SEASONAL MALARIA CHEMOPREVENTION

WITH SULFADOXINE–PYRIMETHAMINE PLUS AMODIAQUINE IN CHILDREN

A FIELD GUIDE

World Health Organization

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ABBREVIATIONS

AQ	amodiaquine
SMC	seasonal malaria chemoprevention
SP	sulfadoxine–pyrimethamine
WHO	World Health Organization

1. BACKGROUND

Malaria remains a major public health problem, with an estimated burden of 216 million clinical episodes and 655 000 deaths worldwide attributable to malaria in 2010.[1] A significant proportion (91%) of reported deaths from malaria occurs in sub-Saharan Africa, where children under 5 years of age bear most of the burden. In 2010, it is estimated that 86% of all malaria deaths occurred in this age group.

Across the Sahel sub-region, most childhood mortality and morbidity from malaria occurs during the rainy season, which is generally short. Giving effective antimalarial medicines at full treatment doses at appropriate intervals during this period has been shown to prevent illness and death from malaria in children.

The interventions currently recommended by the World Health Organization (WHO) for the control of malaria are use of long-lasting insecticidal mosquito nets and/or indoor residual spraying for vector control, prompt access to diagnostic testing of suspected cases and treatment of confirmed cases with effective artemisinin-based combination therapy. In addition to these, other interventions recommended for specific high-risk groups in areas of high transmission include intermittent preventive treatment in pregnancy and infancy.

With the changing epidemiology of malaria, there has been a progressive shift from a 'one size fits all' approach to targeting malaria control strategies to specific populations and/or locations for maximal effectiveness. In line with this approach and on the basis of new evidence, WHO recommends an additional intervention against *Plasmodium falciparum* malaria: seasonal malaria chemoprevention (SMC). This intervention has been shown to be effective, cost-effective, safe and feasible for preventing malaria among children under 5 years of age in areas with highly seasonal malaria transmission.

SMC is defined as "the intermittent administration of full treatment courses of an antimalarial medicine during the malaria season to prevent malarial illness with the objective of maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk."[2]

1 World Health Organization. *World malaria report 2011*. Geneva, 2011. http://www.who.int/malaria/world_malaria_report_2011/9789241564403_eng.pdf.

2 World Health Organization. *Report of the technical consultation on seasonal malaria chemoprevention (SMC)*. Geneva, 2011. http://www.who.int/malaria/publications/atoz/smc_report_teg_meetingmay2011.pdf.

2. WHO POLICY RECOMMENDATION FOR SEASONAL MALARIA CHEMOPREVENTION[3]

SMC is recommended in areas of highly seasonal malaria transmission throughout the Sahel sub-region. A complete treatment course of sulfadoxine–pyrimethamine (SP) plus amodiaquine (AQ) should be given to children aged 3–59 months at monthly intervals, beginning at the start of the transmission season, up to a maximum of four doses during the malaria transmission season (provided both drugs retain sufficient antimalarial efficacy).

The recommended dosing schedule by age is:

- infants 3–11 months old: half of a 153mg tablet of AQ base given once daily for 3 days and a single dose of half a 500/25mg tablet of SP; and
- children 12–59 months: a full tablet of 153mg AQ base given once daily for 3 days and a single dose of a full tablet of 500/25mg SP.

The single dose of SP is given only on the first day, at the same time as the first dose of AQ.

The target areas for implementation are those in which:

- malaria transmission and the majority (> 60%) of clinical malaria cases occur during a short period of about 4 months;
- the clinical attack rate of malaria is greater than 0.1 attack per transmission season in the target age group; and
- SP + AQ remains efficacious (> 90% efficacy).

Contraindications

SMC should not be given to:

- a child with an acute febrile illness or to severely ill children unable to take oral medication;
- an HIV-positive child receiving co-trimoxazole prophylaxis;
- a child who has received a dose of either SP or AQ during the past month; and
- a child who is allergic to either SP or AQ.

Breakthrough malaria infections that occur during SMC administration should not be treated with drug regimens containing either SP or AQ.

[3] World Health Organization. *WHO policy recommendation: seasonal malaria chemoprevention (SMC) for Plasmodium falciparum malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa.* Geneva, 2012 http://www.who.int/malaria/publications/atoz/who_smc_policy_recommendation/en/index.html

Considerations for deployment of SMC

SMC with SP + AQ should not be implemented in areas with high levels of resistance to SP or AQ.

While there are several potential approaches to implementing SMC, there is presently insufficient evidence to recommend a standard strategy, and individual approaches best suited to the local conditions should be used. If possible, SMC should be integrated into existing programmes, such as community case management and other community health worker schemes.

The results of clinical trials indicate that a high level of protection against uncomplicated clinical malaria is likely to be maintained for only 4 weeks after administration of each treatment course of SP+ AQ; thereafter, protection appears to decay rapidly.

For maximum protection, and to minimize selection of drug resistance, children should receive SMC each month during the transmission period and should take the complete 3-day course each month.

In areas where SMC is deployed:

- Pharmacovigilance should be strengthened where it exists and should be instituted where it does not.
- Drug resistance monitoring and system evaluation should be supported or instituted, including systems to assess the number of breakthrough infections and their intervals after the last dose of SMC.
- Health workers must record and monitor the doses of SP + AQ administered in order to evaluate the impact of the intervention. Existing systems for documenting severe malaria, malaria deaths and confirmed cases of malaria should be strengthened.

Treatment of breakthrough *P. falciparum* infections during SMC should not include either AQ or SP or combinations containing either of these drugs, such as artesunate + amodiaquine. Where SMC is implemented, alternative antimalarial combinations must be made available for the treatment of clinical malaria in the target age group.

Existing systems for recording and reporting confirmed cases of malaria and malaria deaths should be strengthened for evaluation of the impact of SMC.

SMC complements existing malaria control interventions and should therefore be deployed concurrently.

Intermittent preventive treatment in infancy and SMC should not be given concomitantly to the same population. Therefore, in target areas for SMC, intermittent preventive treatment of malaria in infancy should not be used.

Expected benefits of SMC

The WHO policy recommendation for SMC is based on the results of seven studies conducted in areas of highly seasonal malaria transmission in the Sahel and sub-Sahel regions of sub-Saharan Africa between 2002 and 2011. Evidence from these studies suggests that SMC with SP + AQ administered monthly for up to 4 months during the malaria transmission season in children aged 3–59 months:

- prevents approximately 75% of all malaria episodes;
- prevents approximately 75% of severe malaria episodes;
- may decrease child mortality by about 1 in 1000;
- probably reduces the incidence of moderately severe anaemia;
- does not result in an increase in clinical malaria cases in the subsequent malaria transmission season after 1 year of SMC, although the consequences of implementing SMC for several years have not yet been evaluated; and
- no serious adverse events have been reported and are probably rare.

3. SEASONAL MALARIA CHEMOPREVENTION

3.1 WHAT IT IS

SMC, formerly known as 'intermittent preventive treatment of malaria in children', is defined as "intermittent administration of full treatment courses of an antimalarial medicine during the malaria season to prevent malarial illness with the objective of maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk". The SMC strategy consists of administering a maximum of four treatment courses of SP + AQ at monthly intervals to children aged 3–59 months in areas of highly seasonal malaria transmission.

3.2 WHEN TO IMPLEMENT IT

SMC should be implemented during the high malaria transmission period, when the incidence of malaria is high. It should be administered to children aged 3–59 months at 1-month intervals (SMC cycle) up to a maximum of four cycles in a year (SMC round). SMC with SP + AQ provides a high degree of protection for up to 4 weeks, and protection decreases rapidly thereafter. It is therefore important to respect a 1-month interval between SMC cycles in order to achieve a high level of protection and to minimize selection for malaria parasites resistant to SP + AQ.

The period of administration of SMC should be chosen to target the period when children are most at risk for malaria attacks. For example, SMC was delivered in August, September and October in field trials in Burkina Faso[4] and Mali;[5] while in Senegal;[6] it was given in September, October and November, covering the period of highest risk for malaria.

[4] Konaté AT et al. Intermittent preventive treatment of malaria provides substantial protection against malaria in children already protected by an insecticide-treated bednet in Burkina Faso: a randomised, double-blind, placebo-controlled trial. *PLoS Medicine*, 2011, 8:e1000408.

[5] Dicko A et al. Intermittent preventive treatment of malaria provides substantial protection against malaria in children already protected by an insecticide-treated bednet in Mali: a randomised, double-blind, placebo-controlled trial. *PLoS Medicine*, 2011, 8:e1000407.

[6] Cissé B et al. Seasonal intermittent preventive treatment with artesunate and sulfadoxine–pyrimethamine for prevention of malaria in Senegalese children: a randomised, placebo-controlled, double-blind trial. *Lancet*, 2006, 367:659–667.

3.3 CHOICE OF SULFADOXINE–PYRIMETHAMINE PLUS AMODIAQUINE

The combination of SP + AQ was chosen for SMC for the following reasons:

- In clinical trials, SP + AQ conferred greater protection than other drug combinations.[7] The use of the two drugs in combination limits the risk for selection for resistance to either SP or AQ used as monotherapy.
- SP and AQ retain their efficacy in areas of Sahel and sub-Sahel with seasonal transmission where SMC is appropriate.[8]
- The SP + AQ regimen is safe, well tolerated and relatively cheap.
- The combination of SP + AQ does not include artemisinin derivatives. Therefore, artemisinin based combinations can be reserved for treatment of clinical cases in which the rapid action of an artemisinin derivative is most useful.

