# Seasonal Malaria Chemoprevention: Supply & Demand Update

**UNICEF Supply Division**

**September 2017**

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## 1. Summary


- Seasonal Malaria Chemoprevention (SMC) is the highly cost-effective[1] intermittent administration of antimalarial medicine during the high malaria transmission season. SMC can prevent malaria by maintaining therapeutic antimalarial drug concentrations in the blood throughout the season of peak malarial transmission.
- SMC comprises a treatment course of amodiaquine (AQ) and sulfadoxine-pyrimethamine (SP), and targets children between 3 and 59 months in the Sahel sub-region of sub-Saharan Africa (SSA), where *P. falciparum* is sensitive to both antimalarial medicines. To achieve universal SMC coverage, UNICEF estimates between 25-30 million children between 3 to 59 months must receive SMC every year, representing approximately 100-120 million treatment courses annually.
- Since 2013, UNICEF has been supporting countries and partners scale up SMC programme implementation by assisting them with SMC procurement, supply chain planning, management, and health systems strengthening. In 2016, SMC programme implementation, including programmes supported by UNICEF, only reached 10.2 million children. The overall target for 2017 is to reach 14 million children, leaving 11-16 million children without protection.
- The scale up of SMC programmes is largely constrained by limited sources of quality-assured AQ+SP. Currently there is only one global manufacturer of quality assured AQ+SP with a production capacity to cater for 5 to 6 million children annually in a market that currently offers limited incentives to manufacturers. Improved demand forecast and advocacy are needed to encourage increased product availability for SMC campaigns and to scale up programme implementation.
- The Malaria Medicines Venture (MMV), as part of UNITAID's partnership with the ACCESS-SMC consortium, is working with partners to improve AQ+SP child-friendly product development, availability, and supports an interactive forecasting platform to improve SMC product demand forecasts.
- UNICEF supplies AQ+SP in dispersible and non-dispersible tablets. UNICEF, WHO, and the Pan American Health Organization (PAHO) will launch a joint tender for antimalarial medicines in 2017, which includes SMC products. UNICEF will seek to diversify its SMC AQ+SP supplier base and award long-term arrangements (LTAs) for SMC supply, as well as encourage suppliers to seek co-packed product WHO prequalification.


## 2. General Brief and Background

Malaria is a leading cause of under-five child mortality accounting for at least five percent of the 5.9 million child deaths in 2015.[2] In 2015, there were an estimated 212 million cases of malaria and 429,000 deaths, of which 90 percent occurred in SSA.[3] In 2015, WHO launched the *Global Technical Strategy for Malaria 2016-2030* to reduce the global malaria burden by 90 percent by 2030. The strategy comprises three pillars. Pillar one focuses on ensuring universal access to quality-assured vector control, chemoprevention, diagnosis, and treatments, including SMC (Table 1).[4]

[1] World Health Organization, *Seasonal Malaria Chemoprevention*, WHO, Geneva, 2017.
[2] World Health Organization, *Under-five Mortality*, WHO, Geneva, 2016.
[3] World Health Organization, *World Malaria Report 2016*, WHO, Geneva, 2016, pp. xii-xiii.
[4] World Health Organization, *Global Technical Strategy for Malaria 2016-2030*, WHO, Geneva, 2015, pp. 11-16.

Table 1 Pillar One of the Global Technical Strategy for Malaria Interventions

| Intervention Pillar | Components |
|---|---|
| Vector Control | - Long-lasting insecticidal nets (LLINs),<br>- Indoor residual spraying (IRS). |
| Chemoprevention | - Intermittent preventive intervention therapies for infants (IPTi),<br>- Intermittent preventive intervention therapies for pregnant women (IPTp),<br>- Seasonal malaria chemoprevention (SMC),<br>- Chemoprophylaxis for non-immune travellers. |
| Diagnostic Testing and Treatment | - Quality-assured microscopy,<br>- Malaria rapid diagnostic tests (mRDTs),<br>- Quality assured artemisinin-based combination therapies (ACTs), and Non-ACTs. |

