POLICY BRIEF

GLOBAL MALARIA DIAGNOSTIC AND ARTEMISININ TREATMENT COMMODITIES DEMAND FORECAST
2017 – 2021
May 11, 2018
INTRODUCTION

This synopsis provides policymakers with a brief summary of the latest forecasts for global need, demand, and procurement of malaria diagnostics and treatments, and the implications of these projections for health and development policy. The forecasts were produced by a consortium including the Clinton Health Access Initiative, Inc. (CHAI), IMS Health (IMS), and the University of California, San Francisco (UCSF). Unitaid funds this consortium, which operates under the guidance of a Steering Committee consisting of representatives from The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), Medicines for Malaria Venture (MMV), Unitaid, the US President’s Malaria Initiative (PMI), and the World Health Organization (WHO).

This is the final forecast in a series of periodic reports, and includes several changes from prior reports. This edition updates baseline demand and procurement forecast outputs presented previously, with emphasis on the impact of continued funding and participation in the Global Fund’s Private Sector Co-Payment Mechanism (CPM) on (quality-assured artemisinin-based combination therapies) QAACT procurement. It also extends the commodity forecasts to the year 2021, introduces estimates around procurement of rectal artesunate, and reflects on how broader trends and uncertainties affecting the malaria epidemic could impact commodities in the future.
KEY MESSAGES

- This analysis distinguishes three forecasting terms that often are used interchangeably but mean very different things: “need”, “demand,” and “procurement”. For this report, “need” represents our projection of the total number of febrile cases where the patient carries malaria parasites currently detectable by microscopy or rapid diagnostic tests (including cases where a separate infection may be the cause of fever). “Demand” represents the number of cases where a consumer would seek treatment for a suspected case of malaria-caused fever (including cases where the fever is not caused by malaria). “Procurement” represents the number of quality-assured products that we estimate public or private sector purchasers will order in the given timeframe.

- In 2017, we estimate global demand for antimalarial medicines to be over 1.6 billion (B) treatment courses, and we forecast this demand will grow to over 1.7B treatments by 2021. Demand for artemisinin-based combination therapies (ACTs) – inclusive of both QA ACTs and non-quality-assured ACTs (non-QA ACTs) – will comprise approximately 36% of global antimalarial demand in 2017. ACTs’ share of market demand is expected to grow to 47% of global antimalarial demand by 2021. Non-QA ACTs comprise about 26% to 32% of estimated global ACT demand, with most of this demand coming from the private sector.

- The latest national funding allocations, recently announced by the Global Fund for 2018-2020, indicate that the total amount of funding available for malaria programs is about $1B lower (31% less) than the amount available during the prior funding window. Because countries tend to prioritize commodity purchases over other expenses, we expect that the impact of a reduction in annual Global Fund funding on ACTs and RDTs procurement will have a limited impact on global procurement estimates. Funding requests are still being reviewed by the Global Fund and the extent to which programs will follow historical procurement strategies remains unclear.

- While financial commitments for the continuation of CPMQA ACT procurement remain somewhat unclear beyond 2017, information from CPM-participating countries that have submitted 2018-2020 funding requests to the Global Fund indicates that there will be a significant decline in the volume of QA ACTs procured through this program; Nigeria, which has accounted for an estimated 49% of all QA ACTs ordered throughout the course of the
Affordable Medicines Facility malaria (AMFm) pilot and the CPM, has not designated within-allocation funding for continuation of the program in their Global Fund funding request, and thus it is likely that Nigeria’s further participation in this program will be halted or, at best, significantly reduced. Due to these reductions in funding allocations for the program, CPM QAACT procurement is projected to decrease from 62 million (M) treatments in 2017 to 23M in 2021.

- Global procurement of QAACTs, including the declining projections for the CPM, is projected to decrease from 286M treatments in 2017 to 268M treatments in 2019, before rebounding to 278M by 2021. Although the market will see an increase in funding from donors like the President’s Malaria Initiative (PMI) – Public sector QAACT procurement will peak in 2018 with the addition of new funding from PMI – and increased use of QAACTs in the premium private sector, the decrease in funding for the CPM, and a flattening in public sector procurement will lead to lower projections for QAACT procurement. Expansion of effective Seasonal Malaria Chemoprevention programs could also push QAACT procurement lower as malaria incidence in children is reduced in regions targeted by this intervention. Procurement forecasts for QAACTs and RDTs are driven in large part by availability of financing as opposed to underlying changes in the burden of disease of patient care-seeking behavior.

- QAACT demand and procurement volumes are substantially higher than World Health Organization (WHO)-reported case estimates. This gap is based in part on differences in methodologies used to estimated malaria cases and demand from fever prevalence. However, procurement volumes exceed reported case estimates while access, for malaria-infected patients, to QAACTs remains low, suggesting ongoing use of ACTs in undiagnosed febrile patients, as well as some ACT use in patients who are treated despite having received a negative diagnostic test.

- Despite guidance from the WHO for the market withdrawal of oral artemisinin-based therapies to halt the spread of artemisinin resistance, there is still evidence, observed through sales data collected by IMS, of continued, albeit declining, sales of oral artemisinin monotherapies. We project procurement of oral artemisinin monotherapies to decline from more than 526,000 treatments to just over 175,000 treatments by 2021. Sustained communication of WHO-recommendations for the cessation of oral artemisinin-based monotherapies is warranted to continue to drive down their use. Pressure needs to be sustained on national regulatory authorities and on suppliers to discourage production and licensing of oral artemisinin-based monotherapies for potential use as stand-alone therapies.
• Since the seminal SEAQUAMAT and AQUAMAT clinical trials demonstrated that replacing quinine with injectable artesunate among patients with severe malaria produced sizable reductions in in-hospital adult and child mortality, there has been a concerted effort to advocate for a revision of treatment guidelines to recommend injectable artesunate as the preferred treatment for severe malaria. However, we forecast public sector orders for quality-assured injectable artesunate (QAINJAS) to decline slightly over the forecast period, with approximately 29M 60mg vials procured in 2017, decreasing to 27M 60 mg vials in 2019 through 2021. The slight decline in QAINJAS procurement between 2017 and 2021 is driven by a decrease in projected funding available through the Global Fund for malaria, with the percentage of funding earmarked for QAINJAS procurement remaining stable for each country. We project QAINJAS procurement through other donors to remain flat over this period.

