

**IDENTIFYING AND MOVING LEVERS  
OF ACCEPTANCE AND UPTAKE  
OF RECOMMENDED QUALITY-ASSURED  
PAEDIATRIC ACTS  
FOR NON-COMPLICATED MALARIA  
IN SIX FRANCOPHONE AFRICA COUNTRIES**

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**November 2012**

## Abstract

Since the late 1990s, global health donors have channelled significant funding to develop new drugs for malaria, TB, HIV-AIDS, and neglected diseases. As part of this focused effort to make up for years of neglect, WHO has encouraged both drug development partnerships and national policy makers to prioritize improvements in therapies for paediatric patients. In the case of malaria, where children comprise approximately 90% of all malaria deaths, the urgency of this WHO advocacy work is particularly relevant.

The good news is that in the past four years, new WHO-recommended options for treating children with uncomplicated malaria have emerged from drug development pipelines, and at least two more child-friendly drugs for malaria should emerge in the next 2-3 years.

However, as has been the case with the introduction of improved therapies in the past it may take several years before these new treatments become widely available in target countries. These delays are the result of a combination of factors that include national processes for revising policy, acceptance by prescribers, drug distribution chains, and patient awareness and understanding of therapeutic improvements.

This study is built on an analysis of six francophone countries in West and Central Africa to determine the most critical barriers to the acceptance and uptake of recommended quality assured drugs for the treatment of malaria in children. Borrowing from a WHO-endorsed framework to assess barriers to essential medicines, it draws out common themes across all the target countries and makes recommendations for interventions which could remove some of the more critical barriers to acceptance and uptake of new therapies for the treatment of malaria in children.

Key findings include:

- Policy and regulatory changes that incorporate new medicines into national essential medicine lists and treatment guidelines can help ensure a better alignment with WHO recommendations regarding the use of quality antimalarials, including in the private sector;
- Drug supply financing and adequate supply chain monitoring represent a significant barrier;
- The lack of sensitization and prioritization of quality assured products, particularly in the private sector, is an important barrier;
- Lack of demand by healthcare professionals – and willingness to change prescribing patterns – remains a barrier to acceptance;
- Patient acceptance of new improved medicines for children can be positively influenced if proper dispensing information accompanies the distribution of these medicines.

The findings from this independent consultancy study are intended to inform Medicines for Malaria Venture (MMV) about possible areas of support which could be undertaken with local, regional and international partners to address these barriers and to support improved acceptance of WHO-recommended paediatric medicines for malaria.

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**Acknowledgement:** *The author is grateful to all the partners and many interviewees for their time and their support for this survey. We particularly would like to thank the National Malaria Control Programme coordinators and teams, the WHO country teams, and the WHO EMP in Geneva, Drs Gilles Forte, Suzanne Hill, Magali Babaley and Lisa Hedman. In addition, we express gratitude to the Global Fund, WHO GMP, RBM, UNICEF and the MMV access team for their guidance and support. This report was prepared by an independent consultant; the recommendations expressed are those of the author, and do not necessarily reflect the views of MMV.*

## I. ABBREVIATIONS

ACT	Artemisinin-based combination therapy
AL	Artemether-lumefantrine
AQ	Amodiaquine
ALMA	African Leaders' Malaria Alliance
API	Active Pharmaceutical Ingredient
AS	Artesunate
ASAQ	Artesunate + amodiaquine
AS+MQ	Artesunate + mefloquine
AS+SP	Artesunate + sulfadoxine-pyrimethamine
DHA-PQP	Dihydroartemisinin-piperaquine
DHS	Demographic and Health Survey
FDC	Fixed-Dose Combination
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
HBM	Home Based Management
HP	Health Professionals
HWG	Harmonization Working Group
IDA	International Development Association
IPTp	Intermittent preventive treatment during pregnancy
IRS	Indoor residual spraying
ITN	Insecticide-treated mosquito net
LLIN	Long-lasting insecticide-treated mosquito net
MIS	Malaria Indicator Survey
MS	Market Share
NEML	National Essential Medicines List
NMRA	National Medicines Regulatory Agency
NMCP	National Malaria Control Programme
PGHT	Wholesalers' prices
PP	Public Prices
PV	Pharmacovigilance
RBM	Roll Back Malaria
RDT	Rapid diagnostic test
SP	Sulfadoxine-pyrimethamine
UN	United Nations
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
PMI	United States President's Malaria Initiative
WHO	World Health Organization
WHO-EMP	World Health Organization – Essential Medicines and Health Products

