case detection, there will not be much epidemiological gain in an individual DRC effort. There are several options in these situations:
  - Systematically inform the patients that if family members or neighbors are experiencing similar symptoms, they should go to a health service to be tested for malaria.
  - Conduct RACD for a cluster of cases instead of a single case. RACD should be conducted where the transmission is suspected to have occurred, or where the cases spend the night. Regular rounds should be planned based on available resources and where cases have appeared. Conduct RACD in a 500-meter radius around a house if it is an urban area, and in a 1–2 kilometers radius in a rural area, or more, if necessary. The population should already be protected with MITLD or RRI. Verify and correct if necessary.

- **In the context of scenario 4 with active foci and <3 cases per health unit per week**, RACD can be conducted around each newly confirmed case. The recognition of the area around a case (around 500m if
urban area or 2km if rural area) will help identify houses and breeding sites, and guide entomological investigations. The results of the entomological investigations will delimit the area where reactive detection will be conducted. The RACD will be conducted therefore as follows [35, 36]:

- 1st week (for entire population): individuals with or without fever with no apparent foci (sweeping)
- 2nd week: individuals with fever with no apparent foci
- 3rd week: individuals with fever with no apparent foci
- 4th week: individuals with fever with no apparent foci

If other cases are found during this search, weekly searches should continue for up to 4-8 weeks with zero cases. In both contexts, the area's health units should be notified about confirmed cases for surveillance and to intensify passive case detection. It is important to underscore that no single recommendation can apply for radius to use; it is often determined by the country’s experience and available resources. Good coverage is important no matter what the radius. Therefore, it will be important to have the census of the population and conduct the RACD when the population is traceable.

In a context with no active transmission but receptive transmission (either a scenario 4 with residual inactive foci or a scenario 3 or 2), it is important to inquire about the history of recent travel to an area recognized as malaria endemic (special emphasis in the two weeks before the onset of symptoms):

- If the individual has travelled, conduct RACD based on 14 days from arrival (considering 8 days for *P. vivax* and 7 for *P. falciparum* as a minimum development period for sporozoites in the vector, and 7 days as a minimum for human incubation period) and up to 30 days after effective treatment of the index case. It should be noted that a recent model shows the interval between first and second generations of *P. falciparum* is 49.1 days (33.0–69.0) [33]; accordingly, case detection actions can be extended to day 69 following onset of symptoms in the index case if possible. The RACD should be conducted as explained above (around the case and according to the area defined by the entomological investigations conducted; in the first week, to the entire population: individuals with our without fever and no apparent foci; in the second week: individuals with fever with no apparent foci; in the third week: individuals with fever with no apparent foci; and in the 4th week: individuals with fever with no apparent foci). In addition, RACD should be conducted with all travelling companions and vector control measures will be applied in the delimited area. If the measure is RRI, a single cycle will be sufficient unless the transmission continues for several months.

---

13 For example, if the entomological investigations identify a vector species with a large dispersion capacity and larval habitats far away from households (eg, *An. Darlingi*), the RACD should cover an area larger than another where the dispersion capacity of the vectors is more limited and the larval habitats are closer to the dwellings (eg: *An. albimanus*). In this analysis, a local multidisciplinary team should participate, if possible, with support from regional or national levels, composed of epidemiologists, entomologists and field technicians. Each situation must be analyzed under local conditions.
• If there has been no travelling, RACD can be undertaken immediately in all areas where overnight stays have occurred from 30 days prior to date of onset of symptoms until 30 days from confirmation of being malaria-free after treatment, in the same way as previously described. If another case is identified during these searches, weekly searches should continue consecutively until 4 weeks has elapsed without a new case; in this situation, the weekly search will be done in four cycles for individuals with and without fever. Confirmed cases also should be notified to the area health units for surveillance and intensification of passive case detection. Intensification can include review of clinical histories to find fever of unknown origin and other symptoms indicative with malaria, such as anemia or splenomegaly of unknown cause in the 30 days prior to case detection.

