POLICY BRIEF

GLOBAL MALARIA DIAGNOSTIC AND ARTEMISININ TREATMENT COMMODITIES DEMAND FORECAST

2015 – 2018

APRIL 25, 2016

Key Messages

- In 2015, global demand for antimalarial medicines was estimated to be 1.3 billion treatment courses and we forecast that demand for antimalarial medicines will grow to approximately 1.4 billion treatments by 2018. Demand for artemisinin-based combination therapies (ACTs) – inclusive of both quality-assured ACTs (QAACTs) and non-quality assured ACTs (non-QAACTs) – comprised approximately 35% of global antimalarial demand in 2015, and is expected to grow to 47% of global antimalarial demand by 2018.

- Despite recent declines in malaria prevalence, global procurement of QAACTs is projected to grow from 378 million treatments in 2015 to 457 million treatments in 2016, due to an increase in public purchases for endemic country malaria programs. QAACT procurement will decline slightly to 431 million treatments in 2017, and 390 million treatments in 2018, with the decline driven by the extension of historical funding allocations over longer timeframes, as we expect many principal recipients of Global Fund grants will allocate projected funding across the entirety of the three year replenishment cycle rather than across just two years in the three year replenishment period, as many have done during the current replenishment period.

- QAACT demand and procurement volumes are generally higher than World Health Organization (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.

- Non-QAACTs comprise about 25% of estimated global ACT demand, with most of this demand coming from the private sector.

- Public sector orders for quality-assured injectable artesunate will reach 25 million 60mg vials in 2016 before declining to 20 million 60mg vials in 2018. The decrease in quality-assured injectable artesunate procurement between 2016 and 2017 is driven by limited visibility of confirmed orders in the Global Fund's next grant making cycle and our expectation that principal recipients of Global Fund grants will allocate projected funding for QA injectable artesunate procurement across the three years in the replenishment cycle, rather than across two of the three years.

- Global procurement of malaria rapid diagnostic tests (RDTs) was approximately 281 million tests in 2015, and will rise to 384 million in 2016, before declining through 2017 to 327 million in 2018.The decline in RDT procurement will be due to similar changes in funding allocations that will lead to a decline in QAACT procurement in 201 and 2018: we expect many principal recipients of Global Fund grants will spend their projected funds over three years rather than two years.
- Artemisinin demand for production of active pharmaceutical ingredients (APIs) will increase from 197 metric tons (MT) in 2015 to 229 MT in 2016, and remain relatively stable through 2018, despite declining malaria prevalence, due to increased share of ACTs among antimalarials and general population growth.

Policy Brief, 2015-2018

This synopsis is intended to provide 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 forecasts for health and development policy. These forecasts have been produced by a consortium including the Clinton Health Access Initiative, Inc. (CHAI), IMS Health (IMS), and the University of California, San Francisco (UCSF). This consortium is funded by UNITAID and 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).

Background

While 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, continuing mortality and morbidity indicate that LLIN and IRS campaigns provide incomplete transmission and infection prevention coverage, and 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.

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 (roughly 25% of artemisinin demand could be met by the current capacity for semi-synthetic production), and this vegetal product requires a 12 to 14-month cycle from initial planting of the crop to production and shipping of an ACT. 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.

In order to address these issues, 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 consortium's forecasts (The forecast methods have been published separately and can be found here: http://unitaid.org/images/marketdynamics/publications/Global_malaria_diagnostic_and_artemisinin_treatment_commodities_demand_forecast_forecasting_methodology.pdf) 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:

- **Procurement** – represents the volume of commodities that will be purchased in a given year
- **Demand** – represents the volume of commodities or services that would be required to meet all consumer demand for treatment or diagnosis of presumed malaria infections.
- **Need** – represents the number of commodities that would be required to treat all febrile illnesses associated with detectable parasitemia (including cases where the malaria parasite itself is not the source of the fever).