## II. THE EVIDENCE

### A. WHO and UNICEF recommend quality solid paediatric ACTs to treat children

**ACTs are recommended to treat non complicated *P. falciparum* malaria.**

Although a significant decrease was seen in recent years, the number of cases of malaria in the WHO Africa region was still estimated at 174 million in 2010<sup>1</sup>. There were between 655,000 and 1,2 million deaths globally<sup>2</sup>, 86% of them in children below 5, and 91% in the WHO Africa region<sup>1</sup>. Malaria accounts for 24% of total child deaths in sub-Saharan Africa<sup>2</sup>. WHO recommends the use of ACTs and advocates for the withdrawal of oral artemisinin-based monotherapies from the market<sup>3</sup>. The global number of ACT treatment courses procured increased to over 200 million in 2010, yet 25 countries, mostly in the African region, were still allowing the marketing of artemisinin-based monotherapies<sup>1</sup>. In addition, many countries allow the use of AQ or SP monotherapy to treat non complicated *P. falciparum* malaria. Five ACTs are recommended by WHO: artemether-lumefantrine (AL), artesunate + amodiaquine (ASAQ), artesunate + mefloquine (ASMQ), artesunate + sulfadoxine-pyrimethamine (AS-SP) and dihydroartemisinin-piperazine (DHA-PPQ)<sup>1</sup>.

**In addition, UNICEF and WHO recommend the use of quality assured solid paediatric ACT formulations to treat children: solid formulations are the only quality assured paediatric ACTs to date** –A quality assured ACT is defined as either WHO pre-qualified and/or authorized for marketing by a Stringent Drug Regulatory Authority<sup>4</sup>.

Recently, the Better Medicines for Children project, funded by the Gates Foundation and coordinated by WHO's EMP, convened expert advisers who suggested that paediatric treatments should use a solid platform technology (multi-particulate solid, including those

that could be dispersed to form a liquid dose), rather than oral liquids<sup>5</sup>. WHO has issued guidance discouraging countries from using oral liquids (either powders reconstituted with water or syrups) to



*Frequently used liquid paediatric antimalarials in francophone Africa*

<sup>1</sup> World Malaria Report 2011 Accessed 2/1/12 at

[http://www.who.int/malaria/world\\_malaria\\_report\\_2011/WMR2011\\_noprofiles\\_lowres.pdf](http://www.who.int/malaria/world_malaria_report_2011/WMR2011_noprofiles_lowres.pdf)

<sup>2</sup> Source C Murray, Lancet, Volume 379, Issue 9814, Pages 413 - 431, accessed on 5/2/12 at

<http://www.lancet.com/journals/lancet/article/PIIS0140-6736%2812%2960034-8/fulltext>

<sup>3</sup> WHO briefing on Malaria Treatment Guidelines and artemisinin monotherapies, 2006

<sup>4</sup> Through WHO's Standard Treatment Guidelines, Prequalification List, and Essential Medicines Programme

<sup>5</sup> Report of the Informal Expert Meeting on Dosage Forms of Medicines for Children, 2008, accessed at

[http://www.who.int/selection\\_medicines/committees/expert/17/application/paediatric/Dosage\\_form\\_reportDEC2008.pdf](http://www.who.int/selection_medicines/committees/expert/17/application/paediatric/Dosage_form_reportDEC2008.pdf) and Hill S, Yang A, Bero L (2012) Priority Medicines for Maternal and Child Health: A Global Survey of National Essential Medicines Lists. PLoS ONE 7(5): e38055. doi:10.1371/journal.pone.0038055

treat malaria in children. This is primarily because of concerns about the inherent instability of these products, specifically those containing artesunate<sup>6</sup>, as well as the difficulty in ensuring consistency in dosing; also, concerns regarding high cost of storage and transport are often cited. The lack of stability is exacerbated when partial dosing is administered and the remainder of a liquid formulation is set aside for subsequent use despite the rapid degradation of the API. In addition, suspensions are reconstituted with a larger amount of water compared to solid formulations, and this water may not be well suited for consumption. Recently, M. Ramharter's meta-analysis clearly indicates the superior efficacy of paediatric ACTs compared to non-ACT formulations for children; this work also shows diminished GI side effects compared to those seen when children take conventional ACT tablet formulations<sup>7</sup>.

## B. Quality assured paediatric ACTs have been developed

Today, the following three ACT treatments are WHO pre-qualified and considered suitable for children in the relevant dosage form: Soluble ASAQ FDC, Dispersible AL and ASMQ FDC. Additional Dispersible AL generics and paediatric formulations of other ACTs are in development but not yet WHO pre-qualified. The following ACTs are likely to have child friendly formulations submitted for WHO prequalification: DHA-PQP and Pyronaridine-artesunate (Status of dossier assessment is available at <http://apps.who.int/prequal/>).