• With the inclusion of rectal artesunate suppositories (100 mg) on the WHO’s Model Essential Medicines List, a product recently receiving approval from the World Health Organization (WHO) Prequalification Programme, and a second product now eligible for procurement according to the Global Fund/Unitaid Expert Review Panel, malaria programs can access quality-assured rectal artesunate (QARAS) for pre-referral treatment of severe malaria. Currently only 28 countries have published treatment guidelines for use of QARAS, and a dozen of them do not have guidelines that align with the WHO’s recommendations for its use. We expect QARAS to be used in limited settings, as per the WHO guidelines, and thus forecast relatively low procurement volumes for this product in countries where guidelines for its use are already in place (288,000 to 351,000 100 mg. suppositories in 2017, expanding to 573,000 to 831,000 in 2021).

• Global procurement of malaria rapid diagnostic tests (RDTs) in the public sector will peak at 274M tests in 2017, and begin a decline, dropping to 243M in 2019, after which procurement may increase slightly to 246M RDTs by 2021. The decrease in RDT procurement after 2017 is driven by a decrease in projected funding available for malaria programs during the upcoming Global Fund funding cycle.

• Despite the declining projections for QAACT procurement during the forecast period, artemisinin demand for production of active pharmaceutical ingredients (APIs) will grow from 176 metric tons (MTs) in 2017 to 218MTs in 2021. This expansion, forecast to occur despite declining malaria prevalence, will be due to increased share of ACTs (including non-QAACTs) among antimalarials and general use of antimalarials in the context of population growth.
BACKGROUND

Sustained international funding for long-lasting insecticidal nets (LLIN), indoor residual insecticidal spraying (IRS) campaigns, quality-assured artemisinin-based combination therapies (QAACTs), and malaria rapid diagnostic tests (RDTs) has led to sharp declines in malaria prevalence and deaths. Mortality from malaria has declined from 839,000 deaths in 2000 to 445,000 deaths in 2016, according to the World Health Organization (WHO).

However, there is evidence that progress against malaria has slowed in recent years, and that the decline in mortality may have reached a plateau. One factor contributing to this slow-down may be the difficulty of ensuring that patients have access to commodities used to prevent, diagnose, or treat malaria. Continuing mortality and morbidity indicate that LLIN and IRS campaigns provide incomplete transmission and infection prevention coverage, and studies indicate that many patients still do not receive prompt and effective treatment. RDTs have not been fully adopted in many markets, especially in the private sector, and a large number of fevers in malaria endemic regions are incorrectly presumed to be caused by malaria, resulting in extensive inappropriate use of antimalarial treatments.

Challenges also extend to the markets for intermediate products and raw materials. Most of the global supply of artemisinin, the key raw material in production of artemisinin-based combination therapies (ACTs) (the WHO’s recommended treatment for uncomplicated malaria), and injectable artesunate (the WHO’s preferred treatment for severe malaria) is derived from agricultural sources. This vegetal product requires a 12 to 14-month cycle from initial planting of the crop to production and shipping of an ACT. Semi-synthetic artemisinin production has a shorter lead-time, but current total global capacity for synthesis of the semi-synthetic product is equivalent to only 25% of global artemisinin demand. Volatility in the artemisinin market has led to concerns over possible ACT supply tightening, resulting in significant risk for market participants and patients whose lives depend on ready access to these medicines.

The emergence of drug and insecticide resistance presents a looming threat to commodity markets and disease control efforts as well. There have been growing signs that resistance to
ACTs is causing declining or delayed treatment efficacy in parts of Southeast Asia. Similar declines in vector sensitivity to insecticides may be causing reduced effectiveness in IRS and bed-nets. Over time, as resistance spreads, new tools will be needed to revitalize malaria control and elimination programs.

In order to address challenges facing the malaria commodity market, the forecasting consortium was established to provide global malaria treatment and RDT forecasts, to identify and assess the uncertainties, and to provide better information to policy makers and market participants on potential shifts in these markets. The forecast methods have been published separately and can be found here: https://unitaid.eu/assets/ACT-and-RDT-Methodology-UNITAID.pdf. The consortium's forecasts project the impact of different trends on the market for malaria commodities at three levels, based on analysis of data from multiple sources including incidence of malaria-like fevers, surveys of treatment-seeking behavior, market data on product imports and sales, surveys of treatment penetration in private and public channels, and country-level procurement trends.

Demand has been projected across three access channels: public sector, formal private sector, and informal private sector, where the formal private sector includes private not-for-profit and for-profit hospitals, clinics, and pharmacies, and the informal private sector includes private drug shops, vendors and general retailers that sell medicines. ACT procurement has been projected across three market categories as well: public sector, subsidized private sector market, and the non-subsidized (premium) private sector market.

Several caveats are important to keep in mind when assessing these forecasts. The antimalarial need and demand forecasts are based on extrapolation of historical household survey data on fever prevalence, malaria prevalence, treatment seeking, testing, and antimalarial treatment, collected from children under age five. New and dramatic shifts in any of these trends would alter the forecasts. ACT and RDT procurement forecasts are based in large part on currently committed funding and historical trends, as opposed to shifts in burden of disease or patient behaviors; changes to contributions by international donors or annual national funding allocations could change overall procurement estimates. Other unforeseen events – such as the use of ACTs for mass drug administration campaigns, the impact of malaria vaccine rollout on
ACT demand, and others – could also alter the outlook for these products at regional and global levels.

In addition, several other factors are likely to inject significant uncertainty into the malaria commodity market in the coming years, and shape the effectiveness of malaria control and elimination programs. Three factors in particular may have a much greater impact in the short term than some of the elements identified in near-term forecasts through 2021. These include:

- Changes in donor funding: Given the importance of donor funding for malaria commodity markets, even small shifts in the size, composition, or procurement requirements related to donor funding could have a dramatic impact on the price and availability of these malaria commodities.
- Expansion of antimalarial drug resistance: Continued progress against malaria is dependent on effective tools, and the intensification or spread of resistance to drugs or vector control tools could cause significant disruptions in the malaria commodity markets and disease control programs.
- Innovation in tools: Continued investment in research and development (R&D) could lead to the launch of new products with superior profiles over the current tools used in prevention, diagnosis and treatment; such innovations could have a dramatic effect on the focus of malaria control efforts and the resulting composition of commodity markets.