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 will not be reflected in the current forecasts, and we expect to incorporate such changes in disease and market dynamics with the addition of updated survey data, which is made available periodically. ACT and RDT procurement forecasts are based in large part on currently committed funding and historical trends; new or expanded funding could change overall procurement estimates. Unforeseen events – such as a change in the donor funding landscape, the use of ACTs for Mass Drug Administration campaigns, the impact of malaria vaccine rollout on ACT demand, and others – could alter the outlook for these products at regional and global levels, and we aim to analyze additional hypothetical scenarios in future reports.

Key Findings

ACTS AND ANTIMALARIAL MEDICINES

FIGURE 1
ACT Need, by region, 2015 - 2018 (millions)
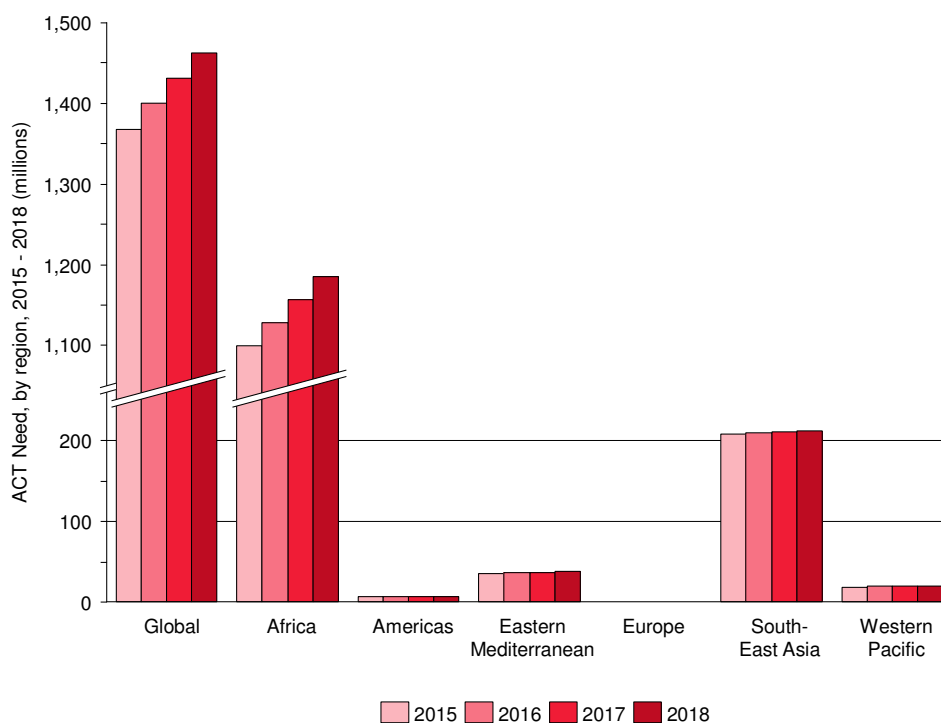
We estimate that the need for ACTs will rise between 2015 (1.37 billion) and 2018 (1.46 billion), largely in line with population growth among at-risk populations (Figure 1). This is driven by estimates of 13.7 billion fevers in 2015 among-at-risk populations, approximately 10% of which likely were associated with detectable parasitemia. While associated with malaria infection, not all of these fevers were necessarily caused by malaria, and thus, we expect estimations of antimalarial need (based on 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 achieved 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 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.

Despite recent declines in malaria prevalence, global procurement of QAACTs is projected to grow from 378 million treatments in 2015 to 457 million treatments in 2016, due to an increase in public purchases for endemic country malaria programs (Figure 2). Barring further reductions in ACT pricing or the introduction of additional funding for their procurement, the number of procured QAACTs will decline slightly to 431 million treatments in 2017, and 390 million treatments in 2018. This post-2016 decline in forecast QAACT procurement will be driven by the extension of historical funding allocations over longer timeframes, as we expect many principal recipients of Global Fund grants will allocate projected funding across the entirety of the three year replenishment cycle rather than across just two years in the three year replenishment period, as many have done during the current replenishment period. 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.