Source: World Health Organization, GTS 2016-2030

In 2012, WHO recommended SMC with AQ+SP for children aged 3-59 months, in areas in SSA with high seasonal malaria transmission, where *P. falciparum* is sensitive to both antimalarial medicines. SMC is the intermittent administration of a full course of antimalarial medicine at monthly intervals throughout the peak high malaria transmission season (which can be up to four months) (Table 2).[5] SMC can prevent malarial illness by maintaining therapeutic antimalarial drug concentrations in the blood. Evidence suggests that SMC can prevent 75 percent of all malaria episodes, 75 percent of all severe malaria episodes, and reduce child mortality by one in a thousand.[6]

Table 2 SMC Intervention Protocol in Geographical Target Criteria

| Target caseload | Protocol |
|---|---|
| **>95% Infants 3 - 11 months** | 1 x 3 days x 76.5mg tab amodiaquine base<br>1 x 1 day x 250/12.5mg tab sulfadoxine-pyrimethamine (on 1st day)<br>1 x month - up to 4 months maximum |
| **>95% Children 12 - 59 months** | 1 x 3 days x 153mg tab amodiaquine base<br>1 x 1 day x 500/25mg tab sulfadoxine-pyrimethamine (on 1st day)<br>1 x month - up to 4 months maximum |
| **Alternative antimalarial interventions should be sought if breakthrough *P. falciparum* malaria infection occurs during SMC administration** | |

Source: World Health Organization

WHO recommends the parasitological confirmation of malaria in all settings prior to treatment using quality assured diagnostics. It recommends countries to use malaria Rapid Diagnostic Tests (mRDTs) or microscopy for clinical malaria diagnosis in all transmission settings.[7] The availability of mRDTs is essential in SMC-targeted areas to determine whether febrile children receiving SMC suffer from breakthrough malaria infection. Should they detect breakthrough cases of *P. falciparum* malaria, WHO recommends the use of ACTs.

Although different approaches to SMC implementation exists, WHO recommends SMC should be integrated into existing programmes, where possible, with individual approaches best suited to local conditions, such as through community case management (CCM) or community health workers (CHW). UNICEF seeks AQ+SP co-packed products to encourage course compliance and adherence.

[5] World Health Organization, *Seasonal Malaria Chemoprevention with Sulfadoxine-Pyrimethamine plus Amodiaquine in Children: A Field Guide*, WHO, Geneva, 2013, p.3.
[6] Ibid., p. 5.
[7] World Health Organization, *Policy Brief on Malaria Diagnostics in Low-Transmission Settings*, WHO, Geneva, September 2014.

The co-packaging component simplifies the administration instructions, which the CHWs give to the parents or the caretakers of children.

Countries need to consider the seasonality in rainfall, malaria endemicity, as well as the therapeutic efficacy of AQ+SP in targeted areas. Countries considering SMC implementation should do so against alternative intervention considerations, such as intermittent preventive intervention therapies for infants (IPTi).[8]

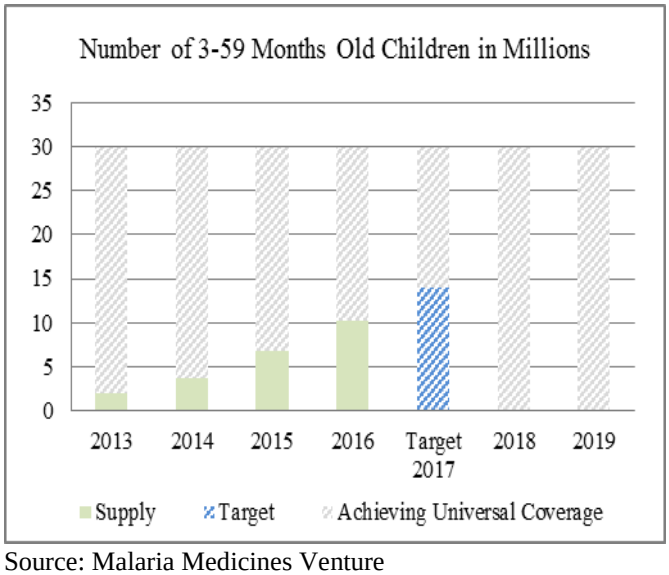
UNICEF, in collaboration with partners, supports SMC implementation through national malaria control programmes in target countries. Partners include the Global Fund to Fight AIDS, Tuberculosis, and Malaria (the Global Fund); Médecins Sans Frontières (MSF); the Roll Back Malaria (RBM) Partnership; WHO; and the World Bank (WB). In addition, UNICEF collaborates with UNITAID's partnership with ACCESS-SMC's consortium, which is comprised of Catholic Relief Services (CRS); the London School of Hygiene and Tropical Medicine (LSHTM); the Malaria Consortium; Management Sciences for Health (MSH); Medicines for Malaria Venture (MMV); and Speak Up Africa (SUA).