3.4 AREAS SUITABLE FOR IMPLEMENTATION

SMC is recommended for use in areas with highly seasonal malaria transmission, and it is likely to be most cost-effective where the burden of malaria is highest in children. The suitability of an area for SMC is determined by the seasonal pattern of rainfall, malaria transmission and the burden of malaria. SMC is recommended for deployment in areas:[9,10]

- where more than 60% of the annual incidence of malaria occurs within 4 months;[11]
- where there are measures of disease burden consistent with a high burden of malaria in children (incidence ≥ 10 cases of malaria among every 100 children during the transmission season);
- where SP and AQ retain their antimalarial efficacy.[12]

3.5 DRUG RESISTANCE

The areas in which SMC with SP + AQ is suitable are those in which the efficacy of the combination remains > 90% (see Annex 1). Resistance to SP or AQ will reduce the efficacy of SMC in protecting children against clinical malaria, although the relation between the degree of resistance and the effectiveness of SMC has not yet been clearly defined. There is, however, a threat that deployment of SMC with SP + AQ will increase drug pressure on the malaria parasite and lead to increased resistance to the combination. It is therefore essential to continue to monitor the development of resistance to SP and AQ both *in vivo* and *in vitro*.

3.6 SAFETY

SP + AQ are safe and well tolerated when used at the recommended doses and regimens. Both drugs have been used for decades for malaria treatment, and SP is currently used for intermittent preventive treatment of malaria in pregnancy and in infancy. Both AQ and SP are also used in combination with artesunate as artemisinin-based combination therapy, which is used for the treatment of uncomplicated malaria in many endemic countries. Mild side-effects may occur, of which the commonest is vomiting associated with intake of AQ. Severe side-effects include severe skin reactions and blood dyscrasia, but they are rare. In Senegal, where nearly 800 000 treatment courses of SP + AQ within SMC have been given to children, no serious adverse events attributable to these drugs were observed during intensive pharmacovigilance based on spontaneous reporting.

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7 Sokhna C et al. A trial of the efficacy, safety and impact on drug resistance of four drug regimens for seasonal intermittent preventive treatment in Senegalese children. *PLoS One*, 2008, 3: e1471.

8 World Health Organization. *Global report on antimalarial drug efficacy and drug resistance 2000–2010*. Geneva, 2010. http://www.who.int/malaria/publications/atoz/9789241500470/en/index.html.

9 Note that that in some countries, eligibility for SMC might apply only to part of the malaria-endemic area.

10 SMC with SP + amodiaquine is not currently recommended for countries in southern and eastern Africa, even though there are some locations where the transmission pattern would suggest suitability, because of the high level of *P. falciparum* resistance to amodiaquine and/or SP and the absence of adequate data on the efficacy and safety of other antimalarial regimens for potential use in SMC.

11 In these areas, more than 60% of the average annual rainfall falls within 3 months.

12 Based originally on assessments of the therapeutic efficacy of SP + amodiaquine in children < 5 years of age in the WHO therapeutic efficacy testing protocol. Methods to assess the continued efficacy of SMC will be developed.

- **To minimize the risk for overdosing, it is recommended that SP + amodiaquine not be given for SMC to children who received either drug or a combination containing one of the drugs in the past 30 days.**
- **SP + amodiaquine should not be given for SMC to children with a history of allergy to sulfa-based drugs or to amodiaquine.**
- **SMC with SP + amodiaquine is not recommended for children with the Human immunodeficiency virus receiving co-trimoxazole prophylaxis against opportunistic infections.**
- **Pharmacovigilance should be maintained, and existing systems might have to be improved.**

3.7 DELIVERY

The method of delivery must be such that > 95% of eligible children receive SMC at monthly intervals during the period of highest malaria risk. This strict timing is best suited for community delivery, in which community health workers reach each household once a month, and a sufficient number of health workers can be deployed in each area to treat all children over a period of 3–4 days; community case management schemes are also suitable, in which health workers living in a village deliver SMC a few days each month. SMC drugs can be dispensed door-to-door or by gathering children at a pre-agreed location in each area of residence. Combining SMC with community case management has particular advantages: there are more opportunities for catching up missed doses; breakthrough cases can be diagnosed and treated, providing information about the effectiveness of SMC; and use of the same person to deliver SMC and to provide diagnoses and treatment is more economical.

SMC can also be delivered in programmes at health facilities, e.g. in outreach clinics of the Expanded Programme of Immunization. Field trials have shown, however, that such programmes are less effective in achieving high coverage.

3.8 IMPORTANCE OF ADHERENCE TO THE 3-DAY REGIMEN

SMC provides protection for up to 1 month after each complete (3-day) course. It is therefore important that children receive SMC each month during the main risk period and complete the course each month in order to obtain the maximum degree of protection. Good adherence also reduces the risk for selecting drug resistant parasites. Health workers should give the dose of SP and the first dose of AQ to the children under their direct observation and should advise the children's caregivers on how to give the second and third doses of AQ to the child at home.

Adherence to the full regimen should be one of the main messages in advocacy and behaviour change communication during the launching and promotion of SMC. The importance of adherence should also be stressed in communication activities at each monthly cycle.

3.9 LIKELY COST

Evaluation of the cost of delivering SMC in large field trials shows that the greatest costs are for delivering the drugs and the incentives paid to health workers. In The Gambia, the cost of SMC delivery by village health workers was estimated to be US$ 1.63 per child per year.[13] In Senegal, where SMC was delivered by community health workers paid a daily rate and supervised by the health post nurse, the overall cost at 46 health posts was estimated to be US$ 0.5 per child per month, or approximately US$ 1.50 per child per year. The cost of SMC is similar to those of other malaria control interventions.

[13] Bojang KA et al. Comparison of two strategies for the delivery of IPTc in an area of seasonal malaria transmission. *PLoS Medicine*, 2011, 8:e1000409.

4. NATIONAL ADOPTION OF SEASONAL MALARIA CHEMOPREVENTION

The decision to adopt and implement SMC at national level should involve all relevant stakeholders, including technical and financial partners. The process should be led by the national malaria control programme, with the involvement of its advisory committee or technical working group (if one exists), regional and district health authorities, local health and research institutions and civil society, including local community health organizations.

In order for the SMC strategy to have an impact on malaria control, it should achieve high, sustained coverage during successive transmission seasons. It is thus essential to plan for long-term, sustained financing. Identifying and securing the necessary resources should be an integral part of the implementation plan; therefore, all potential national and international funders, including the government and the private sector, must be involved at an early stage.

4.1 STEPS IN ADOPTING THE POLICY

Steps in deciding to adopt SMC:

- Identify stakeholders at national and international levels, including potential funding agencies.
- Establish a taskforce to oversee the process and coordinate stakeholders.
- Collate and review available data on malaria seasonality and incidence and the latest available data on the therapeutic efficacy of SP and AQ to determine the suitability of the SMC strategy in the local context.
- Prepare an implementation plan, and estimate the human, logistics and financial resources required.
- Identify funding sources, including national and/or local government, the local private sector and international donors.
- Formulate and disseminate a recommendation on adopting SMC via all available communication strategies to reach key stakeholders, including the community.

Issues to be considered in deciding to adopt SMC:

- the seasonality of malaria transmission and rainfall patterns in the country or region;
- the incidence of malaria in the country or region (transmission intensity);
- potential delivery mechanisms; and
- the efficacy, availability and cost of SP + AQ for use in SMC.

4.2 UPDATING THE NATIONAL MALARIA CONTROL POLICY

After a decision has been made to adopt SMC, the national malaria control policy should be updated to include SMC. Information useful for integrating SMC into a long-term programme includes:

- previous experience in integrating malaria control strategies into the national malaria control policy or other service delivery programmes at community level, such as integrated community case management, vitamin A supplementation and de-worming;
- information on malaria:
  - transmission and rainfall patterns;
  - reported incidence from surveillance and trends over time;
  - overall and area-specific distribution of incidence per month during a year;
  - proportion of cases that occur during the high transmission season; and
  - distribution by age group.
- programme objectives:
  - target or expected coverage; and
  - reduction in disease reduction that might be attributable to SMC.
- implementation issues:
  - delivery by community health workers;
  - implementation during the high transmission season;
  - strategy for integrating malaria control into other disease control strategies;
  - communication and advocacy to sensitize and mobilize communities;
  - monitoring of adverse drug reactions after SMC implementation;
  - revision of reporting forms; and
  - monitoring and evaluating the impact of SMC.

5. PLANNING IMPLEMENTATION OF SEASONAL MALARIA CHEMOPREVENTION

Once the SMC policy has been adopted, a detailed implementation plan should be prepared. A communication strategy should be in place to ensure that all partners and implementers understand what SMC involves. In countries with no previous experience of SMC, implementation might be begun in a few pilot districts, and the lesson learnt used to guide more widespread implementation of SMC. The components of an implementation plan are described below.

5.1 SITUATION ANALYSIS

A situation analysis should to be carried out at all levels to obtain information on:

- the monthly distribution of malaria in various parts of the country, in order to decide where SMC should be implemented;
- existing malaria prevention and control activities, including current first- and second-line treatment regimens;
- interventions with which SMC might be delivered in combination;
- human resources for SMC;
- existing, functional procurement and supply chain management at community level in the areas targeted for SMC implementation;
- strengths and weaknesses of the existing pharmacovigilance system;
- strategies for advocacy for community and social mobilization; and
- potential sources of funding.

5.2 DELIVERY SYSTEM

Delivery of SMC by community health workers has been evaluated in several studies, including a large-scale study in Senegal. Delivery by community health workers achieved high coverage at a lower cost than delivery by reproductive and child health teams or health personnel at health centres.[14] Community health workers delivered more than 790 000 courses of SP + AQ with a very high (> 90%) coverage rate in Senegal. Furthermore, community health workers can undertake both SMC and community case management of malaria,[15] and integration of these two complementary activities has been recommended by several authors.[16]

[14] Kweku M et al. Options for the delivery of intermittent preventive treatment for malaria to children; a community randomised trial. *PLoS One*, 2009, 4:e7256.

