INTERSECTION MSF POLICY ON MALARIA

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Version with explanatory endnotes

1. Introduction

The overall aim of MSF's policy on malaria is to provide a framework for a combination of optimal case management of malaria patients, and the implementation of appropriate preventive measures, accompanied by appropriate advocacy.

Since 2002 it has been MSF's policy to use artemisinin based combination therapy (ACT) for the treatment of parasitologically confirmed malaria due to Plasmodium falciparum (P.f).

Although MSF has been a major actor in piloting and advocating for optimised case management for malaria patients, the role of MSF in malaria prevention has been, for several years, more low profile and less ambitious, leading to insufficient and poorly tracked implementation of vector control measures.

Recently however there has been a renewed interest in optimising vector control, with increasing investment in entomological insight ("vector intelligence"), greater awareness in the projects of the role of vector-based prevention measures, and piloting innovative tools. This has been triggered by recognition of the inadequate implementation of vector control within projects, as well as concerns regarding increasing resistance to the currently used insecticides threatening much of the gain made in recent years.

Pharmaceutical prevention was previously limited to the prevention of malaria in pregnant women and expatriate health care. However, there has been a rapidly growing interest since 2011, when MSF was amongst the first actors to implement the seasonal malaria chemoprevention (SMC) strategy in the Sahel countries outside a research context, offering monthly antimalarial drugs to children under 5 years old during the narrow transmission season. The observed impact and feasibility has triggered discussions on a wider use of pharmaceutical prevention in several other situations, such as complex emergencies, malaria epidemics and in elimination settings, as well as for vulnerable groups outside the Sahel.

Therefore MSF must invest much more in vector control as well as in pharmaceutical prevention, given that effective malaria control requires integrated interventions targeting both case management and prevention, and that the latter has significant potential to become a game changer in both chronic and complex emergencies.

Although MSF was on the forefront in the monitoring of drug efficacy at the time of ACT rollout, currently despite global concern, MSF has insufficient involvement in the fight against the developing artemisinin resistance, which is at present limited to the Mekong sub region.

2. THE DIAGNOSTIC STRATEGY

2.1. MSF projects will ensure that each suspected malaria patient gets an appropriate parasitological diagnosis, based on microscopy or rapid diagnostic test[1]
MSF opts now for the use of pan pLDH tests as first choice in hyper- and holo-endemic areas as well as in areas with intense seasonal transmission, in malaria outbreaks and in complex emergencies. In other contexts the HRP2 based tests or combo-tests remain the first choice for the time being[2].

In general practice, RDTs should not be used to screen for malaria, but only to confirm clinically suspected malaria. Screening is limited to screening of blood donors, pregnant women at prenatal consultation, patients on admission in a nutrition program, and in specific contexts such as pre-elimination settings where persons with a high risk of infection may be screened.

In each project, there should be clear guidance on the management of patients presenting with symptoms of malaria and a negative RDT or blood smear.

2.2. Systematic confirmation of clinical diagnosis may not be appropriate in an epidemic where a high proportion of patients have a positive RDT and the workload linked to testing has a negative impact in access or quality of care[3]

2.3. The use of RDT and microscopy must be subject to quality assurance (QA)[4]

3. The treatment of malaria

3.1. The treatment of patients with uncomplicated P.*f* malaria is based on correct use efficacious quality-assured ACT[5]. All patients with confirmed P.*f* should be treated with ACT, including children under 5 kg and in all trimesters of pregnancy.

As there are now alternative ACTs for each context, a second line ACT to be used in case of treatment failure or contra-indication should be identified and provided[6].

To date there is no artemisinin resistance confirmed outside the Mekong region, therefore treatment failures elsewhere are either due to host factors, or failing efficacy of the partner drug.

It is mandatory to invest in measures to optimise adherence to treatment[7].

3.2. The treatment of severe malaria is based on the use of injectable artesunate IV, or IM when the IV route is not feasible or would delay significantly the administration[8]
Severe malaria in pregnant women should also be treated with injectable artesunate as first line, including during the first trimester.
Advocacy to ensure national protocols include the treatment of pregnant women including during the first trimester with artesunate injections, followed by 3 days ACT, is still needed.