There will be a marked shift in channel mix for QAACTs in this timeframe. We project that procured QAACT volumes in the subsidized private sector will decline from approximately 150 million treatments in 2015 to roughly 100 million in 2016 (owing to changes in the funding structure for the private sector co-payment mechanism program (CPM; formerly the Affordable Medicines Facility for malaria (AMFm)); it has been incorporated into the program budget for Global Fund principal recipients, whereas prior to 2014 it was directly funded by the Bill and Melinda Gates Foundation, Government of Canada, UNITAID and DFID), and according to our projections is expected to hold steady through 2018. This decline in the subsidized private sector will be more than offset by the expansion of public sector orders, which we project will grow from less than 200 million treatments in 2015 to approximately 320 million in 2016. Since estimates of public channel procurement is based on historically committed funding, unless new

funding is made available, public channel procurement is expected to decline to 283 million in 2017, and 236 million in 2018.

FIGURE 2
QAACT market: Historical and forecast growth, 2005 – 2018 (millions)
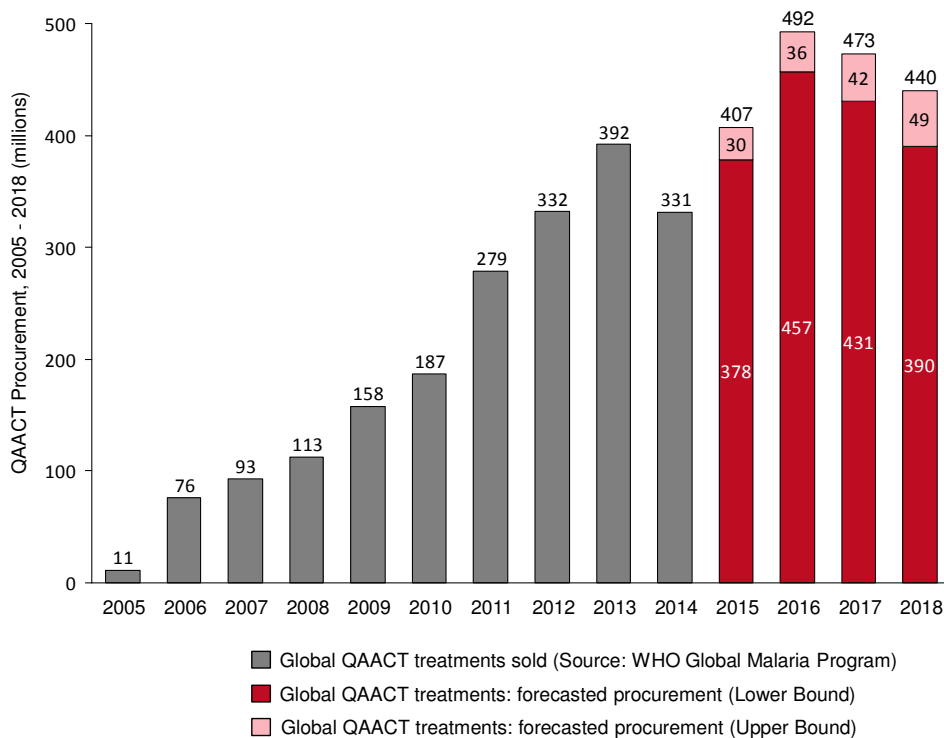
In 2015, the global demand for antimalarial medicines was estimated to be 1.3 billion treatment courses. We forecast that demand for antimalarial medicines will grow to approximately 1.4 billion treatments by 2018. ACTs, both quality-assured and non-quality assured, currently make up roughly one third of the antimalarial market with demand for ACTs in 2015 projected to be 458 million 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 655 million treatments in 2018 (Figure 3).

