



Technical note on accelerating *P. falciparum* elimination in the Americas

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*This technical note offers guidance to national malaria programs and organizations that support malaria elimination efforts in the Region, so that they are able to intensify policy/strategic actions and implement operational changes to accelerate the elimination of *P. falciparum* as part of national malaria elimination strategies.*

1 BACKGROUND AND SCOPE OF ACTION

Due to the risk of emerging *P. falciparum* resistance to artemisinin derivatives in the Americas, in 2015 the Pan American Health Organization (PAHO), together with the countries of the Region, developed a framework for artemisinin resistance prevention, containment, and elimination in South America (1). This framework outlined a combination of activities aimed at preventing and containing the development of artemisinin resistance in South America in general and in the Guiana Shield in particular. Since the emergence of artemisinin-resistant *P. falciparum* in the Guiana Shield would seriously jeopardize malaria elimination throughout South America, prevention of resistance to artemisinin-based combination therapies (ACTs) should be considered a top priority for malaria elimination in the Region. A long-term goal of the framework was to eliminate *P. falciparum* malaria as the only sure way to avoid the selection of resistant parasites. The ultimate goal of this framework was to preserve the efficacy of ACTs (both the artemisinin component and associated drugs) against *P. falciparum* malaria in the Region.

The dynamics of *P. falciparum* and *P. vivax* transmission in the Americas are such that the elimination stage is reached earlier for *P. falciparum* than for *P. vivax*, mainly due to: i) the absence of hypnozoites and relapses, which reduces recurrences; ii) a shorter treatment period, which favors adherence to treatment; and iii) the appearance of gametocytes 7-10 days after onset of symptoms, which facilitates the interruption of transmission chains.

As of 2019, additional epidemiological events continued to show the need for stronger actions to eliminate *P. falciparum* in the Americas. On one hand, *P. falciparum* was reintroduced in territories that had interrupted or drastically reduced malaria transmission by this species (Bolivia, Honduras, Nicaragua, and municipalities in some South American countries), while the situation remained relatively unchanged in Brazil, Colombia, Peru, and Guyana (the only country where resistance mutations have been recorded). On the other hand, a significant reduction in cases in Venezuelan municipalities (which between 2017 and 2019 had recorded the highest transmission rate) is considered a window of opportunity to pursue *P. falciparum* elimination.

Worldwide, three new events since 2019 have led the Regional Malaria Program to reconsider the need to review the relevance of stronger actions to accelerate the elimination of *P. falciparum* in the Americas:

- Significant progress in *P. falciparum* elimination in the Mekong region, with accelerator strategies and innovative approaches: case- and focus-based surveillance systems and interventions to eliminate malaria with specific innovative approaches involving targeted drug administration (TDA) and intermittent preventive treatment (IPT) for at-risk populations.
- Emergence of *P. falciparum* resistance in Africa.
- World Health Organization (WHO) conditional recommendations on chemoprevention interventions to accelerate elimination.

In this context, in 2019 and 2022 the PAHO malaria team presented a proposal to the Technical Advisory Group (TAG) for more intensive actions for the elimination of *P. falciparum* malaria in South America. In 2022, the TAG recognized the importance of accelerating the elimination of *P. falciparum* with the understanding that this effort contributes to the elimination of all malaria species, while noting that *P. vivax* elimination efforts should not be neglected.

2 OBJECTIVES OF THIS TECHNICAL NOTE

The main objective of this technical note is to provide guidance on actions to **accelerate *P. falciparum* elimination** in areas already close to elimination, without compromising unified malaria elimination efforts (*P. vivax* + *P. falciparum*), while contributing to **the country's ultimate goal of eliminating malaria overall**.

The specific objectives related to the acceleration of *P. falciparum* elimination are to:

1. Prevent the emergence and spread of resistance to artemisinin and associated drugs from becoming a further obstacle to malaria elimination in the continent.
2. Accelerate the reduction in the total number of malaria cases in areas with a significant proportion of *P. falciparum*.
3. Develop capacities through the experience of *P. falciparum* elimination, thus reducing the time needed to achieve malaria elimination.
4. Empower different actors, including high-level authorities, donors, municipalities, and other entities involved in malaria elimination, by inspiring them with the achievements of *P. falciparum* elimination. Use the concept of "early wins" as a catalyst. Early wins are needed.

3 ACTIONS TO ACCELERATE *P. FALCIPARUM* ELIMINATION IN THE AMERICAS

The main action to accelerate *P. falciparum* elimination is to strengthen the unified *P. vivax* - *P. falciparum* elimination strategy and, in particular, to ensure access to early diagnosis and treatment of malaria.