3.3. Pre-referral treatment of patients with confirmed or suspected severe malaria is based on injectable artesunate and rectal artesunate where injectable is not possible[9]

3.4. Treatment of non-falciparum malaria: in areas where < 5 % of malaria diagnoses are due to (mono-infections) with non P.*f* malaria, patients with species other than P.*f* will also be treated with the first line ACT of the country. In areas where more than 5 % of malaria diagnoses are due to non P.*f* species, the recommended treatment for species other than P.*f* remains 3 days of chloroquine where still efficacious.
In case of P.v or P.*ov* infection, initial treatment should be followed by radical treatment to eliminate the liver stage hypnozoids[10]

3.5. To extend coverage and access, MSF supports the involvement of trained and supervised outreach workers for first line case management[11] and supports the implementation of iCCM (integrated community case management)[12] where indicated.

Importantly at the community level the management of the patients with a negative malaria test has to be clear and feasible, either through further case management at the community level as in iCCM, or through referral.

MSF does not support the practice of encouraging families to keep antimalarial drugs at home for stand-by treatment in case of fever[13]

3.4. Ensure safe blood transfusion wherever severe malaria patients are treated.

4. Vector control based prevention

4.1. Vector control measures must be implemented in all in-patient facilities in endemic areas with IRS and LLINs for patients, caretakers and staff.

4.2. In a closed setting such as a refugee camp in an endemic area, the entire population must be protected by adequate vector control measures, i.e. LLINs, and where indicated additional measures such as IRS or larviciding may be considered.

4.3. In emergencies in endemic areas timely implementation of vector control measures is mandatory. Both LLINs and IRS can be used, possibly in combination[14].

4.4. Appropriate vector control measures of proven efficacy should be implemented in MSF projects in open setting in malaria endemic and epidemic prone areas. As a minimum LLINs should be provided to the most vulnerable[15], and broader vectorcontrol measures also considered to achieve a community effect.
High LLIN coverage in the project catchment (e.g. estimated at 80% in average setting) will reduce the vectorial capacity of the malaria-carrying mosquito, and thus reduce transmission[16].

4.5. Distribution of LLINs or the implementation of IRS has to be accompanied by appropriate health promotion. A survey to evaluate the coverage and the use is recommended.

4.6. MSF opts for the use of WHOPES approved or WHO prequalified resistance-overcoming new generation of LLINs where appropriate[17]
Because of the increasing resistance to pyrethroids, MSF opts for the next- generation LLINs where indicated,taking into account existing information on insecticide resistance. The new generation LLINs combine a pyrethroid with insect growth regulator, or two insecticides of different classes (the former expected to become available in 2017, the latter several years later). Until these next-generation LLINs are available, MSF's interim recommendation is to use LLINs combining a pyrethroid insecticide with a synergist, piperonyl butoxide (PBO)[18].

4.7. For IRS, MSF opts for the non pyrethroid products, and should aim at rotation of products from differet classes[19].

4.8. Larviciding should be considered as an additional tool where LLIN or IRS have insufficient impact (due to vector characteristics and/or human behavior) and where it is technically feasible such as in slums or camp setting[20]

4.9. MSF strives to remain closely involved with innovative VC tools. The distribution and intensity of insecticide resistance threatens the effectiveness of "core" malaria interventions. New paradigms of vector control and personal protection tools are being designed and evaluated. Recognising the need for novel vector control tools, MSF is actively involved in the identification and integration of novel products and approaches to vector control.

Information describing the vector ecology and insecticide susceptibility profile is central to the selection of appropriate vector control tools and operational planning of interventions. Where this information is not available or if not possible to generate in a reasonable timeframe, this should not lead to a delay in the intervention, especially not in emergencies.

5. Pharmaceutical prevention of malaria

5.1. MSF supports the WHO recommended strategy in **intermittent preventive treatment in infancy (IPTi)**, providing one curative doses of SP at the occasion of each EPI vaccination in the first year if life[21].