[15] Sesay S et al. A trial of intermittent preventive treatment and home-based management of malaria in a rural area of The Gambia. *Malaria Journal*, 2011, 10: e22.

[16] Greenwood B et al. Community case management (home management) and intermittent preventive treatment of malaria in children. *Trends in Parasitology*, 2011, 27:477–480.

5.2.1 Community-based approach

Community-based delivery of SMC by community health workers in Senegal

In Senegal, SMC was implemented by trained community health workers throughout the health system, regionally, in districts, in health centres and in 'health huts'. Researchers at Cheikh Anta Diop University in Dakar worked with the national malaria control programme to train regional and district health officers in implementing SMC. The activities included information and planning meetings with health authorities at national, regional and district levels, developing implementation tools and training health workers in their use and procuring supplies, including the drugs.

SMC was pilot-tested in three districts, each with several health centres that serve several villages or catchment areas. A minimum of two pairs of community health workers delivered SMC in each village, depending on the number of children under 5 years. Each pair of workers was expected to treat 25–30 children per day, and each cycle of drug administration per village lasted an average of 5 days. The pairs were chosen such that at least one was literate and could complete SMC administration forms. If there were insufficient community health workers to deliver SMC in a village, suitable community members were identified and trained to administer SMC.

At the end of each day, the health workers travelled to the health centre to submit a report and obtain provisions of drugs, forms and other supplies for the next day. The completed forms were compiled by nurses at the health centres. Unused drugs were returned to health centres at the end of each administration cycle. When children missed a drug administration during the visit of the health worker, their caregivers were advised to take their children to the health centre within the next few days. One cycle of drug administration was coupled with delivery of vitamin A and a de-worming drug (albendazole); however, information on SMC was recorded on a separate form. The community health workers were directly supervised by nurses at peripheral health centres, who in turn were supervised by district health senior staff. Information was thus channelled from community health workers to nurses, to the district medical officer and to the regional health officer, who reported to the national malaria control programme.

Lessons learnt during wide scale implementation of SMC in Senegal

- Delivery of SMC by community health workers requires a functional community-based health system.
- Involvement of regional and district health authorities from the start and holding regular meetings improved understanding and trust and generated a feeling of ownership at both those levels.
- Participation of community members in sensitization and mobilization helped build confidence between the health workers and the community.
- Provision of incentives played a major role in the commitment of community health workers and heath personnel during SMC implementation. Monetary incentives were used in Senegal, whereby the health workers were paid a rate (determined by the project) that was comparable to that paid in similar community-based delivery projects but higher than the Government rate. The provision of incentives in cash or kind must be discussed before implementation.
- Coupling SMC with administration of vitamin A and albendazole was a successful example of combining several health interventions.
- The appropriate period for SMC might differ slightly by locality within a country because of differences in the pattern of transmission and other local factors.

5.2.2 Facility-based system

There is limited experience on health facility-based delivery of SMC. This approach was evaluated in a study in Ghana, in which about 60% of the children received all SMC courses. SMC was delivered by health personnel at an outpatient department or at the outreach clinic of the Expanded Programme of Immunization to a small number of children. These limited data and the importance of ensuring high coverage for the maximum impact of this intervention indicate that a community-based delivery strategy is preferable to a fixed facility-based approach.

5.3 PREPARING A PLAN

5.3.1 List of key activities

The following activities should be addressed in the implementation plan:

- training personnel;
- procurement and supply chain management;
- advocacy and community mobilization;
- SMC delivery;
- supervision;
- monitoring and evaluation;
- time lines;
- defining roles and responsibilities; and
- costing and budgeting.

A 3- to 5-year implementation plan with a supporting budget is recommended. It should be synchronized with the national plan for other malaria control interventions. A calendar for implementation of activities should be prepared each year (Annex 2).

5.3.2 Estimation of requirement for drugs

Good quantification of supplies is a key determinant of successful implementation of SMC. Estimating the quantity of drugs requires a close approximation of the number of children aged 3–59 months per village, health zone, district, region or country. If such estimates are not available but the fraction of children in this age group in the population is known, the quantity of SMC drug can be estimated. Population data can be obtained from the most recent national census or demographic and health survey or the national bureau of statistics. For example, in the wide scale study in three districts in Senegal, a *demographic surveillance system* was set up as part of the research project. The average percentage distribution of children by age was 5% aged < 3 months, 18% aged 3–11 months and 77% aged 12–59 months.

SMC is delivered in two dosage groups: 3–11 months and 12–59 months. This grouping was determined to be convenient for administering 153 mg of AQ base with a low risk for over- or under-dosing.

If the number of children aged < 5 years is *N*, the number of tablets required is calculated from:

N x 0.18 aged 3–11 months and *N* x 0.77 aged 12–59 months

The number of SP tablets for 1 month is then *N* x 0.18/2 for infants (who receive half a tablet each) and *N* x 0.77 for the older children, which equates to *N* x (0.18/2 + 0.77) = *N* x 0.86.

Increase this by 15% to allow for wastage and uncertainty in the estimates of the number of children:

N x 0.86 x 1.15 = *N* x 0.99.

Therefore,

- The number of SP tablets required each month is approximately equal to *N*, the number of children aged 0–59 months.
- The number of AQ tablets required each month is three times as many, *N* x 3.
- For 4 months, *N* x 4 SP tablets and *N* x 3 x 4 AQ tablets are required.

For example:

For a population of 30 000 children < 5 years, the SMC drug supply required for 4 months to treat an estimated 30 000 x 0.95 = 28 500 children aged 3–59 months will be:

- **30 000 x 4 = 120 000 SP tablets; and**
- **120 000 x 3 = 360 000 amodiaquine tablets.**

5.3.3 Training staff

All staff implementing SMC, including health personnel at district level (where applicable) and community health workers, should be trained for delivery and reporting to ensure that they have a clear understanding of the strategy and activities involved.

- Training should be planned ahead, and the personnel involved should be informed weeks or months ahead of time in order to avoid overlap with other activities.
- Ideally, the training sessions will be held not too long before the start of SMC delivery (2–4 weeks).
- During the first year of SMC, it may be preferable to hold separate training sessions rather than training sessions that also cover other interventions.
- In subsequent years, refresher training or training new staff can be integrated into the routine training activities of the national malaria control programme.
- Pictorial examples are useful for training personnel which applicable.
- The training material should be updated regularly at national level.
- The content of training courses should be adapted to suit the roles and responsibilities of the trainees.

Instructions to community health workers and district health staff

Caregivers and the community should receive the following information about SMC:

- SMC drugs protect children against malaria by reducing the risk for malaria attacks.
- SMC drugs should not be used to treatment children when they are sick.

- SMC is given to children aged 3–59 months.
- A full SMC course (SP+AQ) is administered three or four times (SMC cycles) at 1-month intervals during the rainy season (SMC round).
- A full SMC course is given over 3 days.
- Caregivers should not interchange SMC drugs if they have more than one child who should receive SMC.
- Caregivers should keep empty drug packs and sachets at the end of each SMC cycle for inspection and verification purposes.
- Caregivers must report any adverse event observed.
- Caregivers must take children to the community health worker or to a health centre if they are unwell.
- Drug administration should be recorded on each child's SMC card and in the register.

At the end of each day, community health workers should:

- count the number of SMC courses administered (annexes 3 and 4);
- count the number of children who did not receive drugs;
- discard broken tablets;
- take completed forms to the health centre;
- give a brief report to the head nurse (Annex 4); and
- prepare material for the next day (clean cup, spoon, check availability of SMC drugs).

5.3.4 Transport and supply chain management

In most countries, there is an established channel for dispatching health commodities, including antimalarial agents and long-lasting insecticidal mosquito nets, from central to peripheral level. These channels can be used, and if necessary strengthened or adapted, to supply districts, health centre and villages with SMC drugs and supplies. It is important to keep in mind that SMC supplies are delivered during the rainy season, when some locations may be difficult to reach during heavy rainfall.

SMC courses of SP + AQ given to caregivers to be administered at home should be packed in user-friendly packaging to ensure that the integrity of the medicine is preserved and that it is easy to use.

At each level of the transport chain for SMC drugs, the following must take place:

- recording of stocks received;
- dispatching of stocks to districts, health centres and villages;
- counting remaining stocks at the end of each round of SMC and reporting to health centre, district, regional and national levels;
- returning remaining doses of SP + AQ to the health centre or district at the end of the third cycle of SMC (or at the end of a fourth cycle, depending on the malaria transmission pattern);
- transferring remaining stocks received at the health centre from the community health worker to the district level for appropriate storage and return for the next malaria transmission season if the expiry date has not been reached; and
- factoring in remaining stock, depending on the expiry date, when estimating the amount of SMC drugs required for the following year.

5.3.5 Supervision

The role of supervision is to support SMC implementation by ensuring that activities are carried out in compliance with agreed procedures.

A supervision plan should be prepared at each level; from the national malaria control programme to the community (annexes 4–7). Intensive supportive supervision should be in place, especially during the early stages of SMC implementation (first cycle and first round) in order to identify and resolve problems. If required, retraining can be offered on site to community health workers who experience difficulties.

5.3.6 Advocacy for community and social mobilization and behavioural change communication

The role of advocacy for community and social mobilization and behaviour change communication is to raise awareness in the community and among local authorities, technical and financial partners of the national malaria control programme and nongovernmental organizations. These activities are important for fostering community ownership of the SMC strategy. Delivering key messages about SMC should reduce the risk of misunderstanding and any negative perceptions about the strategy. Community members can be involved in advocacy for community and social mobilization.