METHODS AND DATA UPDATES SINCE THE PREVIOUS REPORT

Since the publication of the previous report, a number of minor updates have been made to the source data: We updated source data for the fevers, need, and demand models based on newly released data from domestic household surveys. Major updates include a decrease in the growth rate assumption for ACTs in the demand forecast (from ~4% annual growth to 2.8% annual growth), and the changes in funding allocations for the CPM in Tanzania, Uganda, and Nigeria.
KEY FINDINGS

ACTs AND ANTIMALARIAL MEDICINES

NEED

We estimate that the need for ACTs will rise between 2017 (999M) and 2021 (1.1 B), largely in line with population growth among at-risk populations. This is derived from estimates of nearly 16B fevers in 2017 among-at-risk populations, approximately 6% of which likely were associated with detectable parasitemia. While associated with Plasmodium falciparum (malaria (P. falciparum)) infection, not all of these fevers were necessarily caused by P. falciparum malaria, and thus, we expect estimations of antimalarial need (based on P. falciparum malaria prevalence applied to febrile incidence) to be greater than reported malaria case estimates; these estimates should be interpreted as a high ceiling to the overall need for antimalarial medicines, rather than as a guide to a necessary volume of ACTs that must be produced by manufacturers and whose procurement must be funded by governments and donor agencies. Substantial reductions in this measure of antimalarial need will require additional large and sustained reductions in P. falciparum malaria prevalence in areas of risk and/or elimination of malaria from large areas (i.e., shrinking the malaria map) – both of which are longer-term objectives.

DEMAND

In 2017, the global demand for antimalarial medicines was estimated to be 1.6B treatment courses. We project that demand for antimalarial medicines will grow to over 1.7B treatments by 2021. ACTs, both quality-assured and non-quality-assured, currently make up 36% of the antimalarial market, with demand for ACTs in 2017 estimated at 576M treatments, and (assuming continued trends in product availability and usage, and owing to population growth in endemic areas and a shift away from use of other antimalarials), will rise to 820M treatments in 2021, comprising 47% of the antimalarial market (Figure 1).
Demand for QAACTs is estimated at 428M treatments in 2017, rising to 539M treatments in 2021 while demand for non-QAACTs is estimated to grow from 147M treatments in 2017 to 250M treatments in 2021, with non-QAACTs comprising about 26% to 32% of estimated ACT demand (Figure 2). Although there is some use of non-QAACTs in the public sector (for example, in Viet Nam), most demand for non-QAACTs is in the private sector, split almost equally between informal and formal sources.
Among QAACT product combinations, artemether-lumefantrine will remain the leader, with consumer demand rising from 328M treatments in 2017 to 433M treatments in 2021. Artesunate-amodiaquine is projected to remain the second most commonly used ACT, with demand growing from 93M treatments in 2017 to 126M in 2021.

Demand for oral artemisinin monotherapies will continue to decline, from 526,000 in 2017 to 175,000 in 2021.

**Figure 2 ACT global demand, by Quality-Assured drug classification and distribution channel, 2017 - 2021 (millions)**
PROCUREMENT

The new Global Fund funding allocations for countries applying for funding during the 2018-2020 period is approximately $3.2B, a figure that is about $1B (31%) lower than the funding allocated for spending on malaria programs in the prior Global Fund funding round (2014-2017). Many high burden malaria-endemic countries have new funding envelopes that are 25% or more below the funding allocations they had during the previous funding round. Since some countries were able to extend that prior envelope over a four-year period, the annual reduction in funding available for procurement of commodities from the Global Fund may not reflect as sharp a decline as the headline number suggests. However, many countries may feel that their funding, over a three-year period, has been reduced, and will have to manage their program needs accordingly. The deadlines for submission of Global Fund funding requests have stretched across the 2017 calendar year, and while we assume that countries will prioritize QAACT, RDT, and QAINJAS commodity purchases over other programmatic expenses, there is a possibility that some countries may reduce commodity purchasing in order to assure that all programs receive, at least, minimally adequate funding. This also means that some countries that have previously participated in the AMFm and CPM have reconsidered their commitment to that program, and we have seen some countries reduce their funding allocations for the CPM, or apply for such funding as an “above allocation” request (e.g., Nigeria).

Barring further reductions in ACT pricing or the introduction of additional funding for their procurement, global procurement of QAACTs is projected to decline from an estimated 286M treatments in 2017 to 268M in 2019 and then recover to 278M treatments in 2021 (Figure 3). QAACT demand and procurement volumes are generally higher than WHO-reported case estimates owing to the use of ACTs in undiagnosed febrile patients, as well as some ACT use in patients who are treated despite having received a negative diagnostic test. The QAACT market could see further declines due to the impact of seasonal malaria chemoprevention (SMC); with the reduction of malaria incidence, and therefore treatment, in children provided SMC in target settings, ACT use may decline, and with continued operation of SMC programs in these regions, we expect a reduction in ACT procurement based on the reduction in malaria cases.
The QAACT procurement forecast contains considerable uncertainty caused by the unclear status of the CPM in countries that have participated in this program in the past. Our model assumes that subsidized QAACT procurement through the CPM will decrease significantly with the reduction in volumes in some CPM countries and the likely termination of the CPM program in Nigeria, a country that accounted for nearly half of all QAACTs procured through AMFm and the CPM. While the scope of CPM-allocated funding among national funding requests remains unclear, if known budget estimates are agreed upon and addition funding commitments do not materialize or new funders do not step in to fill need gaps for the CPM program, then we project a precipitous decline in QAACTs procured through this program; CPM QAACT procurement volumes could fall from an estimated 62M in 2017 to 23M in 2021 (Figure 4). However, if additional funds were committed to sustain or revitalize CPM programs that have planned for funding reductions, and if use of non-subsidized QAACTs continued to expand in the private
sector in both CPM and non-CPM countries, QAACT procurement could potentially rebound toward 396M treatments in 2021.

**Figure 4 Historical and Forecast CPM QAACT Procurement, 2010 – 2021 (millions)**

The forecast period will see steady growth in QAACT volumes in the premium private sector, (from 47M treatments in 2017 to 73M in 2021), and, outside of a spike to 186M treatments in 2018 owing to the influx of additional PMI funding, steady volumes in the public sector (176M to 182M treatments). Among QAACT product combinations, artemether-lumefantrine will remain the market leader, although procurement volume will decline from 217M treatments in 2017 to 194M treatments in 2019 before regaining some volume to reach 204M treatments in 2021, following QAACT procurement trends. Artesunate-amodiaquine is projected to remain the

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second most commonly used ACT, with procurement volume growing from 67M treatments in 2017 to plateau after 2018 at 71M to 72M treatments per year.