5.2. MSF recommends the implementation of the standard **SMC (seasonal malaria chemoprevention),** as recommended by the WHO in areas where at least 60 % of the malaria cases are concentrated in 4 months, within the Sahel sub region only[22].

5.3. **IST combined with IPTp in pregnancy**: MSF uses a combination of the WHO recommended IPTp (intermittent preventive treatment in pregnancy) and IST (intermittent screening and treatment) in pregnancy, see below chapter 6 on malaria and pregnancy

5.4. **Mass drug administration and intermittent preventive treatment with ACTs**

Mass Drug Administration (MDA) covers the entire population, while *targeted Mass Drug Administration* targets specific groups or areas, and may eventually be scheduled to be repeated thereby becoming *intermittent preventive (presumptive) treatment (IPT)*. Thus this may also cover the entire population in a specific area or *target* a specific age group as children (ITPc), a season (ITPs), or refugees.

The principle is based on the combination of a *presumptive treatment effect*, that is the elimination of parasites if present, as well as a *preventive effect* due to the long half-life of the partner molecule (*intermittent presumptive and preventive treatment, IPPT*). This effect can be estimated at 2-6 weeks depending on the ACT combination used. Currently the partner molecules with the longest half-life are Mefloquine and Piperaquine.

MSF recommends the choice of dihydroartemisinin-pipearquine (DP) as ACT of choice for IPT or MDA[23].

The implementation of these strategies may be considered in the situations listed below aiming for a rapid reduction of malaria morbidity and mortality:

1. A complex emergency in a region and period of high incidence of malaria, especially before having the opportunity to implement the appropriate vector control measures or to ensure access to diagnosis and treatment.
2. A malaria epidemic in a similar situation, with the same reasoning as above
3. An emergency situation in an unstable region, with a mobile population (for example due to permanent insecurity), where proper use of mosquito nets or other measures of vector control by the population is not possible and where access to health structures is increasingly difficult,
4. Experimental: In the context of seasonal transmission with high malaria burden, with the aim of contributing to a reduction in morbidity and mortality[24].

The notion of “exceptionality” is important, as these strategies are not yet externally validated, their feasibility and acceptability still have to be further documented, and the impact further quantified. Moreover these strategies that need a heavy investment only provide a short term solution, and there is a risk of contributing to ACT resistance if adherence to treatment is insufficient.

These strategies should not replace the investment in the standard preventive and curative services, and one has to realize that this implies the repurposed use of ACTs as these are not validated for prevention.

Further research on the use of ivermectin as an addition to mass drug administration is in the phase of research[25]

Table: overview pharmaceutical prevention

context	***strategy***	***molecule***
permanent high transmission & SP effic	IPTi	SP
seasonal high transmission Sahel	SMC	SP-AQ
complex emergencies high transmission area, malaria epidmics	IPPT or MDA	ACT(DHA-PQ)
experimental : seasonal transmission outside Sahel	IPTseasonal	ACT(DHA-PQ)
pregnancy endemic area	IST + IPTp	ACT if pos, SP if neg.

5.5. Malaria vaccination

MSF will not use the RTS,S malaria vaccine because of lack of well documented significant efficacy, the need to further clarify the safety profile, and the concerns regarding the feasibility of implementation (4 doses not corresponding to EPI calendar)[26].

6. Malaria and pregnancy

6.1. Pregnant women should sleep under an LLIN: at the antenatal consultation the woman should receive two LLINs[27] at the first antenatal consultation.

6.2. Only ACTs should be used during pregnancy for the treatment of uncomplicated malaria, including during the first trimester[28].

6.3. Only injectable artesunate should be used for the treatment of severe malaria in pregnancy, including during the first trimester (as recommended also by WHO)

6.4. At antenatal consultations, MSF opts to combine the (WHO recommended) IPTp with IST: at each ANC the woman is screened with an RDT, receives ACT if positive and SP if negative[29] (maximum monthly from the second trimester onwards)**.** For HIV positive pregnant women, IST will be done monthly. SP should not be administered to the women who test negative on RDT if they are already taking cotrimoxazole prevention (CTX)[30].