A plan should be prepared as part of the implementation plan and integrated into existing programmes, if possible. These activities should be undertaken before and during SMC implementation (ideally before each SMC cycle) and should emphasize:

- the benefits of SMC;
- the target age group for SMC;
- when SMC should be administered;
- the number of SMC cycles in the round;
- compliance with a full SMC course, cycles and round;
- potential adverse events and serious adverse events and action to be taken in the event of a serious adverse event;
- the fact that children receiving SMC are not fully protected and may still get malaria;
- the difference between malaria prevention and treatment;
- malaria case management;
- the importance of other malaria control strategies (such as long-lasting insecticidal nets); and
- addressing negative rumours, if required.

Material for advocacy and behaviour change communication should be prepared and reviewed carefully, with assistance from local experts, and translated into the main local languages. The activities should be implemented through a variety of resources, including:

- the mass media (radio, television and local newspapers);
- community-based organizations;
- community leaders;
- community health workers;
- community volunteers;
- the health system;
- markets and other gathering places.

As SMC is delivered during the rainy season, which is a period of intense farming activities in rural areas, advocacy and communication should include related issues that may affect coverage rate. The results of previous SMC programmes could be used in subsequent advocacy activities.

5.3.7 Administration

Children who should receive SMC with SP + AQ

All children aged 3–59 months living in areas where conditions for the implementation of SMC are met are eligible. A child is eligible for SMC if he or she meets the following criteria:

- aged 3–59 months;
- does not have confirmed malaria;[17]
- does not have history of allergy to SP or AQ or of adverse reactions to SP or sulfanomide-containing drugs (show drugs or the package to the mother or guardian), such as co-trimoxazole (Bactrim and Metaflekin), Fansidar®, Facilidin®, Malafan® and Novidar®;
- has not received an antimalarial agent containing SP or AQ in the past 30 days;
- does not have any other acute illness; and
- is not receiving co-trimoxazole prophylaxis.

Children who should not receive SMC or whose treatment must be delayed

- children who received SP + AQ or other drugs containing sulfonamide in the 30 days preceding the date of SMC. These children should be given an appointment for the next cycle of SMC.
- children who have malaria at the time of SMC. These children must be referred to a health centre for care or, when applicable, treated for acute malaria through a community-based mechanism such as *community case management*. Caregivers should be advised to bring these children back after 30 days for the next cycle of treatment.
- children who are < 3 months old.
- children with a history of allergy to either SP or AQ.

Missing one course of treatment does not prevent a child from receiving the next course of SMC drugs, if there are no contraindications.

Target period for SMC

SMC is conducted during the high transmission period. The start and end dates depend on the pattern of malaria transmission, which generally correlates with rainfall. This differs within and between countries. If the plan is to administer three SMC treatment cycles during the high malaria transmission season, the second cycle should be given at the peak of the transmission season. The delivery schedules were August, September and October in Mali and Burkina Faso and September, October and November in Senegal.

[17] Defined as fever (body temperature ≥ 37.5°C) or a history of fever in the past 24h and a positive diagnostic test (rapid test or microscopy). In the absence of a rapid diagnostic test or microscopy (within 2h), a diagnosis of malaria should be based on clinical signs and symptoms.

Depending on the date of the first dose of treatment, the second, third and fourth cycles (if applicable) should follow at 1-month intervals.

First cycle (first month)

Day 0: single dose of SP + first dose of amodiaquine (by a health worker)
Day 1: second dose of amodiaquine (by the caregiver)
Day 2: third dose of amodiaquine (by the caregiver)

Second cycle (second month)

Day 0: single dose of SP + first dose of amodiaquine (by a health worker)
Day 1: second dose of amodiaquine (by the caregiver)
Day 2: third dose of amodiaquine (by the caregiver)

Third cycle (third month)

Day 0: single dose of SP + first dose of amodiaquine (by a health worker)
Day 1: second dose of amodiaquine (by the caregiver)
Day 2: third dose of amodiaquine (by the caregiver)

Fourth cycle (fourth month) –*if applicable*

Day 0: single dose of SP + first dose of amodiaquine (by a health worker)
Day 1: second dose of amodiaquine (by the caregiver)
Day 2: third dose of amodiaquine (by the caregiver)

The aim is to administer complete 3-day courses of SP + amodiaquine to each eligible child at least three times during the period of high malaria transmission. Protection against clinical malaria is associated with administration of the second and third doses of amodiaquine. Therefore, it is important that a child receives the full doses of SP + amodiaquine during each course of SMC.

A maximum of four courses may be given, depending on the pattern of malaria transmission. If a child misses one SMC course because of illness or absence, he or she should receive the next round of SMC if he or she is present and well.

What doses of SP and AQ should be given?

For practical reasons, the doses of SP and AQ for SMC are based on the child's age: information on age is easier to obtain in rural communities than weight.

Widescale studies have shown that administration of tablets of 153mg AQ base maximizes the number of children aged 3–59 months who receive the required dose of 10mg AQ base per kilogram of body weight.

The doses of SP and AQ should be:

SP tablet (500mg + 25mg)

- **Children aged 3–11 months receive half tablets as a single dose on the first day.**
- **Children aged 12–59 months receive a full tablet as a single dose on the first day.**

AQ tablet (153mg base)

- **Children aged 3–11 months receive half tablets as a single daily dose for 3 days.**
- **Children aged 12–59 months receive a full tablet as a single daily dose for 3 days.**

It is important to split the tablets carefully when required. If the two halves are not equal, they must be discarded.

Procedures for administering SP + AQ

- Determine or confirm the child's eligibility for SMC. If necessary, ask the caregiver to show any document that could give the child's age.
- If SMC is being given for the first time, write down the names of the child and mother or caregiver and the ages of all eligible children on the card (Annex 8), and give the card to the caregiver after completing administration in the household.
- Determine the doses of SP and AQ that the child should receive (half a tablet or a full tablet).
- Obtain clean potable water. Caregivers can be asked to give community health workers clean water; however, it is recommended that each health worker carries a bottle of clean water as a precaution.
- Crush SP and AQ drugs separately into a powder if the brands that are available do not dissolve easily. Place the tablets in between two spoons in a folded paper, or use another appropriate tool for crushing the tablets.
- Make sure that all the powder is transferred into an appropriate container and mixed with clean potable water. The addition of sugar is recommended to mask the bitterness of AQ.
- Seek assistance from the caregiver or another member of the family if necessary.
- Keep the child under observation for 30min to ensure that he or she does not vomit the drugs.
- If a child vomits, spits or regurgitates the drugs within 30min, give a replacement dose after allowing the child to rest for about 10min.
- After drug administration of the dose for the first day, the health worker gives the rest of the tablets (AQ) in the sachet to the caregiver for treatment on days 2 and 3. For children < 11 months who receive half tablets of AQ, the tablet should be split with a tablet cutter before being packed in the sachet for the mother to take home. This ensures that the child receives an accurate dose. The caregiver should be advised to bring the child for the next course in 30 days (second or third course).
- Provide instructions on giving treatment at home.

Administration of SMC should be recorded in a register with the child's age and any other relevant information.

Cups and spoons should be cleaned with soap and rinsed before being used to give SMC drugs to another child. It is convenient to have several sets of spoons, cups and pots to save time.

SMC should not be given to children who have received antimalarial treatment during the past 30 days, as there is a risk for overdosing and severe adverse drug reactions if the drug combination for treatment of clinical malaria contained a drug that is also used in SMC. These children should therefore receive the drugs at the next SMC administration cycle if they have no other contraindication at that time.

As one cycle of SMC administration for all eligible children in a village lasts up to 7 days, good judgement and planning are required to minimize the number of children who do not receive SMC because they received an antimalarial agent in the past 30 days. Administration to these children can be delayed for a few days if it can be done within the 7 days planned for the SMC administration cycle.

What happens if a child misses a course of SMC?

Children who miss SMC during the visit of the community health workers should be given the opportunity to receive the drugs later, and the workers should arrange to make another visit to find such children. They could give an appointment to the children's caregivers to meet at a certain place in the village at the end of the day or another convenient time, such as after completion of each treatment course. The health workers should record the names of children who are absent during their door-to-door visits to facilitate tracking them later, and the names should be given to community leaders, who can help in finding the children and bringing them within the 7 days planned for monthly administration of SMC in the area. If some children still miss treatment, their caretakers should be advised to bring them to the next SMC cycle.

5.4 ACTIVITIES AT VARIOUS LEVELS

5.4.1 National malaria control programme

Responsibilities

- overall supervision of SMC implementation; and
- facilitation of SMC implementation.

Activities

- Organize meetings with stakeholders;
- Prepare overall SMC implementation plan;
- Incorporate SMC into malaria control strategy and guidelines;
- Secure funding;
- Assist in preparation of the district implementation plan;
- Secure, manage and dispatch SMC drugs;
- Design and update SMC training, supervision and reporting tools;
- Facilitate training at all levels;
- Conduct advocacy, information, education and communication at national level;
- Liaise with partners, including those in research and academic institutions;
- Compile data and prepare progress reports.

5.4.2 Regional level

Responsibilities

- supervision of SMC at regional level; and
- facilitation of SMC implementation at district level.

Activities

- Ensure adequate supplies of SMC drugs;
- Conduct advocacy at regional level;
- Facilitate and supervise SMC implementation at district level;
- Facilitate preparation of district microplans and budgets;
- Provide managerial and financial supervision.

5.4.3 District level

Responsibilities

- supervision of SMC implementation at health facility level; and
- facilitation of SMC implementation at peripheral level.