QUALITY-ASSURED ARTESUNATE FOR SEVERE MALARIA TREATMENT

The seminal SEAQUAMAT and AQUAMAT clinical trials demonstrated that replacing administration of quinine with injectable artesunate among patients with severe malaria resulted in 34.7% and 22.5% reductions in in-hospital adult and child mortality respectively (3,4). Since the publication of those studies, there has been a concerted effort to engage National Malaria Control Programs and advocate for the revision of treatment guidelines toward recommending injectable artesunate as the preferred treatment for severe malaria.

Because the market for quality-assured injectable artesunate (QAINJAS) remains fairly young, there are few data on which to base assumptions around product uptake. Therefore, we have used current Global Fund procurement plans from high burden countries, as well as data from PMI and Unitaid, to build our forecast projections. We do not currently estimate the private sector procurement of QAINJAS but expect that it will be a small fraction of that in the public sector.

We forecast public sector QAINJAS procurement to be 29M 60 mg. vials in 2017, 27M 60 mg. vials in 2019 through 2021. The forecast decrease in QAINJAS procurement between 2018 and 2021 is driven by a decrease in projected funding available through the Global Fund for malaria, with the percentage of funding earmarked for QAINJAS procurement remaining stable for each country. Procurement through other donors is expected to remain flat.

With the inclusion of rectal artesunate suppositories (100 mg) in the WHO’s Model Essential Medicines List, a product recently receiving approval from the World Health Organization (WHO) Prequalification Programme, and a second product now eligible for procurement according to the Global Fund/Unitaid Expert Review Panel, malaria programs can access quality-assured rectal artesunate (QARAS) for pre-referral treatment of severe malaria. Currently only 28 countries have published treatment guidelines for use of QARAS, and a dozen of them do not have guidelines that align with the WHO’s recommendations for its use. We
expect QARAS to be used in limited settings, as per the WHO guidelines, and we forecast relatively low procurement volumes for this product in countries where guidelines for its use are already in place (288,000 to 351,000 100 mg. suppositories in 2017, expanding to 573,000 to 831,000 in 2021).

**RDTs**

Our model for RDT procurement, which is based on announced and committed funding for public sector procurement, forecasts global public sector procurement of RDTs at 274M tests in 2017, declining to 263M in 2018, and plateauing at 243M in 2019 and 246M in 2021 (Figure 5). This decrease in public sector RDT procurement is driven by a decrease in projected funding available for malaria, with the percentage of funding earmarked for RDT procurement remaining stable, during the coming funding cycle. Conversely, global demand for RDTs is expected to grow over this timeframe, from 754M tests in 2017 to 952M in 2021.

Forecast demand for malaria RDTs is significantly higher than our public sector procurement forecast as the demand estimates rely on test data from household surveys, and extend data on the portion of diagnostic tests conducted using an RDT across all sectors, while the procurement estimates focus on historical orders and procurement plans for the public sector, and do not include estimates of private sector RDT use.
**ARTEMISININ DEMAND**

The market for artemisinin for production of derivative active pharmaceutical ingredients (API) will be influenced by the decline in QAACT procurement (owing to decreases in CPM programs), the growth of non-QAACT usage over the 2017-2020 forecast period, the expansion of general antimalarial use with population growth, and shifts in ACT use as a share of antimalarial treatments (36% in 2017 increasing to 44% in 2020). Artemisinin demand will increase steadily from 176 metric tons (MTs) in 2017 to 218MTs in 2021) with the influx of PMI’s additional funding for malaria programs, and sustained growth in demand for QAACTs and non-QAACTs in the premium private sector. ACTs (both QAACTs and non-QAACTs) comprise the majority of global artemisinin demand (97%), with QAACTs accounting for a large share (50 to 63%) of artemisinin demand.
LONG-TERM OPPORTUNITIES & RISKS

In this final forecast report, it is appropriate to consider longer-term trends and uncertainties that could affect the malaria diagnostic and treatment commodity markets beyond 2021. While there are a number of important issues that policymakers can address to strengthen these markets during the next three years, some of the most important uncertainties in malaria will become clear only after 2021. In highlighting these issues now, we hope to identify potential actions that policymakers can take in the near term to mitigate risks and exploit opportunities in the long run.

There are three major uncertainties that are likely to affect the malaria market after 2021. They are:

1. Changes in the donor funding landscape
2. Intensification and spread of antimalarial drug resistance
3. Innovation in tools

CHANGES IN FUNDING

The decline in malaria-related mortality over the past 15 years has largely been the result of a massive global scale-up of effective interventions targeting malaria control and reduction: the widespread distribution and use of insecticide treated bed nets (ITNs), indoor residual pesticide spraying (IRS), adoption and uptake of effective malaria treatments (ACTs), and expanding use of diagnostics in patients with febrile illnesses. The success of these interventions has been achieved owing to significant investments from governments in malaria-endemic countries, as well as international aid and donor organizations, including the Global Fund, USAID, UKAID, AusAID, Unitaid, UNICEF, CIDA, and countless others. According to the WHO, annual global funding for malaria control and elimination programs has grown from approximately $0.3B in

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2003\textsuperscript{2}, to $2.7B in 2016\textsuperscript{3}. More than half of the $2.7B was directed through the Global Fund, which is funded by contributions from 38 countries and more than 14 foundations and non-governmental organizations. Among donors to the Global Fund, European Union countries contribute approximately 41% of all funding (with the United Kingdom accounting for 12% of the Global Fund’s funding commitments for 2017 – 2020), while United States governmental donations comprise 35% of all pledged contributions to the Global Fund. Countries that are members of the Organization for Economic Co-Operation and Development (OECD) contribute 92% of all funding for the Global Fund, with foundations and other non-governmental organizations contributing approximately 7% of all funding for the Global Fund. The remaining funds are provided by non-OECD countries, including some malaria-endemic countries that are also recipients of Global Fund grants. In addition to funding the Global Fund’s activities, many OECD nations support malaria interventions through their own international development efforts. Chief among these is the USAID’s President’s Malaria Initiative (PMI), which launched in 2005 and in Fiscal Year 2017 (October 2017 through September 2018), will spend $723M on malaria interventions in 24 countries and the Greater Mekong Sub-region (GMS: Cambodia, Lao PDR, Vietnam), including procurement of diagnostic and treatment commodities.