6.5. For diagnosis and screening, the use of RDT is preferred over microscopy, because of the possible sequestration of parasite in the placenta during pregnancy with associated increased risk of false negative microscopy.

7. ACT efficacy and early detection of emerging artemisinin resistance

Where the results of recent reliable ACT efficacy studies are not available, MSF should initiate such studies or lobby for other actors to do so.

Outside the particular situation in the Mekong with emerging artemisinin resistance, the efficacy studies should, in the first place, evaluate the efficacy of the partner drug: if below 95% efficacy a change should be considered and if below 90% efficacy the ACT should be changed, in line with WHO recommendations. Lobbying at the national level may be indicated.

Priority should be given to areas where previous studies have indicated existing compromised efficacy, or where molecular marker studies have indicated an increasing proportion of mutations known to correspond to resistance[31].

Where artesunate/amodiaquine (AS/AQ) is the first line treatment and there is proven high efficacy, switching to artemether/Lumefantrine (A/L) should be avoided, as this in effect would mean increasing the number of doses from 3 to 6. In addition it would avoid increasing drug pressure on A/L as this is already the most widely used ACT.

8. Malaria in (pre)-elimination context

A country or a region can be considered to be in pre-elimination phase if the (microscopy or RDT) positivity rate for fever cases is permanently below 5%, and in elimination phase when there is less than 1 case/1000 per year (N.B. this is arbitrary, and varies depending on diagnostic strategy used).
If MSF is involved in malaria in such a context, the programmatic approaches must be adapted, and may include more sensitive diagnostic tools, strategies such as active case-finding, intense follow-up of patients after treatment and stringent measures to improve adherence as well as the addition of single-low dose primaquine (i.e. for its gametocytocidal effect), and increased preventive measures. The approach may eventually include MDA but also measures focusing on mobile populations to avoid (re-) introduction of malaria.
In case of active involvement of MSF in (pre)-elimination interventions in such a context, sustained activities over several years have to be guaranteed by MSF or other actors, because of the expected rapid rebound.
In these cases HQ advice is mandatory.

9. Operational research and advocacy

9.1. Operational research (OR) and publications using data and experiences from MSF projects are encouraged.
OR and publications are important to demonstrate the effectiveness and/or feasibility of our strategies, especially the innovative strategies.
MSF prioritizes research on operationalization of strategies, especially in places where other actors are less active, and with a specific focus on vulnerable populations
The focus of vector control related OR is on adapted tools for displaced populations and populations in precarious situations; OR linked to pharmaceutical prevention focuses on adapted strategies for complex emergencies and epidemics. FInally, OR linked to drug resistance focuses on the Mekong where artemisinin resistance is spreading and on the efficacy of other antimalarials in countries neglected from that perspective.

9.2. MSF will advocate on access to optimal malaria management, as well prevention as case managelent
Advocacy, especially when benefitting from field experiences and observations, is encouraged and should contribute to better access to appropriate preventive and curative management for all patients.
Advocacy and lobbying towards sufficient attention for vulnerable populations and high burden countries, towards donors and other actors is a permanent task of MSF

- Medical-technical advocacy aiming at the further development of quality assured tools and strategies has to be continued.

ENDNOTES

[1]For diagnosis of malaria, both microscopy and malaria Rapid Diagnostic Tests (RDT) are recommended. The decision on which to use should be guided by the availability of quality microscopy and the practical feasibility of offering timely diagnosis to all. If used, microscopy results should be available within a reasonable time to orient the clinician (N.B. more than two hours is not acceptable).
In practice, because of the rapid availability of the results, user-friendliness and reliability of RDTs on the one hand, and the often poor quality of microscopy on the other hand, the initial diagnosis is based on RDT in the vast majority of projects.