✓ In a context of non-receptive zero transmission (scenario 1), RACD is only necessary for all travel companions.
### Annex 3. Suggested indicators for malaria programs

<table>
<thead>
<tr>
<th>N</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Breakdown</th>
<th>Norm or target</th>
<th>Data source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IMPACT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Number and incidence rate (per 1000 population) of malaria cases: • by species, classification, sex, age group; • by source (e.g. imported, indigenous), • by ACD and PCD, • by sector</td>
<td>Number of confirmed malaria cases identified through active and passive surveillance activities over a 1-year period \times 1000</td>
<td>Mid-year number of persons at risk for malaria infection during reporting year. When computing national incidence use the population of the whole country.</td>
<td>Geographical area/foci, risk group, ACD versus PCD, age, sex and species</td>
<td>Target values to be projected by the programme year by year</td>
<td>Malaria case database. Verification local/national level.</td>
</tr>
<tr>
<td>2</td>
<td>Number of foci by classification</td>
<td>Number of foci by classification (active, residual non-active, cleared)</td>
<td>Target values to be projected by the programme year by year</td>
<td>Malaria focus database</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Number of people and percentage of population living in active foci</td>
<td>Number of people in foci by classification (active, residual non-active, cleared). Number of people living in an active foci</td>
<td>Target values to be projected by the program year by year</td>
<td>Malaria focus database</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Number of malaria deaths by species and by imported or locally acquired</td>
<td>Number of malaria deaths by species and by imported or locally acquired</td>
<td>Target values to be projected by the program year by year</td>
<td>Malaria case database</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SURVEILLANCE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Annual blood examination rate by district and focus and by RDT or microscopy</td>
<td>Number of patients receiving a parasitological test over a year</td>
<td>Mid-year number of persons at risk for malaria</td>
<td>Geographical area/foci, risk group, active versus passive, time (year and month)</td>
<td>Without target, based on context. Surveillance follows clear criteria</td>
<td>Malaria case and case detection databases. Verification local/national level</td>
</tr>
<tr>
<td>6</td>
<td>Percentage of expected monthly/periodic reports received from health facilities and other service providers (with number of patients tested for malaria and number positive)</td>
<td>Number of periodic reports received from health facilities and other service providers (with number of patients tested for malaria and number positive)</td>
<td>Number of periodic reports expected from health facilities and other service providers (with number of patients tested for malaria and number positive)</td>
<td>100%</td>
<td>Malaria case and case detection databases</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Percentage of patients with suspected malaria who received a parasitological test</td>
<td>Number of suspected malaria cases receiving a parasitological test. <em>(Define suspected cases: fever without another diagnosis (FUO), fever and epidemiological link like travel to endemic region)</em></td>
<td>Number of suspected cases of malaria</td>
<td>Geographical area, type of facility, time (year and month)</td>
<td>100%</td>
<td>Routine system, Health facility surveys or community surveys</td>
</tr>
<tr>
<td>8</td>
<td>Percentage of cases notified within 24 h of detection</td>
<td>Number of case reports received &lt;24 hours after detection</td>
<td>Total number of malaria case reports</td>
<td>Geographical area/foci, risk group, time (year and month), type of facility</td>
<td>100%</td>
<td>Malaria case and case detection databases</td>
</tr>
</tbody>
</table>
## Diagnosis

<table>
<thead>
<tr>
<th>9</th>
<th>Percentage of microscopy results cross-checked by national reference laboratory</th>
<th>Number of positive and negative microscopy results cross-checked</th>
<th>Number of positive and negative results</th>
<th>Microscopy post</th>
<th>100% of positive results 10% of negative results</th>
<th>Reference laboratory database Verification local/national level</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>10</th>
<th>Percentage of testing laboratories participating in WHO-recommended microscopy quality assurance assessments (direct-NCA and external QA)</th>
<th>Number of testing laboratories participating in QA assessment</th>
<th>Number of testing laboratories</th>
<th>100%</th>
<th>Reference laboratory database</th>
</tr>
</thead>
</table>

| 11 | Proportion of health facilities without stock outs of key commodities for diagnostic testing | Number of health facility without stockouts of key commodities for diagnosis. *(In countries with very low cases it will be necessary to define which facilities should have commodities for diagnostic testing)* | Number of health facilities that should have commodities for diagnostic testing | Geographical area, type of facility, time (year and month) | 100% | Routine and health facility survey |
|---|---|---|---|---|---|