The **basic interventions for *P. vivax* and *P. falciparum*** are:

1. Malaria risk stratification, taking into account receptivity, risk of malaria importation, and number of cases.
2. Microplanning at the level of foci or operational units.
3. Expanding access to diagnosis and treatment, the DT component of the diagnosis, treatment, investigation, and response (DT-IR) strategy promoted by PAHO.
4. Vector control.

In areas close to *P. falciparum* elimination, the following additional **acceleration/reactive interventions** are promoted to accelerate the process:

1. Case investigation and reactive case detection (the IR component of the diagnosis, treatment, investigation, and response [DT-IR] strategy promoted by PAHO) of *P. falciparum* cases, regardless of the *P. vivax* burden.
2. Reactive drug administration.
3. Other chemoprevention and reactive interventions: mass drug administration (MDA), targeted drug administration (TDA), reactive indoor residual spraying (IRS).
4. Prevention of *P. falciparum* re-establishment at the subnational level.

3.1 Basic interventions

3.1.1 Malaria risk stratification

Malaria risk stratification based on receptivity, number of cases, and risk of malaria importation is the first step to plan elimination interventions. PAHO promotes the following stratification to establish differences in the intensity of interventions:

- **Stratum 1.** Non-receptive.
- **Stratum 2.** Receptive, with no indigenous cases and no risk of parasite importation. This includes eliminated foci, with no imported cases and no immigration from endemic territories.
- **Stratum 3** Receptive, with no indigenous cases but with risk of parasite importation. This includes eliminated foci, with imported cases or with immigration from endemic territories.
- **Stratum 4.** Receptive, including residual foci and areas with active transmission and very few cases.¹
- **Stratum 5.** Receptive, with active transmission and with a caseload that makes investigation and reactive actions in response to each case neither possible nor relevant.

¹ To guide differentiation between strata 4 and 5, *Malaria surveillance, monitoring and evaluation: a reference manual* (3) proposes three cases per week per investigation team as an example of criteria for which reactive case detection should be performed. However, technical discussions should be held at the country level to identify the point at which differentiated actions should be taken for each species.

Once the country has been stratified, interventions will be planned according to strata (see annex). A main differentiating element is the need for intensified surveillance and response in strata 3 and 4 (eliminated and residual foci, or active foci with very few cases), while in stratum 5, the higher number of cases means that a response to each case is neither relevant nor possible. The same criteria can be used to stratify the territory according to *P. falciparum* transmission.

Prioritization is an essential element in planning malaria interventions and is part of the stratification exercise. This means identifying populations and geographic areas (foci, municipalities) that require greater attention and efforts aimed at effective resource management and greater impact on public health. Once the geographic units have been classified into strata, it is necessary to prioritize certain units according to their epidemiological importance within a given stratum. The 80/20 rule is often useful for targeting interventions and ensuring impact in municipalities with the most cases of *P. falciparum*. Several criteria can be considered for prioritization, including territories with *P. falciparum* (see the PAHO Manual for Stratifying Malaria Risk and the Elimination of Foci (2019)) (2). **The parasite species should be considered when stratifying, since some areas with very high numbers of *P. vivax* (stratum 5), may be in strata 3 or 4 for *P. falciparum*, requiring intensive surveillance. Without this analysis, these areas will not benefit from effective action to accelerate elimination and prevent reestablishment. Furthermore, priority should be given to areas with *P. falciparum*.**

3.1.2 Microplanning at the level of foci or operational units

Malaria elimination is a field operation that requires the demarcation of a defined geographical area. It is necessary to establish operational units (foci or micro-areas) with assigned personnel for elimination actions. The reduction of transmission in a territory within the country is the result of consolidating malaria-free zones through the elimination of foci. Therefore, it is necessary to delimit these operational units, which may comprise several localities or neighborhoods that should be approached jointly due to their geographic proximity, epidemiological links, or operational advantages if covered by the same field team.

Once the operational unit has been established, the next step is to organize the diagnostic and treatment network (see section 3.1.3) and establish the set of actions for each stratum. The level of *P. falciparum* transmission should be considered at this point. Where there are few cases of *P. falciparum* (e.g., three cases per week per investigation team), surveillance for this species should be intensified, regardless of the burden of *P. vivax* malaria. An increase or reintroduction of *P. falciparum* in a foci or territory should be investigated and addressed with a rapid response (regardless of whether *P. vivax* transmission continues).