While domestically resourced financing for life-saving malaria treatments, diagnostics, and transmission-preventive measures is increasing, these interventions are in large part funded by governments representing a handful of non-malaria-endemic wealthy nations, represents a vulnerability for malaria control and elimination programs, since changes in funding commitments by a few donor countries could significantly impact the continuity of malaria diagnosis, treatment, and transmission reduction programs in endemic countries. Such an event could tragically reverse the hard-earned reductions in malaria-related mortality that has been achieved by a robust, concerted, and global effort during the past 15 years. Historically, countries that have sharply reduced their funding commitments to malaria have often witnessed subsequently sharp increases in mortality and morbidity as once-controlled malaria epidemics demonstrate rapid resurgence\textsuperscript{4}.

\begin{itemize}
  \item \textsuperscript{2} World Malaria Report, 2009
  \item \textsuperscript{3} World Malaria Report, 2017
  \item \url{https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-11-122}
\end{itemize}
While it is difficult to forecast future funding commitments from donor governments beyond 2021, it is possible that major malaria funders could reduce or reallocate their current level of international aid, presenting recipient malaria programs an increasingly difficult challenge in deciding how best to allocate reduced budgets while simultaneously continuing to reduce malaria morbidity and mortality. Faced with reduced funding from global donors, some national malaria programs might prioritize maintaining adequate funding for preventative measures (e.g., IRS, ITNs), diagnosis, or treatment (ACTs), but other national malaria programs might be forced to make significant cuts to their budget for diagnosis and treatment.

Some programs that receive limited donor funding may be able to fill a potential funding gap using additional domestic funding sources, but such a shift could also impact the mix of commodities procured and the effectiveness of malaria interventions. A number of countries are poised to “graduate” from eligibility for grants from the Global Fund, which has recommended that all upper-middle income countries with malaria, and low- and middle-income countries that have low or moderate disease burden should begin preparation to transition to domestic sources of funding. Because many countries are not yet prepared to take on the entire financial burden for maintaining ongoing malaria programs, a transition from aid-based funding to domestic-based funding poses a number of risks to malaria control and elimination efforts, including threats to continuity of commodity supply, and the potential for factors other than treatment efficacy to shape country procurement decisions. Some countries that shift to domestic financing may, for example, move commodity procurement away from WHO-prequalified products and toward products made by domestic manufacturers who may not have sought or obtained WHO-pre-qualification status. It remains unclear what such a shift would mean for overall artemisinin API demand, for overall demand for QAQTs, for the health outcomes of patients receiving locally produced non-QAQTs or other drugs, or for the course of malaria morbidity and mortality in these countries.

**ANTIMALARIAL DRUG RESISTANCE**

Emerging parasitic resistance to drug therapies has been a hallmark of malaria since the first therapeutic interventions were developed. Policies that require artemisinin derivatives to be used for uncomplicated malaria in fixed-dose combination with partner antimalarial drugs, are based in large part on the desire to protect the artemisinin class from emerging drug-resistance
for as long as possible. While ACTs have largely retained their potency despite more than a decade of widespread global use, the emergence of artesunate and partner-drug resistance in Southeast Asia has led to slower parasite clearance rates and longer courses of treatment among patients using ACTs. The rise of antimalarial drug resistance in the GMS is concerning because this region has historically been the index case for global antimalarial drug resistance, and global malaria programs are worried that the ACT resistant *P. falciparum* variants that are currently gaining a foothold among transmitted malaria in the GMS may make their way to Africa and other endemic regions. The global malaria community has mobilized a significant response to this risk, with funding for regionally coordinated efforts spearheading an effective response to artemisinin resistance in the GMS (e.g., the WHO’s Emergency Response to Artemisinin Resistance, and the Global Fund’s Regional Artemisinin-resistance Initiative). The most certain way to reduce the spread of ACT-resistant malaria parasites would be to eliminate malaria altogether, and while programs in the GMS are building surveillance capacity, increasing access to appropriate medicines by expanding village health worker networks, and considering new techniques to block transmission among high malaria-risk populations, eventually continued usage of ACTs in first-line malaria therapy across the globe will render the spread of resistant parasites inevitable.

A rapid acceleration in the loss of parasitic sensitivity to ACTs in Southeast Asia, or the spread of resistant parasites outside the GMS region and into Africa, could have significant repercussions for both malaria control policies and commodity markets. In such situations, policymakers would have several possible responses to consider. The most immediate goal would be to ensure that patients with ACT-resistant infection are able to survive the infection using the treatment tools at our disposal. This might mean revising treatment guidelines to recommend longer treatment durations, the adoption of triple drug combinations (e.g., artemether + lumefantrine + an additional partner drug), or a rapid shift in treatment regimen across a district or nation. Clearing an infection could reduce the period of time during which an infected individual can transmit malaria to another person. However, another approach for reducing transmission is to administer antimalarial drugs that block the sexual-stage of the parasite (such as primaquine) along with the regular ACT.

Given the uncertain and rapidly shifting state of ACT drug-resistance and the limited arsenal of antiparasitic medicines currently in use, programs have had to cycle through different drug
regimens in pursuit of effective treatment options; there has been some evidence that older antimalarials that had been previously deemed ineffective due to widespread resistance, can be brought back into use after long periods of non-use, owing to the effect of the relaxation of selective drug pressure on parasite populations\textsuperscript{5,6}. The WHO has established guidelines for programs to use to coordinate their response to antimalarial drug resistance\textsuperscript{7}. These guidelines include establishment of a system to monitor therapeutic efficacy, and thresholds and an algorithm for determining when it’s appropriate to switch drug regimens. Beyond these guidelines, regimen shifts would require a coordinated effort across the commodity supply chain, and rapid deployment among care givers located across broad geographies. To enable this, programs must have a flexible policy environment capable of revising and implementing new guidelines or programmatic solutions as scientific evidence changes – despite all remaining uncertainty. Programs that employ regimen shifts are taking shape, particularly in the GMS, but the process has been slowed by concerns about drug wastage, training of care givers who are negotiating the regimen shift, and time-intensive evaluations of the efficacy of a regimen shift in the context of underlying drug sensitivities. The global community and national programs need to develop more rapid and effective approaches to respond to antimalarial drug resistance, developing new approaches (e.g., triple combination therapies), and perhaps applying some lessons learned from clinical management of antibiotic resistance.