## 3. Current Market Situation

### 3.1.Demand and Forecast

WHO identified fifteen countries suitable for SMC implementation in accordance with geographical target criteria.[9]. In 2013, only three countries had adopted and implemented SMC interventions, which gradually increased to reach nine in 2015. As of 2016, 11 countries (Burkina Faso, Cameroon, Chad, Gambia, Ghana, Guinea, Mali, Niger, Nigeria, Senegal, and Togo) have adopted and implemented SMC interventions with an aggregate estimated target population of approximately 25-30 million children of 3-59 months of age, as projected by current country-consolidated demand.

Figure 1 SMC Coverage of Children Aged 3-59 Months 2013-2016 and 2017 Forecast




Source: Malaria Medicines Venture

As of 2016, only 10.2 million children received SMC, leaving 15-20 million children without protection for the season. The target in 2017 for all countries implementing SMC intervention is 14 million children, leaving 11-16 million children without protection (Figure 1). The 2017 target excludes any proposed expanded age range coverage by some countries, which if confirmed, would significantly increase current demand requirements even further. Some countries, like Burkina Faso and Guinea, are looking to extend their target age group for children from under five up to ten years of age, potentially increasing demand requirements further beyond the 30 million estimated caseload.

[8] **Note**: IPTi is a full course of SP administered to infants at routine immunization visits during the 1st year.
[9] World Health Organization, *World Malaria Report*, WHO, Geneva, 2015, p. xii

The current demand for 25-30 million children equates to an estimated need for 100-120 million courses, assuming the maximum WHO recommended AQ+SP administration of four rounds per season during the high transmission season, equating to one per month for four months.[10] Although there are uncertainties and limitations attached to each country's target caseload estimates, as these draw from population censuses and programmatic plans, UNICEF considers the demand for the SMC products high for the current 11 SMC implementing countries.

### 3.2. Supply

Country SMC implementation to date has been limited due to a number of factors. Not all target countries have adopted SMC policy intervention protocols into their national guidelines. In the absence of a policy, intervention resource mobilisation and implementation becomes difficult.

Currently, 50 percent of the global SMC target is unmet, largely due to limited supply of quality assured product. UNICEF procures AQ+SP for approximately ten percent of the global SMC target, while the ACCESS-SMC consortium procures for approximately 35 percent of the global target.

WHO recommends whenever possible to use fixed dose combination (FDC) tablets, rather than co-blistered or loose, single agent formulations to facilitate treatment adherence.[11] However, even though both AQ and SP are available as individual tablets, currently there is no proven technology to produce a FDC of AQ+SP. The best alternative is to co-blister AQ+SP treatment course for SMC administration by CHWs. At present, there is one quality assured source of co-blistered AQ+SP on the market (manufactured by Guilin Pharmaceutical Company). As there are uncertainties around both the future size of the market and the return on investment for a low-margin product, the market offers limited incentives for manufacturers to invest in AQ+SP research and development (R&D).[12]

UNICEF only procures quality assured pharmaceutical products, which comply with recognised international standards[13].Current AQ+SP global supply availability and security is vulnerable, as it is dependent on Guilin Pharmaceutical Company as the single source supplier. A few manufacturers have indicated having AQ+SP both dispersible and non-dispersible presentations in their R&D pipeline, and it is anticipated that one of them will have the product commercialised in 2018.