Local-level surveillance routines, analyses, and decision-making should take into account the specific situation with regard to *P. falciparum* (e.g., tables of case numbers per locality/week disaggregated by species), and analyses should be conducted to understand the underlying causes (e.g., increased importation of *P. falciparum* or decreased surveillance, *P. falciparum* reservoir dynamics, subpatent infections) and implement the response.

3.1.3 Expanding access to diagnosis and treatment

Early diagnosis and treatment are the key interventions in any malaria elimination scenario in the Americas. The earlier the patient is diagnosed and treated, the lower the probability of parasite transmission and the greater the impact. This is especially important in the case of *P. falciparum*. Despite the efforts made by countries on the path to malaria elimination, significant gaps persist in access to timely diagnosis. For this reason, PAHO proposes a framework to improve access to malaria diagnosis and treatment based on expanded diagnosis, including greater use of rapid diagnostic tests (RDTs) and prompt, full treatment.

This is a call to expand the offer of diagnostic and treatment using all possible tools, maximizing the use of RDTs, leveraging the presence of all service providers, and intensively involving the community in all areas with *P. falciparum* and *P. vivax* transmission. This includes the elements presented in the 2015 Framework for the Prevention, Containment and Elimination of Artemisinin Resistance in South America in relation to the multiple actors that could participate in diagnosis and treatment in gold mining areas, to ensure early treatment and discourage monotherapy and the circulation of unregulated antimalarial drugs.

A microplanning approach is proposed for the organization of a local diagnostic and treatment network, based on an understanding of the links and dynamics between communities, access routes, and the structure of the health service network (see section 3.1.2).

As part of policies aimed at simplifying and expanding access to treatment in *P. vivax/P. falciparum* co-endemic areas, a unified (ACT-based) drug treatment scheme could be considered (4, 5). Separate treatment remains the preferred option in the Region, where *P. vivax* is chloroquine-sensitive and diagnostic strategies can distinguish between *P. vivax* and *P. falciparum*. However, in some co-endemic settings, a unified ACT-based strategy for *P. vivax* and *P. falciparum* malaria could be beneficial. Even if a microscopic diagnosis of *P. vivax* is correct, sub-patent co-infection with *P. falciparum* is common and is not detected by RDT. If a significant proportion of patients with *P. falciparum* infection are treated with chloroquine alone, there may be a consequent increase in *P. falciparum* transmission and morbidity. At the same time, the potential detrimental effects and operational challenges of this policy on *P. vivax* should be considered.² In summary, unified treatment of *P. vivax* and *P. falciparum* should be carefully analyzed in each epidemiological context. *P. falciparum* and *P. vivax* rates, the specificities of *P. vivax* and *P. falciparum* dynamics, and other aspects should be taken into account.

Finally, PAHO offers encouragement and support for countries to monitor in vivo responses of *P. falciparum*, not just molecular markers. At a minimum, all malaria cases should be monitored and microscopy should be performed at the end of treatment, with follow-up after 28 or 42 days (depending on the combination used for *P. falciparum*). In countries with very few cases, WHO recommends follow-up at 0, 3, 7, 14, 21, 28, 35, and 42 days, thus integrating drug efficacy monitoring into routine surveillance systems. This is also a component of case management aimed at ensuring a cure.

3.1.4 Vector control

Recommended vector control measures (long-lasting insecticidal nets [LLINs] and IRS) should be guided by the local analysis at foci level. The delimitation of operational units (foci or micro-areas), combined with entomological surveillance, provides the necessary elements to guide the selection and prioritization of interventions. The presence of *P. falciparum* may be an important factor in the identification and **prioritization of foci that require LLINs and IRS.**³ However, decision-making and prioritization of vector control should be guided by other elements related to the magnitude and risk of the overall malaria situation (*P. vivax* and *P. falciparum*).

² Considerations against a unified strategy focused on artemisinin-based combination therapy (ACT) include: i) the efficacy of 8-aminoquinolines in preventing relapses of *P. vivax* may be lower with ACT than with chloroquine, so their introduction may lead to a relative reduction in relapse prevention; ii) the higher costs of ACT; and iii) two doses/day of artemether-lumefantrine versus only one dose/day of chloroquine for *P. vivax*.

³ An additional element in favor of such prioritization is that, due to the shorter duration of sporogony in *P. vivax* than in *P. falciparum*, interventions aimed at reducing vector longevity (LLINs and IRS) may be more effective for *P. falciparum*.