FIGURE 3
Antimalarial and ACT Demand, by region, 2015 - 2018 (millions)
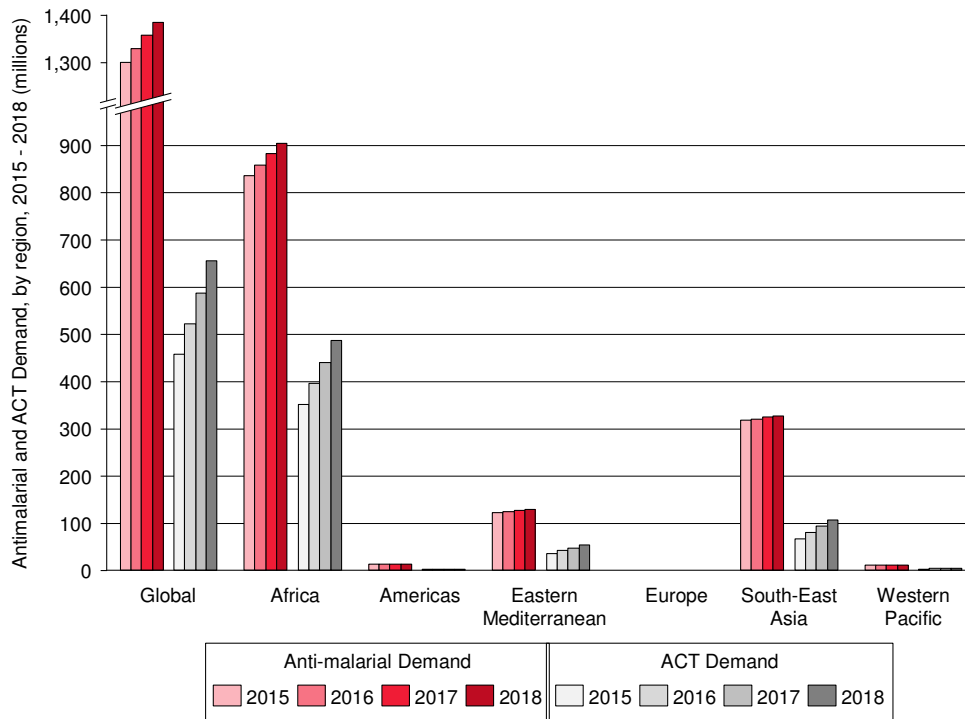

Demand for QAACTs is estimated at 349 million treatments in 2015, rising to 484 million treatments in 2018 while demand for non-quality-assured ACTs (Non-QAACTs) is estimated to grow from 108 million treatments in 2015 to 171 million treatments in 2018, with non-QAACTs comprising about 25% of estimated ACT demand (Figure 4). Although there is some use of non-QAACTs in the public sector (for example, in Viet Nam), most of this demand will be in the informal private sector, where 53% to 55% of non-QAACT treatments will be sold.

Among QAACT product combinations, artemether-lumefantrine will remain the leader, with consumer demand rising from 237 million treatments in 2015 to 327 million treatments in 2018. Artesunate-amodiaquine is projected to remain the second most commonly used ACT, with demand growing from 80 million treatments in 2015 to 111 million in 2018. Demand for artesunate-sulfadoxine-pyrimethamine is expected to increase from 31 million treatments in

2015 to 44 million treatments in 2018, with India as the product's main market. The non-subsidized private sector (premium private sector) market for QAACTs is projected to increase over the next few years from 35M treatments in 2015 to 55M treatments in 2018.