Although UNICEF can supply both non-dispersible tablet and dispersible tablet formulations for SMC through LTAs with Guilin Pharmaceutical Company, UNICEF continues to advocate for the child-friendly dispersible presentation (Table 3).

Table 3 UNICEF Available Products and Packaging Specifications

| Material Number | Short Description | Shelf Life | Indicative Price |
|---|---|---|---|
| **Non-Dispersible Tablets** | | | |
| S1532005 | SP 500/25mg tab/3+AQ 150mg tab/1/PAC-25 | 36 Months | US$ 6.87 |
| S1532006 | SP 250/12.5mg tab/3+AQ 75mg tab/1/PAC-25 | 36 Months | US$ 6.12 |
| **Dispersible Tablets** | | | |
| S1532008 | SP 250/12.5mg disp tab/3+AQ 76.5mg disp tab1/PAC-50 | 24 Months | US$ 13.25 |
| S1532009 | SP 500/25mg disp tab/3+AQ 153mg disp tab/1/PAC-50 | 24 Months | US$ 14.75 |

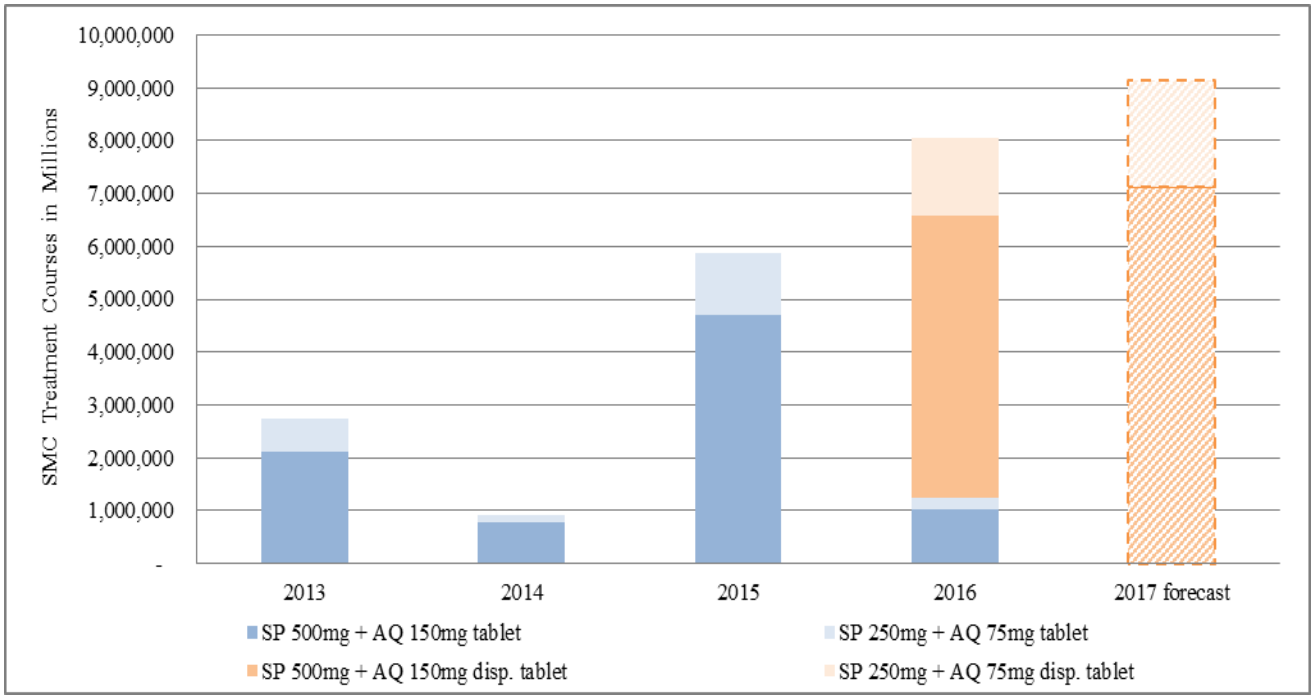
Source: UNICEF Supply Division

[10] World Health Organization, *WHO Information Note: Addressing the Current Medicine Shortages for Seasonal Malaria Chemoprevention.* WHO, Geneva, April 2015.
[11] World Health Organization, *Guidelines for the Treatment of Malaria*, 3rd Edition, WHO, Geneva, 2015
[12] UNITAID, *Malaria Medicines Landscape*, Geneva, 2015
[13] UNICEF Technical standards - Pharmaceutical products, https://www.unicef.org/supply/index_52844.html