It is necessary to improve the coverage and quality of vector control and to recognize that these interventions may have a greater impact on *P. falciparum*. Furthermore, more actions are needed to control insecticide resistance and ensure the quality and efficacy of mosquito nets and insecticides.

3.2 Acceleration/reactive interventions in areas approaching *P. falciparum* elimination

3.2.1 Case investigation and reactive case detection in response to each *P. falciparum* case

The DT-IR strategy emphasizes the importance of timely investigation and response to cases and foci after diagnosis and treatment; in this regard, investigation and reactive case detection play a key role. Actions should not stop once a case has been diagnosed and treated; it is necessary to continue detecting and treating other possible cases related to each identified case. This cascade of surveillance-driven actions is a key element in operationalizing the concept of surveillance as intervention and response to cases.

This response to an individual case is recommended when the number of cases is very low (WHO suggests less than three cases per week per investigation team). **Among the interventions to accelerate *P. falciparum* elimination, this intensified response should be activated when the number of *P. falciparum* cases is low, regardless of the magnitude of the *P. vivax* situation.**

3.2.2 Reactive drug administration

Reactive drug administration (RDA) could be included as a new component of reactive interventions. **Reactive treatment may be indicated in situations with a very low number of *P. falciparum* cases (regardless of the number of *P. vivax* cases)**, where the risk of transmission is considered to be higher in family members or others living with the patient. This reactive intervention may be supported by prior information that shows that the cases are grouped in a specific location. Care should be taken not to confuse treatment based on clinical suspicion or presumptive treatment (which is no longer used in the Region) and RDA. RDA should be monitored and reported in case investigation and response activities.

3.2.3 Other chemoprevention and reactive interventions

Based on WHO recommendations, two groups of interventions can help to accelerate *P. falciparum* elimination: i) **MDA** (full course of an antimalarial drug to all members of a defined population or to everyone living in a defined geographic area); and ii) **TDA** (full course of an antimalarial drug to persons at higher risk of malaria infection compared to the general population).

Countries should identify the specific situations in which these chemoprevention interventions may be indicated. For each situation eligible for a chemoprevention intervention, the starting point is an analysis of **the transmission burden and the dispersion/concentration of transmission** in the area (cases per locality and trends, distance, access, and human dynamics between localities); **deficiencies in surveillance** (passive or active case detection); **coverage** of diagnostics, treatments, and vector control interventions; the dynamics of **mobility and importation**; and **hypotheses** as to why transmission has not been disrupted or has stabilized. Based on WHO recommendations on chemoprevention, **PAHO encourages countries to identify areas where these interventions could be implemented to interrupt *P. falciparum* transmission.**

Reactive IRS has also been recently recommended by WHO and is included among reactive interventions. In situations where the number of cases is very low or where reestablishment of the transmission is being prevented, reactive IRS could be considered, if feasible, among reactive interventions in response to a case.

3.2.4 Prevention of *P. falciparum* re-establishment at the subnational level

Consolidation of the national territory as free of malaria transmission is the result of keeping subnational territories free of transmission and consolidating this achievement. **Countries must take decisive action to prevent the re-establishment of *P. falciparum* transmission at subnational levels where it has been disrupted (even if there are more *P. vivax* cases in the area).**

All these measures are aimed at interrupting *P. falciparum* transmission and preventing its re-establishment. Foci and municipalities that have been classified as stratum 4 for *P. falciparum* because they are residual foci (one year without transmission) should be identified and monitored at the national level. The intensified *P. falciparum* surveillance and response actions mentioned above should be complemented with proactive measures to manage the risk of imported *P. falciparum* cases from neighboring municipalities or other territories. Analyses should prioritize situations where there is a risk of *P. falciparum* importation.

An important consideration:

For a more effective strategy against *P. falciparum*, it is essential not only to investigate cases and conduct reactive interventions, **but to develop local capacity to analyze and understand each specific situation, the dynamics of the *P. falciparum* reservoir, and the risk of importation and subpatent infections, and to organize interventions in each specific area.**

Due to limited evidence and the “conditional” nature of WHO recommendations on the chemoprevention strategies indicated here, the approach proposed by PAHO to implement these strategies consists of controlled implementation in selected situations. This will make it possible to collect evidence, gain experience, and consolidate policies that can be subsequently expanded as needed.^a

The entire set of actions should be complemented by other measures found in the 2015 Framework for the Prevention, Containment and Elimination of Artemisinin Resistance in South America, in particular actions to monitor *P. falciparum* resistance, as well as policy, regulatory, and surveillance measures to contain self-medication, monotherapies, and the unregulated market for artemisinin-based combination therapies (ACTs).