ACT global demand, by Quality-Assured drug classification and distribution channel, 2015 - 2018 (millions)
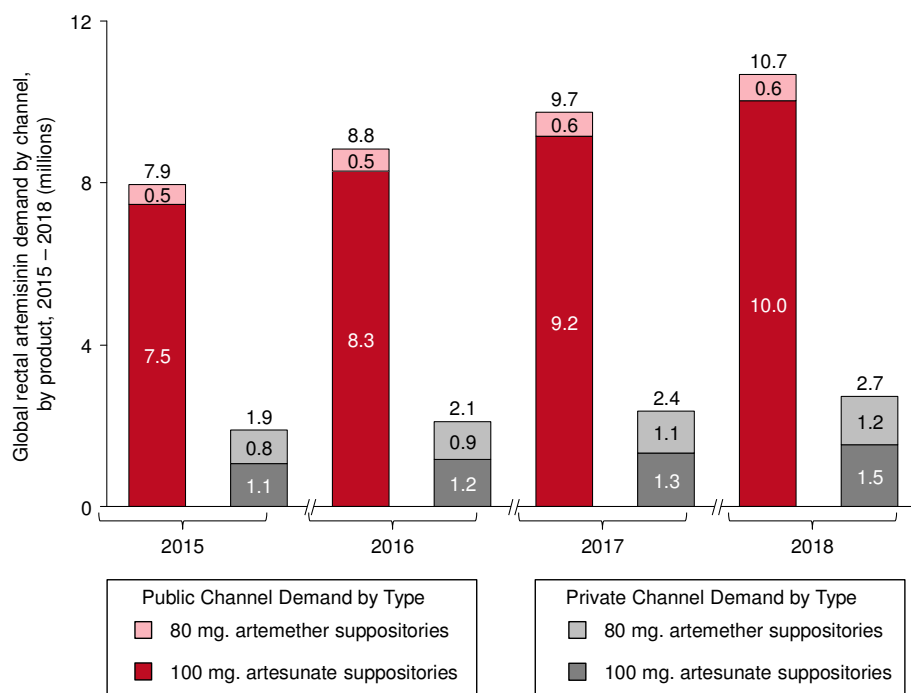
Demand for oral artemisinin monotherapies will continue to decline (from 0.8 million in 2015 to 0.4 million in 2018), and with multiple donor agencies conducting a concerted funding effort to shift severe malaria treatment away from the use of quinine and on to injectable artesunate, public sector orders for quality-assured injectable artesunate will reach 25 million 60mg vials in 2016, before declining to 20 million 60mg vials in 2018. The decrease in quality-assured injectable artesunate procurement between 2016 and 2017 is driven by limited visibility of confirmed orders in the Global Fund's next grant making cycle and our expectation that principal recipients of Global Fund grants will allocate projected funding for QA injectable artesunate

procurement across the three years in the replenishment cycle, rather than across two of the three years.

RDTS

Our model for RDT procurement, which is based on announced and committed funding for public sector procurement, and a subset of estimated private-sector testing demand, forecasts global procurement of RDTs at 281 million tests in 2015, rising to 384 million in 2016, and declining in 2017 to 327 million in 2018, unless additional funding is made available (Figure 5). As it was for the decline in forecast QAACT procurement after 2016, the post-2016 decline in forecast RDT procurement will be driven by the extension of historical funding allocations over longer timeframes, as we expect many principal recipients of Global Fund grants will allocate projected funding across the entirety of the three year replenishment cycle rather than across just two years in the three year replenishment period, as many have done during the current replenishment period. Demand for RDTs is expected to grow over this timeframe as well, from 406 million tests in 2015 to 438 million in 2018. Most of this demand will be met in the public sector, although the private sector will meet up to a quarter of global demand.