**INNOVATION IN TOOLS**

The final major uncertainty facing future malaria diagnostic and treatment commodity markets is the impact of novel tools and approaches to malaria diagnosis, treatment, and prevention. In recent years, several important innovations have been tested and incorporated into malaria control and elimination programs, including injectable and rectal artesunate formulations for treatment of severe malaria, pediatric dispersible formulations of ACTs, and expanding use of SMC in regions where malaria transmission occurs during a period of time that is both predictable and of limited duration. In addition, the recent submission of tafenoquine for


\textsuperscript{7} http://www.who.int/malaria/areas/drug_resistance/overview/en/
regulatory approval offers promise in treatment of *Plasmodium vivax* (*P*. *vivax*) infections, providing a single dose administration (replacing a 14-day primaquine regimen) for radical cure of patients who do not have enzymatic deficiencies (Glucose-6-phosphate dehydrogenase (G6PD) deficiency) that would preclude them from taking this medicine. Each of these interventions benefits a specific patient segment or type of community and together they have contributed to reductions in the burden of malaria.

However, future breakthroughs in diagnosis, prophylaxis, and treatment may hold even greater promise than these several successes. Since its founding in 1999, MMV have promoted the development of many of the world’s early stage malaria drug candidates. MMV’s portfolio includes several products with the potential to reach market after 2021, including candidates from new drug classes with potentially superior characteristics for first-line use in treatment of uncomplicated malaria, when compared to the current ACTs. A single dose radical cure for falciparum malaria, for example, could transform current models for product distribution and case management in malaria control programs. Other drugs might open new paths for prevention campaigns that would also lead to a new era of accelerated progress toward elimination.

Similarly, emerging advances in diagnostics may also have a material effect on epidemic control programs and commodity markets. More reliable or affordable RDTs could enable health programs to expand diagnostic testing of all febrile illness into the private sector market, or into remote geographies where access to laboratory-based diagnosis is limited. Deployment of more sensitive RDTs would be useful in settings that are focused on eliminating malaria and identifying all potential sources of transmission. New diagnostics that are able to detect malaria parasites that lack the phenotypic markers currently detected in today’s RDTs would be helpful in both identifying infections that would have normally gone undetected, and increase the public’s perception of test reliability. Finally, development of broader tests that could be used in integrated fever case management would help ensure that febrile patients receive the appropriate care.

While these innovations appear promising, they remain speculative and will require sustained investments in R&D to complete testing, regulatory approval, and registration. They will also require policymakers to adjust treatment guidelines, overhaul caregiver training programs, and
reinvent procurement processes to enable transformative interventions to be put into practice quickly. Historically, global health innovations have suffered from slow uptake due to the complexity of these processes at both the local and global level, and the multitude of stakeholders involved. Recent experiences with the adoption and use of SMC, injectable artesunate, and future tafenoquine interventions may provide the malaria community with lessons that it could draw on to accelerate the implementation of even more transformative innovations in the future.

Finally, product developers and innovators need to be given clear guidance on the utility gaps and needs in the malaria diagnostic, prophylactic, and treatment landscape, as well as a clear picture of how products that fill those gaps and niches will be used in the context of existing tools. For example, pharmaceutical developers may need to consider whether replacing ACTs is the development goal, or whether the future drug landscape for malaria will look more like that of antibiotics (e.g., novel innovative therapies may be withheld from widespread use to preserve them for use in second- or third-line therapy, or novel therapies might be used only after specific diagnostic testing either of parasite drug sensitivities or the patient’s suitability to withstand potential drug side effects). Developers of novel diagnostics will likewise want to understand how their product would be used, and any niche markets that might be impacted.

All of these concerns and innovations will have lasting impacts on the global market for malaria diagnostic tests and artemisinin-based therapies. While it is difficult to predict how today’s interventions will hold up for the next five to ten years, it’s safe to say that goal will always be to reduce morbidity and mortality, and to use the tools that we have intelligently to achieve these goals and preserve our ability to continue combatting this disease.
POLICY IMPLICATIONS

Sustained and predictable donor funding for QAACTs, injectable artesunate, and RDTs is essential for continued progress toward reducing malaria mortality and morbidity, and maintaining stable and healthy markets for suppliers of malaria treatment and diagnostic commodities.

POLICY IMPLICATIONS FOR ACTs AND ANTIMALARIAL MEDICINES

- The WHO’s 2016 World Malaria Report showed that the median proportion of children under five with recent or current *P. falciparum* malaria who received an ACT was 14% (Figure 4.5, 2016 World Malaria Report). While it is unclear why the remaining 86% of recent or current cases did/do not receive an ACT, our estimates of approximately 1B parasitemic fevers per year indicate that the currently available supply of QAACTs is insufficient to meet overall need; even if all fevers were tested and only confirmed parasitemic fevers were treated with a QAACT, the current procurement of such drugs would cover only one third of all detectable infections. This indicates that as more patients have better access to proper disease diagnosis, the supply of QAACT should grow to meet the need for appropriate treatment of all confirmed infections.

- As national programs (and donors) retreat from supporting private sector access to QAACTs through the CPM, without stemming the resulting degradation of QAACT access through introduction of new and innovative initiatives, the past decade’s achievement – expanding access to QAACTs for people in high-burden countries – may be at risk. ACTs currently comprise approximately 36% of the global antimalarial demand. We forecast that this share will grow to 47% by 2021. However, much of this growth will be from the use of non-QAACTs in the private sector, which will be exacerbated by the projected reductions in funding for the CPM, and QAACT share of ACT demand decreasing from 74% to 68% over this period. As countries begin to shift from donor-funded programs to domestically-funded national malaria programs, some may look to reduce costs and bolster domestic industry by buying commodities manufactured locally. This could lead to an increase in non-QAACT use, and this potential shift may test the global malaria community’s resolve
on the use of QAACTs vs non-QAACTs in both the public and the private sector. The use of non-QAACTs is concerning owing to the varying, unknown quality of these products, potentially leading to a higher risk for mortality and/or induction of artemisinin-resistant malaria with the use of ACTs of substandard quality. With growth in ACT usage, and the likely increased use of non-QAACTs, the global malaria community should consider ways to either renew interest or funding in programs that maintain or increase the use of QAACTs to treat malaria infections in the private sector as a component of targeted case management, phase out the use of non-QAACT medicines, or support pathways for more products to be reviewed by a stringent regulatory authority.

- Sustained support for procurement of malaria commodities is heavily dependent on international funding sources. The 31% decline in Global Fund funding envelopes in the current funding cycle will force countries to make difficult decisions around their health spending priorities. Given the need to sustain robust malaria case management programs, procurement of quality-assured malaria commodities, at least in the public sector delivery channel, will likely be prioritized over other investments. In addition, the malaria community will need to monitor the funding situation and advocate for continued substantial investments to combat this disease.