The current global production of quality SMC pharmaceuticals falls far short of demand. Guilin Pharmaceutical Company's overall current capacity is limited to seven million tablets per month, which equates to 84 million tablets a year, equivalent to 21 million courses, covering five to six million children with four cycles per season. In 2015, Guilin commercialised dispersible tablets of AQ+SP tablet, which addressed some of the challenges related to course administration feasibility, acceptance, and adherence. Previously, caregivers had to crush and mix AQ+SP tablets with water and sugar to ensure acceptance by children.[14]

UNICEF represents approximately 20 percent of total global AQ+SP supply, while ACCESS SMC consortium represents approximately 70 percent, and the balance shared between Médecins Sans Frontières (MSF) and Global Fund to Fight AIDS, Tuberculosis, and Malaria (the Global Fund), with some of the Global Fund's supply going through UNICEF. From 2013 through 2016, UNICEF cumulatively procured over 17 million SMC treatment courses for children. In 2017, UNICEF anticipates to procure 9 million treatment courses, which translate into covering 2.25 million children (approximately ten percent of global targets) (Figure 3) with SMC.

Figure 2 UNICEF SMC Procurement in Courses 2013-2017 (forecast)




Source: UNICEF Supply Division

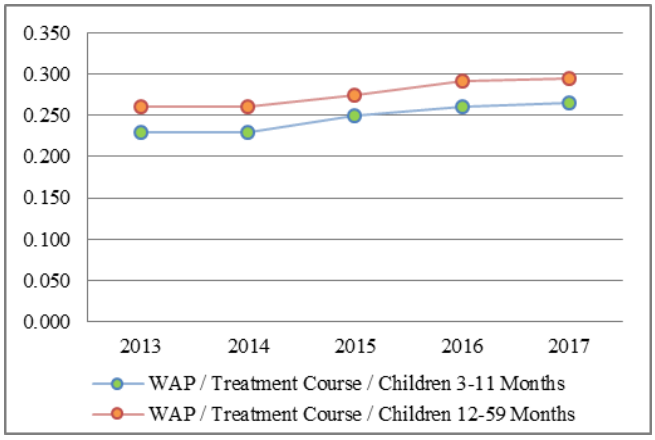
AQ+SP timely delivery is also incredibly important given the seasonality of increased disease transmission, and the necessary timing of associated catch-up campaigns. WHO reported that Guilin Pharmaceutical Company, as a single source manufacture, had difficulty in fulfilling some orders,[15] which undermined supply security for quality assured AQ+SP, and limited SMC programme implementations in a number of countries.

[14] Misiorowska, Aleksandra, *AQ+SP for Seasonal Malaria Chemoprevention*, Roll Back Malaria, Geneva, October 2013.
[15] World Health Organization, *WHO Information Note: Addressing the Current Medicine Shortages for Seasonal Malaria Chemoprevention*., WHO, Geneva, April 2015

To support national and global efforts to increase access to and the affordability of care and treatment of malaria, WHO, together with UNICEF, UNAIDS and UNITAID, invite manufacturers of selected pharmaceutical products to submit Expressions of Interest (EOIs) for product evaluation. WHO has listed AQ+SP products amongst the medicinal products for the annual EOIs since the 10th invitation in 2012, and have continued to list them in all the subsequent EOI invitations, including the most recent one, the 15th Invitation.

## 4. Pricing

Figure 3 Supply Cost of SMC Treatment Course Per Child through UNICEF 2013-2017




Source: UNICEF Supply Division

The cost of SMC supply through UNICEF has remained relatively stable, increasing by approximately 0.035 USD per treatment, per child between 2013 and 2017. Cost increases reflect costs related to treatment course pack-size reductions from 50 to 25, and a change from non-dispersible tablets to dispersible tablets. UNICEF estimates the cost to supply AQ+SP at US$ 0.30 per child per cycle / month or US $ 1.20 per child, per year.[16] WHO estimates the cost of the whole SMC package to be US$ 0.50 per child per month, or US$ 1.50 to US$ 2.00 per child per year.