^a This is based on WHO recommendations for malaria chemoprevention. PAHO has developed a framework to guide national malaria programs in the Americas in the implementation and evaluation of chemoprevention strategies conditionally recommended by WHO in 2022.

4 HOW THIS FRAMEWORK RESPONDS TO THE PLAN OF ACTION FOR MALARIA ELIMINATION 2021-2025

P. falciparum elimination was highlighted as a priority at several points in the consultation process for the regional plan of action. The following set of actions responds to the following objectives of the Plan of Action for Malaria Elimination 2021-2025:

- **Objective 2.1:** Establish programmatic approaches to ensure early testing, treatment, and investigation of cases, and transform active foci into cleared.
- **Objective 2.2:** Pursue interventions and innovations to accelerate reductions in transmission in key populations or high-burden areas.
- **Objective 2.3:** Sustain key capacities in countries and their subnational territories to prevent re-establishment of transmission; enable, support, and accelerate the elimination of *P. falciparum* and prevent the re-establishment of its transmission, including at subnational level.

5 CHALLENGES AND RISKS

- Countries should ensure that the political commitment to eliminate all types of malaria continues after the elimination of *P. falciparum*.
- Similarly, steps should be taken to ensure that local malaria control efforts do not neglect basic actions against *P. vivax* when applying specific measures against *P. falciparum*.
- Attention must be paid to the need to address weaknesses in local teams. The proposed actions depend mainly on local capacity. There is a concerning loss of capacity and weakening of malaria programs at the local level.
- The level of *P. falciparum* transmission at which surveillance actions should be intensified more for *P. falciparum* than for *P. vivax* is a key element in this framework; Technical discussions should be undertaken at the country level to identify the threshold at which differentiated actions need to be taken for each species.
- It is necessary to consider the negative effects that the promotion of RDA may have in some countries, in light of past efforts to avoid presumptive treatment and focus on diagnosis-based treatment. Measures should be taken to mitigate this risk.

6 SUMMARY OF ACTIONS

Complementing unified actions to eliminate malaria (*P. vivax* and *P. falciparum*), PAHO promotes a set of actions to accelerate *P. falciparum* elimination in countries and subnational territories that are close to eliminating this parasite:

1. Countries should differentiate between *P. falciparum* and *P. vivax* when analyzing their data at **local** and national levels. Stratification, surveillance, and operational decision-making should consider the specific situation of *P. falciparum* transmission.
2. Countries are encouraged to expand the availability of diagnostic treatment using all possible tools, maximizing the use of RDTs, utilizing all local structure and opportunities in the health service network, and intensively involving the community in all areas with *P. falciparum* and *P. vivax* transmission.
3. The presence of *P. falciparum* may be an important factor in the identification and prioritization of foci for IRS and LLINs, with interventions of good quality and coverage.
4. When the number of *P. falciparum* cases is low, regardless of the number of *P. vivax* cases, an individual case response should be initiated, with case investigation and reactive interventions. Reactive case detection, reactive drug administration, and reactive IRS could be considered, either alone or in combination.
5. Countries should identify areas where WHO-recommended chemoprevention interventions could be implemented to disrupt *P. falciparum* transmission.
6. Countries should take decisive action to prevent the re-establishment of *P. falciparum* transmission at subnational levels where it has been disrupted (even if there are more cases of *P. vivax* in the area).

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All malaria-endemic countries in the Region of the Americas have taken on the challenge of eliminating the disease and have focused their health programs and strategies on that goal.

This technical note provides guidance on actions to accelerate *P. falciparum* elimination in areas close to achieving this goal without compromising unified malaria elimination efforts (*P. vivax* - *P. falciparum*), while contributing to the country's ultimate goal of eliminating malaria overall. The acceleration of *P. falciparum* elimination has several goals: mitigating the risk that resistance to artemisinin and associated drugs will emerge and spread; accelerating the reduction in the total number of malaria cases in areas with a significant proportion of *P. falciparum*; accelerating malaria elimination (both *P. vivax* and *P. falciparum*), considering that *P. falciparum* is one of the triggers of *P. vivax* relapses; developing capacities in interventions to accelerate malaria elimination by building on the experience of *P. falciparum* elimination; and empowering different actors, including high-level authorities, donors, municipalities, and other entities involved in malaria elimination, by inspiring them with the achievements of *P. falciparum* elimination.