- Malaria case management will continue to be provided through health systems that include both public and private providers. Policymakers can improve malaria outcomes by focusing on effective stewardship of mixed health systems and by addressing issues specific to each sector. The Global Fund’s private sector co-payment mechanism is responsible for a significant fraction of the QAACP market, and any changes or reductions in this program will likely affect the market for QAACTs, and sustained access to quality-assured antimalarial medicines for many people living in high-risk regions.

- Sustained communication of WHO-recommendations for the cessation of oral artemisinin-based monotherapies is warranted to continue to drive down their use. Further pressure needs to be sustained on national regulatory authorities and on suppliers to discourage production and licensing of oral artemisinin-based monotherapies for potential use as stand-alone therapies.
POLICY IMPLICATIONS FOR RDTs

- The WHO-led focus on expansion of RDT use will help identify malaria infections across diverse settings where febrile patients seek treatment. Although we expect public sector RDT procurement to decrease by nearly 11% from 2017 to 2019 (Figure 5), increased uptake of RDTs in and of itself will not lead to a reduction in antimalarial or ACT use. Sustained donor support for RDT use should continue to be coupled with appropriate treatment follow-up: increasing the percentage of malaria-positive patients that receive appropriate treatment while decreasing the percentage of malaria-negative patients that receive an antimalarial. Such coupled interventions could improve targeting so that all confirmed cases are treated, and valuable QA ACTs are not wasted by misuse in patients who do not have malaria.

- The progress that has been made in expansion of diagnostics in recent years has been remarkable. The WHO reports that there are now fewer ACTs distributed in the public sector in sub-Saharan Africa than diagnostic tests conducted in this region (Figure 2.10, 2016 World Malaria Report). We forecast 274M RDTs will be procured in for the public sector 2017, 93% of them in Africa. This RDT deployment estimate and our estimate that Africa accounts for approximately 26% of annual global fevers in malaria-endemic areas, indicate that countries outside of Africa should potentially increase their focus on expanding access to RDTs. The ratio between procured public sector RDTs and QA ACTs will approach 1:1 in 2017. Although we acknowledge that malaria testing extends beyond the use of RDTs, a 1:1 test-to-treatment ratio is not sufficient given annual estimates of over 4B fevers in this region; the ratio of diagnostic tests to ACTs will have to increase significantly to achieve ubiquitous case management targets. These data reinforce the need for the expansion in the use of diagnostics, coupled with deployment of prompt and appropriately targeted follow-up treatments.
POLICY IMPLICATIONS FOR ARTEMISININ SUPPLY

- We project that despite declining malaria prevalence and increase use of malaria diagnostic tools preceding treatment, artemisinin demand for API will increase throughout the forecast period, owing to the steady increase in ACT share as a portion of antimalarial use. Semi-synthetic artemisinin (SSA), which reduces the start-to-finish production cycle to six or fewer months, has a current maximum total production capacity that is equivalent in size to approximately 25% of the global demand for artemisinin. Therefore, agriculturally-derived artemisinin will continue to play a critical role in supplying artemisinin to meet global demand for artemisinin-based medicines for at least the next three years.

- Despite sustained and stable demand that should help stabilize supply there are potential for external shocks that can impact supply such as weather (droughts or floods), and changes in the prices of competing cash crops. Thus, supply should continue to be monitored to make sure global demand can be met, and policymakers should explore whether specific institutions or consortia are best placed to fulfill this monitoring function.

POLICY IMPLICATIONS FOR LONG-TERM DONOR FUNDING

- Given the importance of international donors to the funding of malaria commodities in endemic countries, it is critical for countries to work to sustain and diversify funding sources. The Global Fund currently provides more than half of the funding of malaria control and elimination programs, and successful replenishments of the Global Fund in future cycles will be vital in sustaining momentum against malaria. In addition to securing continued support from current funders, multi-lateral donors should continue their outreach toward countries that have benefitted from recent economic growth and may be in position to begin or increase their contributions to malaria and other global health conditions while malaria-endemic countries should look for additional ways to sustain and increase domestic investments in malaria interventions.
• As more countries “graduate” from eligibility for Global Fund grants, strengthened regulatory approaches and systems may be needed to protect patient’s health and ensure the continued progress and effectiveness of malaria reducing interventions. Countries that fund malaria programs through domestic financing may prefer to procure commodities from local or regional manufacturers. While that preference may offer certain advantages, it also requires that local and global regulatory systems are equipped to ensure that locally procured commodities meet appropriate quality thresholds and are consistent with other global guidelines (e.g., combination therapies for uncomplicated malaria) and quality standards. Policy makers need to strengthen the capabilities of local regulatory systems to provide adequate oversight. In addition, additional resources for technical assistance and oversight of regulatory compliance and quality-assurance should be provided to support poorly-resourced countries.

• During the period leading up to implementation of the AMFm and throughout the duration of the AMFm and subsequent CPM, donors have focused on private sector market interventions supporting malaria diagnosis and treatment. The private sector continues to play a significant role in providing malaria care for patients in many high-burden settings, yet donor focus on innovative private sector malaria case management programs has waned. This decline in attention to the private sector, happening almost simultaneously across all former private sector-related diagnosis and treatment programs, and coupled with a retreat, in some settings, of regulatory approval for diagnosis access in private sector shops, risks disrupting access to appropriate malaria case management and quality-assured treatments for large populations in the malaria endemic world. The global malaria community should recognize that achievement of the common goals set out by the WHO’s global technical strategy for malaria will more likely be achievable if donors and national programs commit to continue efforts to address the needs of patients who access care through the private sector.

Finally, longer-term funding risks also place a premium on robust evidence demonstrating that investments in malaria are effective and sustainable. Many donors justify their funding based on results and evidence that global aid is effective in reducing or eliminating the burden of malaria is crucial in sustaining and diversifying funding. Additionally, as more malaria tools become available, countries rely on available
evidence to prioritize interventions. Regular program evaluations and operational research are needed to inform resource allocation decisions that country malaria programs take to maximize the impact of interventions in the unique context of their epidemic, and to facilitate the transfer of best practices across regions. While national guidelines often call for universal interventions, in practice more targeted allocation of scarce resources (e.g., IRS, bed-nets, RDTs) to areas of highest benefit can help countries stretch their limited program budgets further without compromising impact. Implementation research that examines the operational effectiveness of different interventions and roll-out strategies can help countries steer their malaria investments to areas of greatest return.