[2] Until 2016 there were two types of RDT available as MSF standard: a histidine rich protein-2 (HRP2) based test which identifies only Plasmodium falciparum (P.*f)*, and a "combo-test" having an HRP2 line next to a pan Plasmodium lactate dehydrogenase (pan pLDH line) which reacts to all plasmodial species including P.*f*.
These combotests are advised if mono-infections with species other than P.*f* make up more than 5% of the local malaria infections (N.B. this threshold is based on consensus only).
Developments in 2015/16, namely greater understanding of the very long HRP2 antigen persistence after elimination of malaria parasites, have led to an adaptation in the recommended choice of tests. An MSF/Epicentre study in 2016 showed that median time to become negative was 6 weeks after elimination of parasites (i.e. 50% of HRP2 based tests are still positive 6 weeks) whereas this is two days for pan pLDH based test. This long persistence results in a low specificity of HRP2 tests especially in areas with high reinfection rates, and can lead to overdiagnosis of malaria, missing other potentially important diagnoses and less clear insight in real epidemiology.
Other arguments in favour of pan pLDH tests over HRP2 based tests are: less risk of prozone effect (i.e. a physical effect due to precipitation of antigen leading to a false negative test in cases of very high parasitemia), pan pLDH tests also allow the detection and treatment of the non-P.*f* species (even if they make only up for a small proportion of the patients), and recent information about the existence (and possible spread) of parasite strains with mutations of the HRP2/HRP3 producing genes, no longer producing HRP2 and/or HRP3 and as such potentially lead to false negative tests.

[3] In epidemics or other situations where a very high proportion of patients with suspected malaria have a positive RDT (an arbitrary level of >80% has been proposed) AND the workload of systematic testing has a negative impact on access to quality of care, treatment on clinical basis may be considered. If this is done, the situation must be monitored with regular sampling to determine when to restart systematic testing of suspected cases.

[4] MSF recommendations for the QA of microscopy are available and should be followed
MSF uses only WHO prequalified RDTs, or otherwise validated by the MSF QA referents.

[5] ACT's are a combination of the short acting artemisinin derivate (artesunate, artemether or dihydroartemisinine), with a long-acting partner drug. The choice of the combination is based on the efficacy in the country or area, the ease of use, as well as other factors such as national protocols.

[6] The second line ACT to be used in case of treatment failure after the first line ACT will be most likely artemether-lumefantrine in places where artesunate-amodiaquine is first line, and dihydroartemisinin-piperaquine or artesunate mefloquine in places where artemether-lumefantrine is the first line. The same ACT can be repeated if the treatment failure is most likely due to obviously poor adherence to the initial treatment course.
Strategies for defining treatment failures depend on the context and diagnostic tools available. Therefore these should be prepared locally with advice from the section's malaria advisor.

[7] The first ACT dose has to be given under direct observation. Project staff must invest in appropriately adapted patient information and proper drug dispensing practices, especially for smaller children. Guidance is

available from the malaria WG. It is recommended to consider the evaluation of adherence through studies in case of concerns.

[8] Patients with severe malaria must receive artesunate injections, on the basis of proven superiority in reducing mortality compared to quinine (and to a lesser extent compared to artemether injections),
After a minimum 24 hours of initial parenteral artesunate treatment (i.e. 3 doses), a full course of ACT should be started as soon as the patient can eat and drink if oral treatment is not possible injectable artesunate will be continued for 7 days.

[9] Depending on the capacity of the personnel, use IV or IM artesunate as pre-referral treatment before transfer to an appropriately equipped structure. If this is not possible because of the level of the staff, rectal artesunate should be given as pre-referral treatment for children under 6 years. After a single dose of rectal artesunate, referral is mandatory and the doses cannot be repeated.
Patients with severe malaria need further supportive treatment including monitoring of haemoglobin and transfusions when needed. Hence patients must not be kept at a level of care where these treatment options cannot be offered.

[10] The radical/curative treatment of Pv and Po is based on primaquine for 14 days in case absence of G6PD deficiency has been documented by a quantative test, and where a low rate of reinfection is anticipated.