FIGURE 5

RDT procurement by channel, 2015 - 2018 (millions)
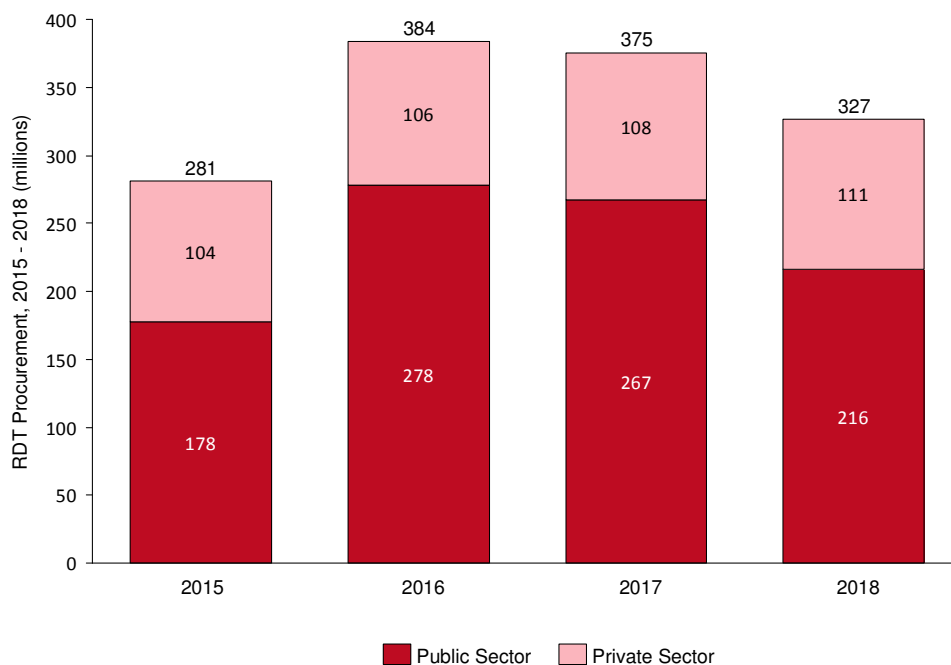
ARTEMISININ DEMAND

The market for artemisinin for production of derivative active pharmaceutical ingredients (API) will remain robust over the 2015-2018 forecast period, given the expansion of general antimalarial use with population growth, and shifts in ACT use as a share of antimalarial treatments (35% in 2015 increasing to 47% in 2018). The increase in artemisinin demand from 197 metric tons (MT) in 2015 to 229 MT in 2016 is largely driven by a forecasted 79 million increase in QAACTs procured in 2016. While current donor funding estimates indicate that QAACT procurement may decline in 2017 and 2018, increasing demand for non-QAACTs, particularly in the private sector market, will sustain global demand for artemisinin at around 227 (MT) in 2017, and 232 MT in 2018. ACTs (both QAACTs and non-QAACTs) comprise the

majority of global artemisinin demand (97%), with QAACTs accounting for a large share (64-73%) of artemisinin demand.

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 2015 World Malaria Report showed that the portion of children under five with confirmed *P. falciparum* malaria who received an ACT was less than 22% (Figure 3.13, 2015 World Malaria Report). While it is unclear why the remaining 78% of confirmed cases do not receive an ACT, our estimates of approximately 1.4 billion 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 supply 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 must grow to meet the need for appropriate treatment of all confirmed infections.

- ACTs currently comprise approximately 39% of the antimalarial demand. We forecast that this share will grow to 47% by 2018. However, much of this growth will be from the use of non-QAACTs in the private sector, as the QAACT share of ACT demand will decrease from 75% to 73%. The use of non-QAACTs is concerning owing to the potentially higher risk for mortality and/or induction of artemisinin-resistant malaria with the use of these potentially sub-standard ACTs. With growth in ACT usage, and the expected increased use of non-QAACTs, the global malaria community should consider ways to either phase

out the use of non-QAACT medicines, or provide a pathway for these products to become quality-assured, at the national, regional, or global level.

- 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 QAACT market, and as such, any changes or reductions in this program might affect the market for QAACTs.

- 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 increase by nearly 50% from 2015 to 2016 (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 must 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 QAACTs 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. We forecast 384 million RDTs will be procured in 2016, 79% of them in Africa. However, given annual estimates of ~3.7 billion fevers in this region, the ratio of ACTs to diagnostic tests will have to drop significantly to achieve ubiquitous case management targets. This reinforces 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 remain stable 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 production capacity that accounts for approximately 25% of the global demand. 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.