Activities

- Explain SMC strategy to district health team;
- Establish an effective communication system for SMC delivery;
- Explore possible combined delivery with other strategies;
- Prepare the district SMC implementation plan and budget;
- Prepare nurses for advocacy for community and social mobilization;
- Train nurses at health centres, and keep training records;
- Deliver commodities to peripheral health centres;
- Allocate resources to peripheral health centres for SMC implementation;
- Plan and organize supervision of SMC implementation;
- Monitor progress and solve problems;
- Prepare a technical and financial report for approval at regional level and submission to the national malaria control programme.

It is important to maintain regular telephone contact with nurses and community health workers during each cycle of SMC delivery in the first year in order to monitor progress and solve any problems. The number of contacts can be reduced once the team has gained experience.

5.4.4 Peripheral health centre level

Responsibilities

- supervision of SMC implementation at community level;
- advocacy and community mobilization;
- management of cases of malaria, including referrals when needed; and
- management of any adverse events (pharmacovigilance).

Activities

- Organize meetings with all personnel to explain the SMC strategy.
- Meet communities to explain SMC.
- In collaboration with community leaders, identify community members who will participate in sensitization and advocacy by making door-to-door visits and delivering messages at suitable gathering places such as markets, mosques and churches.
- Train community members to identify and recognize drug-related serious adverse events.
- Identify, discuss and report community concerns.

- In collaboration with community leaders, identify the community health workers who will administer SMC:
  - Health workers should administer SMC and complete reporting forms in pairs. In each village with fewer than 200 children aged < 5 years, the health workers are expected to visit and administer SMC to an average of 25–30 children per day. The number may increase to at least 100 children, depending on the experience of the health workers, the location of households and whether SMC is given door-to-door or at a central point.
  - In villages with a large number of children, the number of health workers should be increased to ensure that SMC can be delivered within 7 days.
  - If SMC is to be administered with vitamin A and albendazole, a third health worker may be needed.
- Train the health workers in administering SMC, completing drug accountability forms and identifying any drug-related serious adverse events.
- Prepare a delivery plan for each village and a daily circuit for each health worker.
- Dispatch drugs, consumables and monitoring forms to the health workers.
- Supervise the health workers and solve any problems. At least two supervisory visits per pair of community health workers and cycle of SMC treatment is ideal. Once the team has gained experience, the number of supervisory visits can be reduced to one per round.
- Report serious adverse events to the district medical office.
- Compile the daily reports received from health workers for submission to the district health officer.
- Debrief the health workers at the end of each treatment cycle.
- Prepare reports at the end of each treatment cycle for submission to the district (Annex 9), and share with community health workers.

5.4.5 Community level

Responsibilities

- Deliver SMC to children at community level (community health workers).
- Conduct advocacy and community mobilization (community leaders and health workers).
- Manage and refer cases of malaria (community health workers).
- Refer patients to nearby facilities if suspected drug reactions (community health workers).

Activities

- advocacy for community and social mobilization in collaboration with selected community members and nurses at peripheral health centres;
- collecting drugs and other material required for SMC at the health centre;
- administering SMC courses;
- completing forms and registers;
- identifying and reporting adverse drug reaction to nurses;
- delivering information, education and communication to caregivers of children on adherence to treatment, how to prevent malaria and when to refer a child to the nearest point of care; and
- reporting daily on SMC delivery to nurses.

5.5 REPORTING

Tools for reporting should be developed or adapted from existing tools. Generally, the routine health information system does not capture information generated at community level. Adaptation of routine health data collection tools may require time, and interim arrangements may be necessary until the changes can be made. Questions important for updating existing data collection tools are what data reporting forms are already available and whether it would be possible to add new recording forms to the routine health system.

If SMC is delivered in a community-based approach, simple, user-friendly tools should be prepared and, if possible, combined with tools used for other community-based health interventions. Where community case management of malaria is implemented, health workers can be given simple forms that are easy to fill in for recording information. Issuing SMC cards (Annex 8) to caregivers is useful for monitoring SMC programmes.

6. MONITORING AND EVALUATION

Monitoring is conducted routinely to oversee the essential elements of programme performance by record-keeping, regular reporting and surveillance to assess achievements. Therefore, a good monitoring and evaluation system is required. The system is based on both routine health information and periodic household surveys, which should be adapted to include questions relevant to SMC. In the context of results-based management, a clear performance framework should be set up before implementation of the SMC strategy.

6.1 PERFORMANCE FRAMEWORK

The performance framework guides the monitoring and evaluation system. It includes the objectives and indicators in a logical hierarchy, baseline and annual targets, data sources, data collection methods, frequency of reporting and the person responsible.

6.1.1 Potential indicators

Goals are usually measured from impact indicators, while objectives are usually measured from outcome indicators. Input and output indicators are also useful for monitoring implementations of the various interventions of the SMC strategy. Only essential information should be recorded.

Impact indicators

- Number of confirmed malaria cases per 1000 population per month. This indicator can be calculated during the high transmission season (SMC intervention period; between the first dose of the first course and 30 days after the last dose of the third or fourth course). The variable is, however, sensitive to changes in reporting rates, diagnostic practice and use of health facilities. Care should be taken to ensure that reporting has been consistent over time, by examining trends in health facility reporting rates, annual blood examination rates and total outpatient attendance. If these indicators have changed, it may be more informative to examine trends in test positivity rates (slides or rapid diagnostic tests) or confine the analysis to a subset of health facilities that have reported consistently over time.
- Number of inpatient cases of malaria per 10 000 population per month during the high malaria transmission season.
- Number of inpatient deaths due to malaria per 100 000 population per month or per year.

Outcome indicators (coverage)

- Percentage of children aged 3–59 months who received SMC per cycle during the transmission season.
- Percentage of caregivers who gave the second and the third doses of AQ at home.
- Percentage of children aged 3–59 months who received three courses of SMC per transmission season.

Output indicators

- Number of health personnel trained in SMC
- Number of community health workers trained in SMC
- Number of community health workers who received a supervisory visit during the past month
- Number of SMC courses delivered

Input indicators

- Number of health centres with stocks of SMC drugs
- Number of health centres with adequate reporting forms, supervision tools and supply tracking system for SMC

6.1.2 Baseline data and annual targets

Baseline data must be collected for monitoring progress in SMC implementation. They can be obtained from previous reports, by compiling data at facilities or by conducting special surveys with support from local partners. It is important that the baseline for each indicator be defined before implementation of the plan and that the planned target for each subsequent year is set.

6.1.3 Data sources and collection methods

The data source is given for each indicator, and this will define the data collection method. Depending on the nature of the data, routine SMC reports, health information, surveillance systems or special surveys (such as population-based surveys, case–control and case–cohort studies) can be used to collect the data required for monitoring and evaluating SMC.

For example, data collected over time at facility level can be used to assess:

- the proportion of positive rapid diagnostic tests among those tested for suspected malaria;
- the number of cases of malaria reported by health centres;
- the number of hospital admissions for severe malaria; and
- the numbers of deaths from all causes and from malaria in health facilities.

In areas where SMC is implemented within community case management of malaria (integrated or not), the number of malaria episodes can be derived from the number of treatments given to children under 5 years. Free artemisinin-based combination therapy at community level improves access to treatment, and rapid diagnostic tests improve malaria diagnosis. Data collected by health workers in the community can provide useful information about the impact of SMC over time. It is, however, difficult to attribute any reduction in morbidity or mortality to a single intervention, such as SMC. Therefore, data on other contextual factors, collected during routine monitoring, are useful for assessing the impact of SMC.

6.1.4 Frequency of reporting

The frequency of reporting each indicator should be determined. For example, during one round of SMC, some indicators will be collected daily and others weekly or monthly, while surveys to evaluate the impact of SMC on mortality might be conducted every 3–5 years, and surveys to monitor the efficacy of SMC drugs should be conducted every 2–3 years (see section 6.7).

6.1.5 Person responsible for each indicator

A person should be chosen to collect data on each indicator and made accountable. A database can be set up, with support from the national health information system and local research organizations, to facilitate data entry, analysis and reporting. A data quality monitoring system, also set up with help from the local health information system and local research institutions, will increase the credibility of data.

6.2 TOOLS FOR MONITORING PROGRESS

As SMC relies on community health workers, simple, user-friendly recording tools should be designed and adapted to the country context. For instance, pictorial aids are helpful. Data can be presented in tables, bar charts and figures to show stakeholders how the programme is performing globally, by region and district, and highlight areas in which adjustments are required to improve performance. If resources are limited, representative sites in various locations can be selected to monitor the impact of the SMC strategy.

Various data collection instruments can be used to record information for SMC programme monitoring, including registers, tally sheets, SMC implementation cards, children's health cards and survey data collection tools. The monitoring tools should be reviewed carefully and, if possible, integrated with existing tools. It is nevertheless unrealistic to expect full integration of SMC monitoring and evaluation into the local health management information system, at least in the initial stages.

6.3 ISSUES IN RECORDING AND REPORTING HEALTH INFORMATION BY COMMUNITY HEALTH WORKERS

The recording of information and the quality of the data recorded are major concerns in health programmes involving community health workers. These aspects must be emphasized during training. For community health workers who are illiterate, alternative solutions must be found, such as a literate member of the community who can be trained to assist the health worker in recording information (e.g. a school teacher). Support in delivering SMC and recording and reporting information might also be obtained from health workers in neighbouring localities, if SMC is not conducted on the same date.

As SMC is seasonal and coincides with the long school break in many countries in the Sahel and sub-Sahel regions, short-term support might be obtained from secondary school pupils and students returning to the community for holidays, if they can obtain some incentive in return. They could help to complete administrative forms, sensitize the community and participate in surveys for the evaluation of SMC if they receive appropriate training. Their work should be supervised by nurses in a primary health care facility or by senior staff at the district health office.