[11] Access can be largely increased by the involvement of community health workers (malaria village workers, community malaria workers etc.) offering community based case management i.e. parasitological diagnosis, ACT treatment for the positive patients, and a single dose of rectal artesunate as pre-referral treatment in case of symptoms of severe malaria.
Where community case management is implemented, MSF must ensure that support to the health centers remains adequate i.e. to avoid shifting patients from professional health care workers to lay care providers. MSF should also ensure referral pathways for the referral of patients with symptoms of severity

[12] Importantly at the community level the management of the patients with a negative malaria test has to be clear and feasible. This could include a simple management algorithm to treat other recognised priority health problems at the community level e.g. integrated community case management of fever (iCCM) – focussing on the malaria, pneumonia and diarrhoea. In this strategy, as well as using an RDT to investigate fever, the respiratory rate is assessed as an indicator of respiratory tract infection and diarrhoea is assessed on anamnesis or observation

[13] Home based managment in the sense of having the treatment in the hands of the family would most likely not allow for parasitological confirmation (the use of RDTs requires training and correct waste management), and would raise concerns about drug quality e.g. storage conditions, checking expiry dates etc.

[14] Rapid deployment of vectorcontrol in an emergency situation is essential, therefore the choice between undertaking a LLIN distribution or IRS campaign must consider operational elements such as the rapid availability of products and the logistical constraints associated with deployment. Other factors including population characteristics (density, mobility, and acceptance) and the physical characteristics and dispersal of shelters as well as the time in the emergency can be taken into account. Seeking the advice of the vector and malaria advisors is recommended.

[15] I open setting, as a minimum LLINs should be provided to the population subgroups most vulnerable to malaria morbidity and mortality i.e. all pregnant women and children under 5 should receive a net during prenatal consultations and EPI/emergency vaccination opportunities respectively.

[16] The overall reduction in transmission provides a “community effect” by which even those residents not sleeping under a LLIN have increased protection from malaria infection. The coverage threshold where LLINs provide a mass, “community effect” depends on the context.

[17] The use of intact LLINs without an efficacious insecticide will provide personal protection, but no longer induce mosquito mortality and thus may not have a community effect on transmission. Moreover, the impact

of insecticide resistance may lead to a reduction in LLIN-conferred personal protection with gradual hole acquisition. Although there is no clear evidence of impact yet, insecticide resistance threatens to reduce the impact of core vector control interventions on transmission.

[18] The synergist PBO is a non-insecticidal chemical that increases sensitivity to the insecticide by reducing the mosquito's capacity to enzymatically degrade the insecticide component.

[19] Insecticides from four different classes are approved for use in IRS and may be considered as part of an insecticide resistance management strategy. There is evidence that insecticide rotation or mosaics may slow the rate of operationally significant insecticide resistance, and this should be considered in MSF projects.

[20] The availability of new safe and user-friendly larvicides make this strategy more feasible
Larvicides such as growth regulators can be beneficial as they do not target adult mosquitoes (i.e. which is the mode of action for LLINs and IRS) and therefore can be useful as a component of an insecticide resistance management strategy i.e. they have an additive impact when integrated with LLIN or IRS interventions. They may also have an impact on outdoor-biting malaria vectors. Larviciding may not be applicable for certain contexts or species or malaria vectors e.g. if breeding sites are too widespread.
Entomology and malaria advisors should be consulted for the planning of larviciding activities.

[21] IPTi This standard approach is based on the administration of a curative dose of sulphadoxine-pyrimethamine (SP) at the occasion of the EPI vaccinations, to be implemented only in areas with permanent significant transmission and sufficient efficacy of SP

[22] The standard SMC (seasonal malaria chemloprevention) strategy is based on 3 or 4 rounds of monthly sulphadoxine-pyrimethamine + amodiaquine (SPAQ) to children under five, during the transmission season.Variations on the strategy (for example targeting wider age groups, or SMC with different molecules) are currently only considered in the frame of operational research.
This intervention has to be well planned, with appropriate community involvement. The first dose has to be administered under direct observation and only co-blistered SP + AQ should be used.
This strategy must not lead to decreased attention to curative services.
Appropriate vector control measures should be implemented in areas of SMC
Combination of this strategy with other prevention strategies (vaccination, nutrition activities etc.) may be considered, taking into account that the monthly schedule of SMC needs to be respected.