## Case Management

<table>
<thead>
<tr>
<th>12</th>
<th>Percentage of patients with confirmed malaria who received first-line anti-malarial treatment according to national policy</th>
<th>Number of patients with confirmed malaria who received first-line antimalarial treatment according to national policy</th>
<th>Total number of confirmed malaria cases</th>
<th>Geographical area, type of facility, parasite species, time (year and month)</th>
<th>100%</th>
<th>Malaria case and case detection databases</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>13</th>
<th>Proportion of detected cases contacting health services within 48 hours of developing symptoms</th>
<th>Number of cases contacting health services (including CHW) within 48 hours of developing symptoms</th>
<th>Total number of passively detected malaria cases</th>
<th>Geographical area/foci, risk group, type (year and month), type of facility</th>
<th>Target values to be projected by the program year by year</th>
<th>Routine system</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>14</th>
<th>Median time between onset of symptoms and start of treatment by type of surveillance</th>
<th>Median number of days in which malaria cases received treatment from the start of symptoms</th>
<th>Total number of confirmed malaria cases</th>
<th>Geographical area/foci, risk group, time (year and month), type of facility, type of surveillance</th>
<th>Target values to be projected by the program year by year</th>
<th>Routine system</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>15</th>
<th>Proportion of cases with supervised treatment</th>
<th>Number of cases that received supervised treatment</th>
<th>Total number of confirmed malaria cases</th>
<th>More important for countries with very low cases</th>
<th>100%</th>
<th>Routine system</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>16</th>
<th>Proportion of health facility months without stockouts of first-line treatments</th>
<th>Number of health facility months without stockouts of first-line treatments. <em>(In countries with very low cases it will be necessary to define which facilities should have treatment)</em></th>
<th>Number of health facility months</th>
<th>Geographical area, type of facility, time (year and month)</th>
<th>100%</th>
<th>Routine and health facility survey</th>
</tr>
</thead>
</table>