6.4 RECORDING DRUG ADMINISTRATION (MONITORING AND EVALUATION)

The administration of SMC drugs must be recorded in order to monitor progress. The basic information should be recorded on the SMC card kept by the mother or caregiver (Annex 8) and in a register kept by the community health worker.

The register entry should include the name of the village, the name of the child's mother or the head of the household (optional), the child's age group, the SMC cycle and any observations. The name of the child's mother and that of the head of the household will be useful for tracing the child.

At the end of each SMC cycle, the community health workers should compile, for each location (annexes 6 and 9), the total numbers of children treated by age group, SMC courses given and children who missed SMC administration.

6.5 ESTIMATING COVERAGE

In general, SMC involves administration of three courses of treatment during the season of high malaria transmission, although up to four courses can be given. In many field studies, therefore, SMC coverage was estimated as the proportion of children who received three complete courses during the transmission season. In field studies of SMC delivery by community health workers, coverage of children receiving three complete courses was estimated to be 90% in Senegal and 74% in The Gambia. This definition is, however, difficult for programme managers to use in monitoring SMC coverage unless special surveys are undertaken.

Coverage can also be defined as the number of people reached by services offered by a programme. Coverage with SMC could therefore be defined as the proportion of children who received the first dose of each treatment cycle during the transmission season. It would be calculated per treatment cycle, with the number of children aged 3–59 months who received the first dose of SP + AQ as the numerator and the expected number of children aged 3–59 months in the locality during the current transmission season as the denominator. The coverage rates of courses 1, 2 and 3 then determine SMC coverage.

If accurate estimates of the expected number of children are not available, data on the form shown in Annex 3 for counting and recording the number of children who received and did not receive each SMC course can be used to estimate the number of children expected to receive SMC. An example of such calculation is shown in Table 1.

Table 1. Example of calculation of coverage with seasonal malaria chemoprevention in 2011

	August	September	October
Number of children aged 3–59 months who received drugs	950	920	900
Expected number of children aged 3–59 months in 2011	1000	1000	1000
Coverage (%)	95	92	90

6.6 MONITORING ADVERSE DRUG REACTIONS

Drugs can have both desirable and undesirable effects, and no drug is absolutely safe for use in all individuals under all circumstances. It is therefore important to monitor adverse events. In general, adverse events are events associated with exposure to a drug; thus, an adverse event is not necessarily causally associated with the drug. In case of doubt, however, it is better to report the event than not to report it.

Health personnel, community health workers and caregivers should be trained to identify and report adverse events. If health workers identify a serious adverse event, they should report it to nurses at the health centre, who will complete the form in Annex 9 and send it to the district medical office for appropriate action. In many locations, routine pharmacovigilance systems will have to be strengthened to ensure effective reporting of drug-related adverse events after implementation of SMC.

6.6.1 Definitions

An *adverse event* is any untoward occurrence in a patient or in a participant in a clinical investigation who was given a pharmaceutical product, which is not necessarily causally related to the treatment. An adverse event is any unfavourable or unintended symptom or disease (including laboratory findings temporally associated with use of a medicinal product), which may or may not be considered to be related to the medicinal product.

A *serious adverse event* is any untoward medical occurrence in response to a drug that at any dose:

- is life-threatening;
- requires or prolongs hospitalization;
- results in disability or incapacity;
- results in congenital abnormality or birth defect;
- results in death; or
- may require intervention to prevent one of the outcomes listed above.

6.6.2 Recording and reporting adverse events

Occasionally SP and AQ cause mild-to-moderate adverse events; in rare cases, serious adverse events can occur. Mild adverse events associated with SP involve the skin and mucous membranes. In rare cases, serious cutaneous toxicity (Steven–Johnson syndrome) and hepatotoxicity may be observed.

The commonest mild adverse events associated with AQ intake are vomiting, abdominal pain, fever, diarrhoea, itching, headaches and rash. Aplastic anaemia and fatal hepatotoxicity are rare serious adverse events associated with weekly prophylactic use of AQ; such events have not been reported with use of AQ as part of SMC.

Clear guidelines must be in place for effective monitoring of drug safety. They should include:

- definition of the roles and responsibilities of staff;
- lists of adverse events and serious adverse event that must be recorded;
- standard definitions of 'adverse event' and 'serious adverse event' for use by all staff;
- use of standard forms for recording, reporting and investigating serious adverse events;
- guidelines for recording, reporting and investigating serious adverse events;
- criteria for assessing the relation of the event with SMC drugs;
- documentation of action taken; and
- use of a standard database to record all serious adverse events.

Guidance should be provided on identifying and reporting serious adverse events to ensure that the minimum information is available for proper assessment of any reported event. The information could include: patient identity, age, sex, weight, brief description of the event, including severity, date of onset, treatment given, dates of onset and termination of administration of SMC and concomitant medicines, batch number and expiry date and outcome.

Serious adverse events can engender negative perceptions in the community and jeopardize the success of SMC. Therefore, any such event must be documented, whether or not it appears to be related to the SMC drugs. An excellent communication strategy is required to explain the risks and benefits of the intervention and any issue that might affect community acceptance of SMC.

Once an adverse event has been identified, prompt action must be taken by the medical team to minimize the risk for children's health and ensure a positive outcome. An example of the adverse event reporting form used in the wide scale study of SMC in Senegal is shown in Annex 10.

6.6.3 Potential difficulties in reporting adverse events

Lack of experience of community health workers and health staff with adverse events associated with SP + AQ can lead to underreporting of such events. Some may be missed for various reasons, including an assumption that the event is not related to SMC drugs. Staff in charge of reporting adverse events should be encouraged to report any such manifestation. Refresher training and regular discussions with personnel involved in reporting such events is recommended to minimize the risk for underreporting. Where available, pictures of adverse event should be made available to the community, community health workers and nurses at health centres.

6.7 MONITORING THE EFFICACY OF SULFADOXINE–PYRIMETHAMINE PLUS AMODIAQUINE

SMC with SP + AQ may increase drug pressure on the malaria parasite population, which could lead to selection of drug-resistant parasites and the spread of resistance to SP and/or AQ. Therefore, monitoring the estimated efficacy of SP and AQ during SMC is important. Unfortunately, there is currently no recommended way of estimating the efficacy of SP + AQ. A baseline assessment of resistance would be helpful, and surveys should be carried out at 2–3-year intervals in representative locations with techniques such as molecular markers of resistance to SP and in vitro assays of the sensitivity of *P. falciparum* to AQ and SP. Indirect methods, such as monitoring the impact of SMC with SP + AQ on the prevalence of malaria infection or clinical malaria over time, might also be useful for detecting declining efficacy of SP + AQ, which could lead to surveys of markers of resistance or in vitro assays for confirmation.

Collaboration between national malaria control programmes, local research institutions, WHO and other organizations involved in monitoring antimalarial drug resistance is highly recommended.

For ethical reasons, the efficacy of SP + AQ cannot be assessed in children who are ill, because such children should receive only drugs (artemisinin-based combination therapy) that are currently effective for the treatment of clinical malaria due to *P. falciparum*.

6.7.1 Molecular markers of resistance

Genetic mutations associated with parasite resistance to SP and AQ can be assessed by molecular biological techniques such as polymerase chain reaction, single sequence oligonucleide probing or sequencing. *pfdhfr* (51, 59 and 108) and *pfdhps* (437 and 540) mutations are known to be good indicators of SP resistance, and recent reports indicate that mutations at both *pfcrt* and *pfmdr1* are good markers of resistance to AQ.

Surveys must be conducted to determine the prevalence of *pfdhfr* and *dhps* mutations, associated with resistance to SP, and the prevalence of *pfcrt* mutations at codons 72–76 and *pfmdr1* mutations at codons 86, 184 and 1246, associated with resistance to AQ. Filter paper blood spots could be obtained from a random sample of children who have malaria (fever and positive rapid diagnostic test) to monitor the prevalence of these molecular markers at sentinel sites (health centres) in various locations during SMC implementation and 1 month after the last course of SMC. Nurses at health centres can be trained to prepare filter paper blood spots. The filter papers should be labelled with the names of the health centre and district and sent to a local research institution with expertise in monitoring markers of resistance to antimalarial drugs for processing and analysis.

6.7.2 In vitro assays

In vitro assays are tests performed directly on malaria parasites to determine the concentrations of a drug that inhibit parasite growth. The assays require fresh blood, good laboratory equipment and well-trained personnel. They should be conducted by research organizations collaborating with the national malaria control programme. The results can provide additional information for interpreting results, together with studies of efficacy in vivo and surveys of molecular markers of resistance.