[23] Mefloquine and piperaquine offer longer protection than amodiaquine and lumefantrine.
Mefloquine is present in the artesunate/mefloquine (AS/MQ) combination and provides (relative) protection for up to 6 weeks. It is administrated as a single daily dose for 3 days. However, it is often not well tolerated, which can reduce the adherence.
Moreover there are concerns about (long-term) side effects.
Piperaquine is present in the dihydroartemisinin-piperaquine (DP) combination, and provides a (relative) protection of approximately 4 weeks. The DP combination is well tolerated and is administered as a single daily dose for 3 days. Since the duration of protection does not exceed 3-4 weeks, one or more repetitions may be considered.
As DP is now increasingly available and being registered in more countries, for IPT or MDA MSF should only use DP. This choice is on the basis that with the same investment DP provides longer protection than with AS/AQ or A/L and it is preferable that the drug used in MDA or IPT is different from the drug used as first line treatment.
The emergency units of MSF should anticipate stocks of DP for rapid deployment in case of emergency.
In the frame of operational research, other drugs can be considered, such as artesunate-mefloquine or artesunate-pyronaridin.

[24] The biggest impact of the use of IPT with ACT outside the Sahel (where SMC is indicated) can be expected with 3-4 drug administration cycles with 4 week intervals during the months of highest transmission. Each cycle would protect the target population for 2-4 weeks depending on the drug used. This would be *in the framework of operational research* as the best approaches are yet to be defined (target age group, the number of cycles, the interval between cycles, the necessary resistance monitoring etc

[25] the use of ivermectine, an endo-isecticide taken as drug by human to kill the biting mosquito needs to be further investigated and optimized: target product profile, doses, safety, effect on different species, adapted drug formulation with slow release or uptake etc. The MWG is following the ongoing research on this topic and will advise operations according to the developments.

[26] This current position on the malaria vaccine may be revised once the results of the WHO-guided pilot studies that would start in 2018 are available (probably 2022). Other vaccines are in an early stage of development and testing

[27] A pregnant woman should receive two LLIN at the first ANC, as experience shows that if there is only one LLIN distributed, other family members may use it instead. Moreover this is a good way to scale up coverage in the population.
In case there is already a high coverage with LLINs in the entire catchment area, one LLIN may be sufficient

[28] To date, WHO and most national protocols still recommend quinine-based treatment during the first trimester. However quinine is associated with low adherence, poor tolerance and hence is less effective. This is not optimal especially at a time when a woman is more vulnerable to the effects of malaria infection due to pregnancy. WHO however also provides re-assuring information in case ACT has been taken during the first trimester (see WHO malaria treatment guidelines 2015)

[29] The WHO recommended intermittent preventive treatment (IPTp) based on the administration of SP at each antenatal consultation is still expected to have some impact on the birth weight and anaemia when the frequency of administration is increased (previously only 2 doses recommended during pregnancy), but increasing resistance to SP may lower the potential impact.
Intermittent screening and treatment (IST) alone, i.e. providing ACT to pregnant women with a positive RDT on screening at the antenatal consultation did not prove to be superior in recent studies.
MSF combines both strategies to optimise the impact, thus a pregnant woman is screened at each antenatal consultation (2nd and 3rd trimester), and receives ACT if RDT is positive, and a dose of SP (as preventative treatment) if the test is negative.
The test should not be repeated within a month if the previous test was positive due to the long persistence of HRP2 antigen.

[30] Providing SP as prevention to a woman already taking CTX is not recommended as CTX also provides relative protection, and the combination SP-CTX can lead to severe adverse effects. If a woman receiving CTX tests positive, the ACT used for treatment should not be AS-SP due to issues of cross-resistance and safety.

[31] In efficacy studies day 3 smear positivity should be analysed as an increasing positivity rate may indicate development of tolerance to artemisinin (e.g. no suspicion if below 3%, but if above 10% further studies are needed to confirm artemisinin tolerance or partial resistance).