## 5. Issues and Challenges

- Fifty percent of SMC targets are unmet, largely due to the limited supply of quality assured AQ+SP, with only one global manufacturer with a quality assured product.
- Reliance on one manufacturer presents a risk to supply security. In 2014, WHO reported that Guilin Pharmaceutical Company had difficulty in fulfilling some orders,[17] which resulted in supply constraints during 2014 through 2016, including for procurement through UNICEF. UNICEF facilitated cross-country supply of AQ+SP, thanks to the flexibility by some countries that adjusted their campaign schedules in support of neighbouring countries.
- SMC is a timed intervention. To ensure timely availability at the distribution points at the start of the malaria transmission season, SMC medicines must arrive in country well in advance of the rains season. Countries should communicate AQ+SP demand and SMC implementation plans to UNICEF at least 12 months before product is required at distribution sites in country.
- Inaccurate population censuses and ill-defined target age-group definitions risk inaccurate target caseload estimates. Current market supply constraints require accurate country demand forecasts to ensure the effective and efficient use of limited supply.
- Alternative combination therapies are required for SMC adaptation in regions where AQ+SP retains less than 90% efficacy.

[16] UNICEF Supply Division
[17] World Health Organization, *WHO Information Note: Addressing the Current Medicine Shortages for Seasonal Malaria Chemoprevention*., WHO, Geneva, April 2015

- Support for CCM and CHW is required to ensure adequate intervention guideline administration, patient adherence to prescribed regimens, and an understanding of alternative and complementary treatment therapy.
- Key challenges to the scale-up of SMC include the costs and complexities of delivery that requires mass distribution during the rainy season when logistics are most difficult.

## 6. Steps Forward

- UNICEF will work with partners to align with the interactive forecasting platform.[18] ACCESS-SMC intends to aggregate funded demand and give visibility to Guilin Pharmaceutical Company on the timing of requests, to ensure that Guilin Pharmaceutical Company can manufacture AQ+SP at set frequencies throughout the year and allocate supply rationally at the required time.
- UNICEF will engage actively with WHO's prequalification programme, WHO's Global Malaria programme, The Global Fund, UNITAID, and MMV, to accelerate the process for alternative products to enter the SMC market in 2018.
- UNICEF will continue to present the global demand and the unmet needs for SMC products through its regular interactions with suppliers, and at the industry consultation forum, planned for 1H 2018.
- UNICEF will continue to advocate to national malaria control programmes and donors to mobilize resources to scale up SMC implementation and achieve targets.
- During 2H 2017, UNICEF, WHO, and PAHO will launch a joint tender for the procurement of antimalarial medicines, which includes AQ+SP for SMC implementation, with the objective of diversifying the LTA supplier base of AQ+SP, and facilitating market entry. UNICEF will highlight product demand and requirements, and will extend invitations to all suppliers that have AQ and SP products in their R&D pipeline to ensure that UNICEF does not lock out any potential suppliers for an LTA tenure.

Table 4 2017-2018 Expected Antimalarial Medicines Tender Timeline

| Activity | Timeline |
|---|---|
| Request for Expression of Interest | July 2017 |
| Finalisation of Invitee list | August 2017 |
| Request for Proposal issued | September 2017 |
| Closing date for submission of proposals | November 2017 |
| Opening of submitted proposals | November 2017 |
| Clarification and evaluation of proposals | November 2017 - March 2018 |
| Contract Review Committee Meeting | April 2018 |
| Announcements of Awards | May 2018 |
| Long Term Agreement Establishment | May 2018 |
| Quarterly review of Supplier performance | Regularly every quarter |

Source: UNICEF Supply Division

[18] ACCESS-SMC, *SMC Forecasting Platform: A Tool to Support SP+AQ Availability*, the Malaria Consortium, London, 2017.

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Other UNICEF information notes can be found at: http://www.unicef.org/supply/index_54214.html.