6.8 POSSIBLE METHODS FOR MONITORING THE EFFECTIVENESS OF SEASONAL MALARIA CHEMOPREVENTION

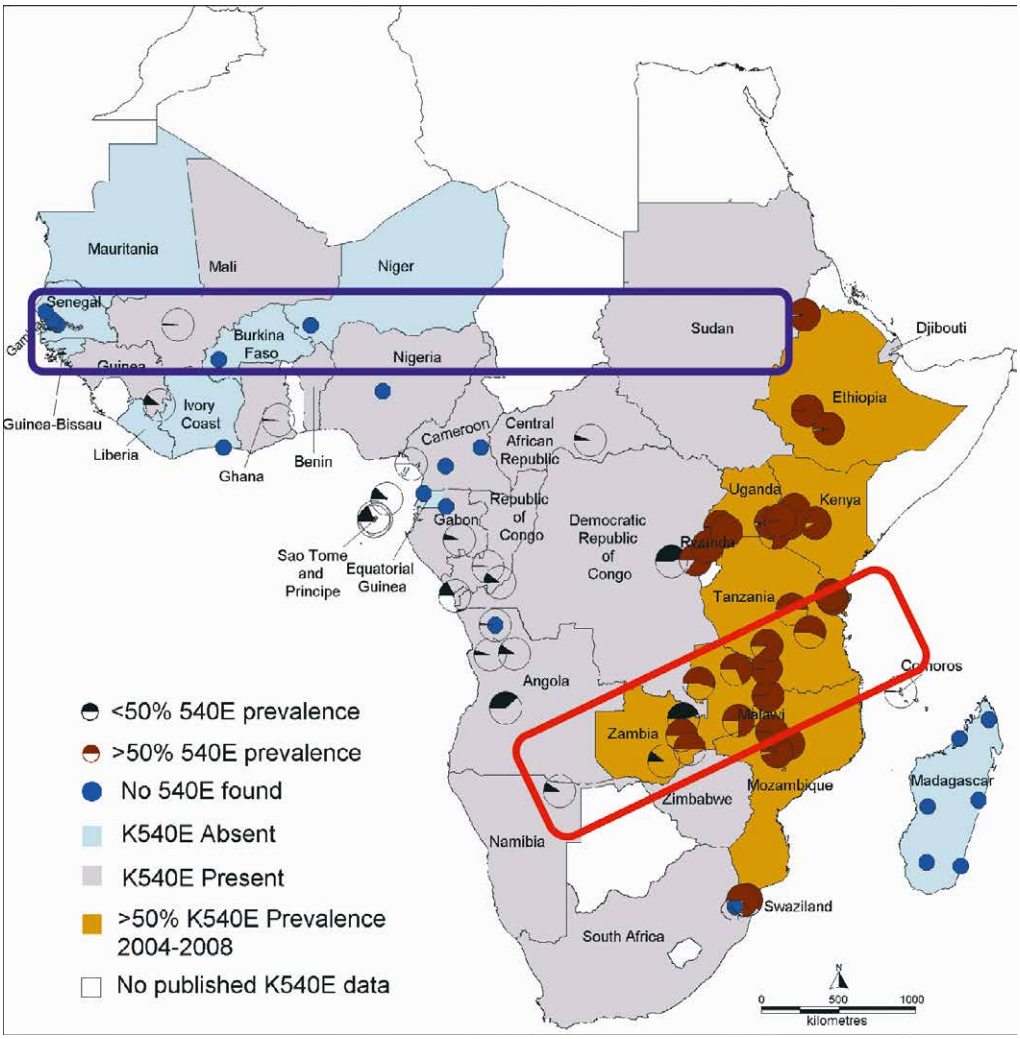
There is no established method for monitoring the programmatic effectiveness of SMC. Approaches that might be explored further in operational research are discussed below.

In the first year of SMC, a random sample of children who received the first course of treatment can be screened for parasitaemia at the time of administration of the second or third course to determine the proportion with breakthrough infections 1 month after a full course. Only children whose parents or caregivers report that no other antimalarial drug was given in the month following the previous SMC course should be included in these surveys and screened with rapid diagnostic tests. This survey should be repeated in subsequent years of implementation during the same SMC cycles of each round. An increase in the prevalence of malaria infections over time may suggest waning efficacy of SP + AQ, if SMC coverage did not decrease.

Monitoring episodes of malaria or the incidence of reported malaria in children under 5 years over time and plotting the number of malaria episodes against SMC coverage gives an indication of the efficacy of SP + AQ. An increase in the number of malaria episodes reported at community or health facility level at constant or gradually increasing SMC coverage may suggest that the efficacy of SP + AQ is decreasing, if the quality of the drugs can be ascertained during the specified period, the reporting system has not changed and other major determinants of malaria transmission (e.g. rainfall or vector control interventions) also did not change. On the basis of these observations, studies of markers of resistance to SP or in vitro sensitivity tests should be conducted to confirm the efficacy of SP + AQ.

ANNEXES

Annex 1. Distribution of resistance to sulfadoxine–pyrimethamine in sub-Saharan Africa



Legend:

Areas suitable for SMC (low prevalence of *K540E* mutation).

Although these areas are potentially suitable for SMC, research showed that they have a high prevalence of *K540E* mutation. Therefore SP + AQ is not recommended (Cairns et al., *Nature,* 2012).

From Naidoo I & Roper C. Drug resistance maps to guide intermittent preventive treatment of malaria in African infants. *Parasitology,* 2011, 138:1469–1479.

Annex 2. Sample calendar for community health workers

	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Month 0	Sensitization campaign in village																															
	Drugs (SP and AQ) distributed to CHWs																															
Month 1 (round 1 of SMC)	Distribution of SMC																															
	Catch-ups at health post																															
	Return unused drugs to health centre																															
	Sensitization for round 2																															
	Drugs (SP and AQ) distributed to CHWs																															
Month 2 (round 2 of SMC)	Distribution of SMC																															
	Catch-ups at health post																															
	Return unused drugs to health centre																															
	Sensitization for round 3																															
	Drugs (SP and AQ) distributed to CHWs																															
Month 3 (round 3 of SMC)	Distribution of SMC																															
	Catch-ups at health post																															
	Return unused drugs to health centre																															
	Inform population of end of campaign																															

AQ, amodiaquine; CHEW, community health worker; SMC, seasonal malaria chemoprevention; SP, sulfadoxine–pyrimethamine.
Months of distribution to be determined by the Ministry of Health. The first day of distribution can be changed; it need not be the first day of the month.

Annex 3. Sample form for counting treated and untreated children

Date : |___|___| |___|___| |___|___| District: ....

Health centre: .... Village/area: ....

Community health worker's name: ....

SMC period |__| Month 1 |__| Month 2 |__| Month 3

Household	Number of children aged 3–59 months					Number of children given SMC						Number of children not given SMC					
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	○	○	○	○	○		○	○	○	○	○		○	○	○	○	○
	Total =						Total =						Total =				

This form is to be used by community health workers to record the total number of children who should receive SMC, the number of children who were actually given SMC and the number of children who were not given SMC. During door-to-door visits for SMC administration, health workers should ask the head of the household or the caregiver how many children aged 3–59 months are present in the household before administering SMC. The health worker should cross-check the information with other members of the household if possible. The health worker responsible for filling in forms should give the household a number according to the order in which households were visited (1, 2, 3, 4 etc.). Each row represents one household. If there are more than five children in a household, the health workers should use the next row and repeat the household number. For each child aged 3–59 months living in the household or compound who is eligible to receive SMC, the health workers should put a cross in the first circle (first row) of the second column (under the heading 'Number of children aged 3–59 months'). If the child received SMC during the visit, the health workers should put a cross in the first circle of the third column (under the heading 'Number of children treated'); if the child was not treated, the health workers should put another cross in the fourth column (under the heading 'Number of children not treated'). A separate form should be completed for administration of each course of SMC.

Annex 4. Sample form for reporting drug use by community health workers

At the end of each course of SMC, community health workers should report to the health centre on the number of SMC courses received, administered and remaining.

Date : |___|___| |___|___| |___|___| District: .....

Health centre: ..... Village/area: .....

Community health worker's name: .....

SMC period |__| Month 1 |__| Month 2 |__| Month 3

All children aged 3–59 months	SP	AQ
Number of SMC tablets received	|__|__|__|__|__|__|__|	|__|__|__|__|__|__|__|
Number of SMC tablets used	|__|__|__|__|__|__|__|	|__|__|__|__|__|__|__|
Number of SMC tablets remaining	|__|__|__|__|__|__|__|	|__|__|__|__|__|__|__|

Comments:

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Annex 5. Sample supervisory checklist for district health officers monitoring implementation

This form should be completed by a senior member of the district health staff who is responsible for supervising nurses at the health centre. The supervisor should visit each village before the first cycle of SMC administration each year, interview one randomly selected community health worker per village and cross-check the information provided.

Date	District	Health centre
|__|__| |__|__| |__|__|	.....	.....
Village	Supervisor's name	Health worker's name
.....	.....	.....

SMC course	|__| Month 1 |__| Month 2 |__| Month 3	
Estimated number of children under 5 years in the locality	|__|__|__|__|__|	
Number of community health workers in the locality	|__|__|	
Number of community health workers who received training to deliver SMC	|__|__|	
Do all community health workers in the locality have sufficient knowledge about the SMC strategy?	|__| Yes	|__| No
Has any sensitization about SMC been provided in the locality?	|__| Yes	|__| No
Has any sensitization material been displayed or distributed in the locality?	|__| Yes	|__| No
Is the community aware of the SMC implementation programme?	|__| Yes	|__| No
Was training organized to teach caregivers how to give SMC drugs?	|__| Yes	|__| No
Were members of the community involved in SMC sensitization activities?	|__| Yes	|__| No
Has the community been told when SMC implementation will start?	|__| Yes	|__| No
Does the health worker have relevant SMC implementation documents (instructions)?	|__| Yes	|__| No
Does the health worker have sensitization material?	|__| Yes	|__| No
Does the health worker have SMC drugs in stock for implementation?	|__| Yes	|__| No
Does the health worker have a register?	|__| Yes	|__| No
Does the health worker have SMC cards for caregivers?	|__| Yes	|__| No
Does the health worker have forms for SMC drug management?	|__| Yes	|__| No

Supervisor's comments:

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Annex 6. Sample form for monitoring the performance of community health workers

This form should be completed by the nurse at the health centre who responsible for supervising community health workers. The nurse should visit the health workers during SMC administration, at least once per transmission season, to obtain the information required by interviewing and observing the health workers at work.

Date	District	Health centre
|__|__| |__|__| |__|__|	.....	.....
Village	Supervisor's name	Health worker's name
.....	.....	.....