## Investigation

<table>
<thead>
<tr>
<th>17</th>
<th>Percentage of cases with case investigation and classification</th>
<th>Total number of malaria cases in the national case register with case investigation (and with case)</th>
<th>Total number of confirmed malaria cases</th>
<th>Geographical area/foci, risk group, time (year and month), type of facility</th>
<th>100%</th>
<th>Malaria case and case detection databases. Verification local/national level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Percentage of cases with completed case investigation form submitted within stipulated delay</td>
<td>Total number of malaria cases in the national case register with fully completed case investigation forms submitted within stipulated delay within the previous year</td>
<td>Total number of confirmed malaria cases</td>
<td>Geographical area/foci, risk group, time (year and month), type of facility. More important for countries with very low cases</td>
<td></td>
<td>Malaria case and case detection databases</td>
</tr>
<tr>
<td>19</td>
<td>Percentage of foci investigated</td>
<td>Total number of new foci in the national foci register that have received full investigations within the previous year</td>
<td>Total number of new foci in the national foci register</td>
<td>Geographical area/foci, time (year).</td>
<td></td>
<td>Malaria focus database</td>
</tr>
<tr>
<td>20</td>
<td>Percentage of foci for which completed investigation form submitted within stipulated delay</td>
<td>Total number of new foci in the national foci register that have received full investigations within stipulated delay within the previous year</td>
<td>Total number of new foci in the national foci register</td>
<td>Geographical area/foci, time (year). More important for countries with very low cases.</td>
<td></td>
<td>Malaria focus database</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RESPONSE - VECTOR CONTROL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Proportion of targeted risk group sleeping under an insecticide-treated net (ITN) or living in house sprayed by IRS in the previous 12 months</td>
<td>Number of persons living in risk areas sleeping under an ITN or living in house sprayed by IRS in the previous 12 months.</td>
<td>Number of persons living in risk areas (Define population at risk: population living in active, residual non-active foci or in highly vulnerable and receptive areas).</td>
<td></td>
<td></td>
<td>Operations records or household surveys-LQAS</td>
</tr>
<tr>
<td>22</td>
<td>Percentage of active and residual non-active foci protected by IRS, by year</td>
<td>Number of active and residual non-active foci protected by IRS, by year</td>
<td>Number of active and residual non-active foci protected by IRS, by focus and year</td>
<td></td>
<td></td>
<td>Independent focus surveys</td>
</tr>
<tr>
<td>23</td>
<td>Percentage of population living in active and residual non-active foci protected by IRS, by focus and year</td>
<td>Number of people living in active and residual non-active foci protected by IRS, by focus and year</td>
<td>Population living in active and residual non-active foci by focus and year</td>
<td></td>
<td></td>
<td>Independent focus surveys</td>
</tr>
<tr>
<td>24</td>
<td>Percentage of active and residual non-active foci protected by ITN, by year</td>
<td>Number of active and residual non-active foci protected by ITN, by year</td>
<td>Number of active and residual non-active foci protected by ITN, by focus and year</td>
<td></td>
<td></td>
<td>Independent focus surveys</td>
</tr>
<tr>
<td>25</td>
<td>Percentage of population living in active and residual non-active foci protected by ITN, by focus and year</td>
<td>Number of people living in active and residual non-active foci protected by ITN, by focus and year</td>
<td>Population living in active and residual non-active foci by focus and year</td>
<td></td>
<td></td>
<td>Independent focus surveys</td>
</tr>
<tr>
<td>26</td>
<td>Percentage of active and residual non-active foci with activities of larval control.</td>
<td>Number of active and residual non-active foci with activities of larval control.</td>
<td>Total active and residual non-active foci</td>
<td>As per national target, depending on breading sites characteristics</td>
<td></td>
<td>Independent vector survey</td>
</tr>
<tr>
<td>PROGRAMME MILESTONES</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>27</strong> Malaria expenditure by source (domestic, external)</td>
<td>Target values to be projected by the program year by year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>28</strong> Malaria expenditure per capita for malaria control and elimination</td>
<td>Target values to be projected by the program year by year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>29</strong> Malaria is a notifiable disease within 24 hours</td>
<td>Yes</td>
<td>Policy documents</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>30</strong> Standard operating procedures for all components of surveillance have been prepared, field tested and are in use</td>
<td>Yes</td>
<td>Surveillance and routine information systems assessment surveys</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>31</strong> There is a national reference laboratory for microscopy, with a slide bank and implementation of external quality assurance</td>
<td>Yes</td>
<td>Surveillance and routine information systems assessment surveys</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>32</strong> There is a focus register and if it was updated in the last 12 months</td>
<td>Yes</td>
<td>Malaria registers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>33</strong> An independent national malaria elimination advisory committee has been set up</td>
<td>Yes</td>
<td>Malaria program reviews</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>34</strong> A comprehensive report on the elimination program is prepared annually and shared with all district health offices</td>
<td>Yes</td>
<td>Malaria program reviews</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>35</strong> The national malaria elimination plan has been approved and endorsed by the minister of health</td>
<td>Yes</td>
<td>Malaria program reviews</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>36</strong> There is functional inter-sectoral collaboration in all districts concerned</td>
<td>Yes</td>
<td>Malaria program reviews</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>37</strong> There is an updated list of all public and private health facilities and community health workers who provide malaria diagnosis or treatment</td>
<td>Yes</td>
<td>Surveillance and routine information systems assessment surveys</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>38</strong> Each facility is registered to receive appropriate supervision</td>
<td>Yes</td>
<td>Surveillance and routine information systems assessment surveys</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Annex 4. Example of focus characterization and response