POLICY IMPLICATIONS FOR RESISTANCE

- Parasite drug resistance to artemisinin and ACT partner drugs remains the greatest threat to the progress countries have made in the reduction of malaria mortality. Ongoing surveillance of malaria treatment efficacy in Southeast Asia and elsewhere should continue to be a top priority for health officials. In addition, national malaria programs need to identify and disrupt the practices of market participants that place undue pressure on the artemisinin drug class. While the use of artemisinin monotherapy for uncomplicated malaria is forecast to diminish, regulatory systems in malaria endemic countries still need to intensify their efforts to enforce existing policies. Local health officials should continue to remove artemisinin monotherapies and counterfeit medicines from distribution channels, and on ensure that all sources of malaria treatments (including village workers, private sector players, non-governmental organizations, and others) understand the risks and consequences of resistance, comply in full with policies, and follow standard protocols for reporting suspected and confirmed cases as well as treatment failures.

- Countries need to expand strategies to block the transmission of resistant parasites to prolong the utility of artemisinin-based therapies. The best way to accomplish this is to aggressively pursue malaria elimination in areas that are facing emerging drug resistance, so that malaria transmission is significantly reduced prior to any critical expansion of ACT-resistant parasites. Programs like Zambia’s targeted mass drug administration would add
to ACT volumes and might be useful in key settings. Prophylaxis or vaccines could be helpful when used in populations whose high risk for malaria infection is an occupational hazard, or for populations in holo-endemic transmission settings. Efforts underway in the GMS hold the potential of forestalling the spread of artemisinin resistance, and sustained funding is needed to ensure alternative therapies are available to protect the utility of artemisinin and its partner drugs. Similar efforts with sufficient funding will be needed in other regions where resistant parasites emerge and threaten the continued utility of ACTs. In addition, countries facing the threat of resistant parasites need to explore other mechanisms for blocking the spread of these infections. Strict enforcement of guidelines around use of RDTs before treatments with antimalarials can help avoid unneeded use of ACTs. Outreach and education programs for populations that are at risk of spreading resistant parasites (e.g., itinerant workers, immigrant populations, etc.) also can help reduce the risks that resistant parasites will spread to new areas.

- Given the seriousness of the resistance threat, health officials also should ensure that policy processes are flexible enough to adapt treatment guidelines appropriately to changes in resistance levels. WHO has established guidelines for changes in treatment policies, and these have been applied in Southeast Asia (e.g., Cambodia’s recent switch from using dihydroartemisinin-piperaquine to using artesunate-mefloquine) to increase treatment success rates and limit the spread of artemisinin resistance. These shifts in ACT usage as a response to ACT-resistance would impact the market share of each ACT formulation. However, even greater policy flexibility may be needed in the future, and health officials can take steps today to prepare for worsening artemisinin resistance. For example, endemic countries could register multiple malaria drug combinations now and train caregivers on their use and how to rapidly deploy treatment regimen shifts, in order to avoid future delays when a treatment regimen shift is deemed necessary.

- Policymakers should also re-assess their recommendations for the policy revision process so that countries can expedite changes in treatment guidelines if required. The current model calls for pilot studies with new treatment regimens before treatment guidelines are to be revised, but it may be possible to build a sufficient evidence base with alternative combinations now so that needed policy changes can be accelerated in the future. Greater clarity around the costs and benefits of a triple combination therapy (e.g., an ACT with an
additional partner drug) could also be studied with an eye toward helping countries decide what conditions would trigger a shift toward this intervention in case management, or which triple combination treatment regimen should be pursued. Modeling analyses could help identify the conditions in which alternative approaches, such as rotations of drug combinations, could be effective in managing the impact of artemisinin resistance, and help build generic strategies to help countries manage their guidelines accordingly. It is clear that an effective strategy to rotate treatment regimens will require extensive coordination across the existing supply chain and distribution channels in country, and proactive planning for such a case is essential to achieving success.

**POLICY IMPLICATIONS FOR INNOVATION IN TOOLS**

- After malaria elimination or eradication, the next best solution to the emerging problem of ACT resistance is the development of new anti-malarial treatments. While the R&D pipeline for novel therapies and diagnostics shows great promise, R&D for drugs and diagnostics is both expensive and slow. Policymakers should continue to advocate for sustained investment in these global public goods to ensure that transformative new products are developed and registered for use. Since all new drug classes have eventually faced parasitic resistance, sustained investment in R&D for new malaria treatment likely will be required until disease elimination. Moreover, new tools are needed for a range of applications in malaria, including seasonal chemoprophylaxis, mass drug administration, and prophylaxis and treatment during pregnancy, among others.

- While the ultimate success of late-stage products remains uncertain, they may offer different performance characteristics than current tools, and may lead to breakthroughs in case management strategies for uncomplicated malaria. Careful coordination is needed across a range of stakeholders: health experts to recommend partner drugs in combinations, to identify appropriate applications for the new tools, and update global guidelines; country malaria programs to adopt global guidelines to a local context, and plan for efficient and effective roll out of a new program; manufacturers and funders to align on pricing, procurement and logistics; caregivers and patients to understand factors that may affect roll-out and uptake. To realize the benefits of these new products fully,
policymakers should prepare for the launch of new products long before they are registered. By proactively developing adoption and roll-out plans for new drugs, policymakers can avoid delays in adoption and speed the impact of innovation.

- In the same vein, better guidance to manufacturers is needed about which product applications are priorities in malaria. As successful new therapies for uncomplicated malaria are developed, their use case may become more narrowly defined and nuanced. By identifying and prioritizing these niche applications for novel treatments, policy makers can help drug developers and manufacturers allocate their investments in innovation toward the greatest need. Improved communication with manufacturers will also be critical if the malaria drug market evolves into a direction comparable to the antibiotic market, where new medicines are sometimes held back in reserve in order to provide an insurance policy against emergent resistance. The more manufacturers understand about how their drugs will be used in the overall arsenal against malaria, the better decisions they can make,

- Innovation in RDTs and other diagnostic tools also requires continued support for development and roll-out. New tests with greater sensitivity and reliability have the potential to improve the performance of malaria elimination programs by identifying sub-clinical cases of parasitemia and enabling health officials to target the reservoir of parasites in a community more efficiently. More affordable RDTs or diagnostic tests that can discriminate malaria from other causes of febrile illness could also help malaria control officials allocate drug resources more precisely and ensure that antimalarial drugs are provided only to patients with parasitemia. Driving down the use of ACTs in cases of fever without malaria could reduce resistance pressures and help preserve the potency of artemisinin therapies.