1. Direct observation of SMC administration		
Does the community health worker have all material for SMC administration?	|__| Yes	|__| No
Does the community health worker have a register for recording information?	|__| Yes	|__| No
Does the community health worker have SMC administration cards?	|__| Yes	|__| No
Did the community health worker give information on SMC to the caregiver?	|__| Yes	|__| No
Did the community health worker explain that SMC is administered on three occasions* during the rainy season?	|__| Yes	|__| No
Did the community health worker check the child's identity and age?	|__| Yes	|__| No
Did the community health worker check whether the child is well and eligible for SMC?	|__| Yes	|__| No
Did the community health worker give the right dose of SP + AQ to the child?	|__| Yes	|__| No
Did the community health worker keep the child under observation for at least 30 min after treatment?	|__| Yes	|__| No
Did the community health workers give the second and third dose to the caregiver?	|__| Yes	|__| No
Did the community health worker explain to the caregiver how to administer the second and third doses?	|__| Yes	|__| No
Did the community health worker give an appointment for the next course of SMC?	|__| Yes	|__| No
Did the community health worker fill in the SMC card correctly?	|__| Yes	|__| No
Did the community health worker record information correctly in the register?	|__| Yes	|__| No
Did the community health worker rinse spoons, syringes and cups used for SMC administration?	|__| Yes	|__| No
2. Sensitization of caregivers		
Did the community health worker explain the difference between SMC and community case management of malaria or integrated case management**?	|__| Yes	|__| No
Did the community health worker inform the caregiver about the side-effects of SMC drugs?	|__| Yes	|__| No
Has the caregiver been told what to do if an adverse event occurs?	|__| Yes	|__| No
Did the community health worker tell the caregiver to seek treatment at any time if their child is sick?	|__| Yes	|__| No

Supervisor's comments:

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* May be changed to four courses, as appropriate

** For areas where community case management or integrated community case management of malaria is being implemented

Annex 7. Sample form for health workers interviewing mothers to assess their knowledge and understanding about seasonal malaria chemoprevention

This form should be completed by the nurse responsible for supervising community health workers at the health centre. The nurse should carry out a survey of a random sample of caregivers to assess their knowledge about SMC and their acceptance of the strategy. This activity should be undertaken during the first cycle of SMC in the first year and can be repeated every 2–3 years.

Date	District	Health centre
|__|__| |__|__| |__|__|	.....	.....
Village	Supervisor's name	Health worker's name
.....	.....	.....

1. Caregivers' knowledge about SMC		
Has the caregiver been informed about SMC?	|__| Yes	|__| No
Does the caregiver know that SMC is given during the rainy season?	|__| Yes	|__| No
Does the caregiver know that SMC is given over 3 months* at 1-month intervals?	|__| Yes	|__| No
Does the caregiver know that she or he should give second and third* doses at home?	|__| Yes	|__| No
Has the caregiver been told how to administer the drug at home?	|__| Yes	|__| No
Does the caregiver know that younger (3–11 months) and older (1–5 years) children are given different doses of SMC drugs?	|__| Yes	|__| No
Did the caregiver receive information on the side-effects of SMC drugs?	|__| Yes	|__| No
Can the caregiver name at least one side-effect?	|__| Yes	|__| No
If yes, ask the caregiver to name one side-effect.....		
Does the caregiver know what the SMC card is used for?	|__| Yes	|__| No

2. Acceptability of SMC to caregivers		
How many children aged 3–59 months are under the responsibility of the caregiver?	|__|___|	
How many of these children received SMC treatment?	|__|___|	|__| NA
If there are children who did not receive SMC, give the reasons: Reason for child 1..... Reason for child 2..... Reason for child 3..... Reason for child 4..... Reason for child 5.....		
Did the caregiver keep the SMC drug packaging?	|__| Yes	|__| No
Is the caregiver satisfied with the community health worker's work?	|__| Yes	|__| No
If no, ask the caregiver to give reasons. 1. ..... 2.		
If yes, ask the caregiver to list at least a few. 1. ..... 2.		

Supervisor's comments: .....
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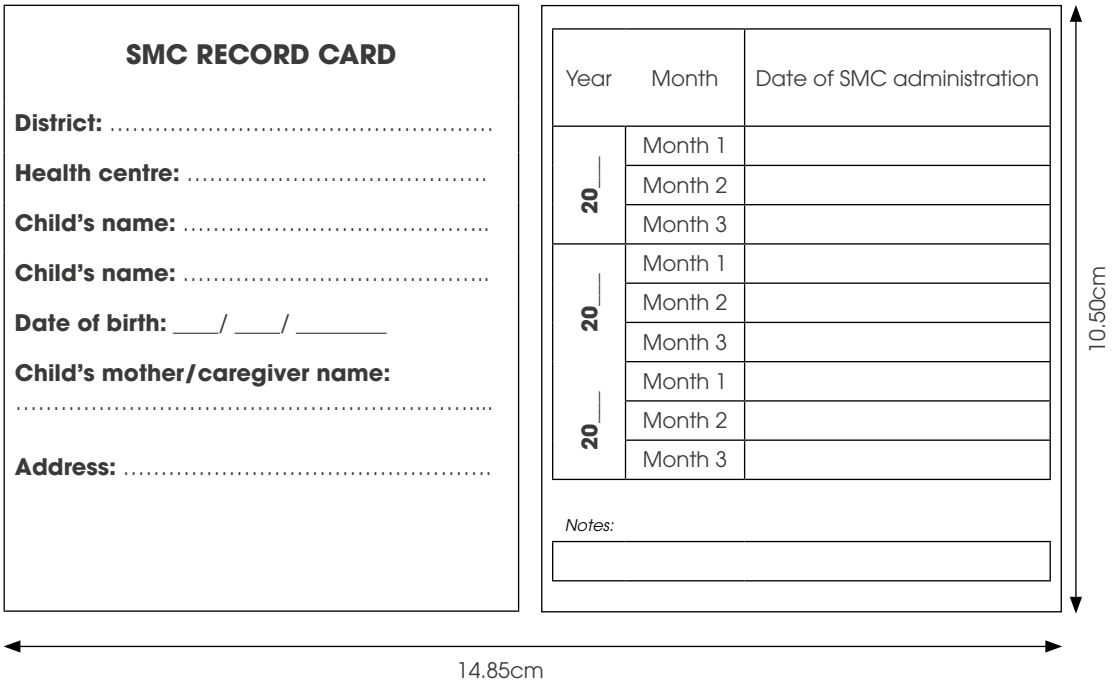
* May be adapted for different number of courses

Annex 8. Sample administration card

All children under the responsibility of each caregiver who are eligible for SMC should be given a card before administration of the first dose of SMC. The community health worker should complete this card by recording the name of the district, health centre and village, the child's date of birth (if available), the child's mother's name and the date of SMC administration. The date of administration must be given for each cycle as proof that the child received SMC. If SMC is not given, the date of administration should be left blank and a comment made at the bottom of the card in the area labelled 'note, such as 'child absent', 'refused' or ineligible ('child sick', 'child received SP + AQ in the past 30 days', 'child allergic to SP or AQ', 'child aged more than 59 months'). The caregiver should be instructed to keep the card safely for the next cycles of SMC.



Annex 9. Sample form for reporting by health centres and districts

Nurses should use this form to compile information provided by community health workers and report to the district medical office at the end of each SMC course

Date : |__|__| |__|__| |__|__| District: .....

Health centre: ..... Village/area: .....

Head of health centre or district: .....

SMC course |__| Month 1 |__| Month 2 |__| Month 3

	SMC administered	Expected	Coverage* rate
Number of children aged 3–59 months given SMC in the health zone	|__|__|__|__|__|__|__|	|__|__|__|__|__|__|__|	

*Coverage is estimated from the number of children who should have received SMC as recorded by the community health worker and the number of children who actually received SMC during each course.

Comments:

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Annex 10. Adverse events reporting form used in a study of the effectiveness of seasonal malaria chemotherapy in Senegal

Ministry of Health and Disease Prevention, Department of Health, Division of Disease Control, National Malaria Control Programme

Drug-related adverse event notification form

This form gives information contained in the 'yellow form' that should be completed by health personnel as part of routine surveillance of adverse drug reactions. Strengthening the local pharmacovigilance system is required to ensure effective reporting of adverse drug reactions during SMC implementation.

<table>
<tr><th>Patient</th><th>Reporter</th></tr>
<tr><td>Name: ……</td><td>Name: ……..…</td></tr>
<tr><td>Date of birth:……../……../…….. or age: ……..</td><td>Medical doctor: /___/ Pharmacist: /___/</td></tr>
<tr><td>Sex: F /___/ M /___/</td><td>Dentist: /___/ Nurse: /___/ Midwife: /___/</td></tr>
<tr><td>Weight: ……..</td><td>Other /___/ (specify): ……</td></tr>
<tr><td>Record number: ……</td><td>Specialization: ……</td></tr>
<tr><td>Medical history/associated factors</td><td>Telephone: ……..
Fax: ……
Email: ……
Institution: ……</td></tr>
<tr><td rowspan="2">Description of event:
……
……
……
……

Date of onset: ……/……./…….
End date: ……/……../…….</td><td>Action taken:
Follow-up: /____/ Hospitalization: /____/
Referral: /____/ Other: /____/ (specify):
……</td></tr>
<tr><td>Treatment:
Yes: /__/ (specify): ……..
No /__/</td></tr>
<tr><td></td><td>Date: ……./……./…….</td></tr>
</table>

Signature of Reporter: _____

World Health Organization

Seasonal Malaria Chemoprevention
with sulfadoxine–pyrimethamine plus amodiaquine in children

A field guide

Global Malaria Programme
World Health Organization
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1211 Geneva 27 - Switzerland
http://www.who.int/malaria/en/

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