Despite this guidance and subsequent Global Fund for AIDS, Tuberculosis and Malaria (GFATM) change of rules, large numbers of prescribers and patients in many francophone African countries continue to use non recommended antimalarials to treat children, including monotherapies, antimalarials of varying quality and syrups and suspensions. This study seeks to understand the barriers and potential levers to facilitate the adoption of paediatric ACTs that are both recommended and quality assured, to treat non-complicated malaria in children in francophone Africa.

## C. Sub-optimal treatments are still used to treat malaria in children

According to NMCP evaluations, IMS Health (<http://www.imshealth.com/portal/site/ims/>), surveys and interviewees in the target countries, few children benefit from correct malaria case management, i.e. with a recommended quality assured paediatric ACT:

- 1) There is a significant « informal » unregulated private sector where many drugs of poor quality may be found, including treatments based on chloroquine, which is no longer appropriate for the treatment of *P. falciparum*.
- 2) Many products from multiple manufacturers are sold in the regulated private sector that don't follow the national malaria policy, including AQ and SP monotherapy, widely (and inappropriately) used to treat *P. falciparum* malaria in children.
- 3) The majority of antimalarials available on the market are not quality assured.

<sup>6</sup> Source: Accessed 26/7/11 at <http://www.essentialdrugs.org/edrug/archive/200503/msg00046.php> and [http://archives.who.int/eml/expcom/expcom15/applications/paediatrics/paed\\_meds/arte\\_lumefantrine.pdf](http://archives.who.int/eml/expcom/expcom15/applications/paediatrics/paed_meds/arte_lumefantrine.pdf)

<sup>7</sup> F Kurth, M Ramharter, et al, The Lancet Infectious Diseases, 2010: 10, 2, Pages 125 - 132, accessed on 12/2/12 at [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(09\)70327-5/abstract](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(09)70327-5/abstract)

4) Many children with fever receive a treatment that was retained at home from past treatment, which is particularly problematic with liquid formulations given their instability and rapid degradation of API.

5) Although solid paediatric formulations are being adopted, syrups and suspensions are still a preferred formulation for children by many providers and patients.

Remarkable progress has been achieved in malaria control in some countries over the last decade, particularly in the public sector. Senegal for instance witnessed a reduction of 41% in all malaria cases and 30% in under 5 mortality from malaria between 2005 and 2009<sup>8</sup>. In Benin, the PNLP performance reviews indicates that 95,5% of children under 5 with fever received an antimalarial in line with the national malaria policy in the public sector in 2011<sup>9</sup>. **However, malaria is still the main cause of morbidity and mortality in francophone Africa, especially in children under 5, and overall, relatively few children benefitted from correct malaria case management in recent surveys.** Only about 5% of febrile children under 5 received an ACT as antimalarial therapy in Burkina Faso<sup>10</sup>, 8% in Mali<sup>11</sup>, and 20% in Benin<sup>12</sup>, only 25% benefitted from correct case management within 24 hours in Gabon<sup>13</sup>. In Benin, the public sector distributes 46% of all ACTs and 68% of all “WHO-approved” ACTs<sup>7,14</sup> used in the country. Since the public sector distributes only 5% of all antimalarials in Benin, patients often don’t get ACTs in the private sector.

**Chloroquine is largely found in the “informal” unregulated private sector along with many drugs of poor quality, and AQ monotherapy is still often used to treat non complicated *P. falciparum* malaria.** Chloroquine was provided to about 20% of the children who received an antimalarial in Mali<sup>9</sup> and Senegal<sup>15</sup>, and 51% in Benin<sup>10</sup> in 2008. In Benin, in the private sector, non-artemisinin monotherapies accounted for a total of 91% of treatment courses sold in a 2009 outlet survey; the breakdown was primarily as chloroquine (54%), followed by quinine (29%) and SP (8%); ACTs accounted for 8% of treatments sold, and artemisinin monotherapies for less than 1%<sup>16</sup>. Non-artemisinin monotherapies were also the first antimalarial sold by registered wholesalers in 2008 in Benin with 56% market share (SP 50%, quinine 3%, other 3%) vs 43% for ACTs (artemether-lumefantrine (19%) followed by artesunate + SP (12%), DHA-PQP (7%), ASAQ (5%) of sales volumes); but there, contrary to the outlet’s survey, chloroquine sale by wholesalers was insignificant<sup>11</sup>. AQ monotherapy ranged from 2% of febrile children under 5 who received an antimalarial in Benin<sup>7</sup>, to 6% in Mali<sup>9</sup> and 12% in Burkina Faso<sup>8</sup>; it was however rarely found in Senegal (less than 1%)<sup>13</sup>. K.

<sup>8</sup> RBM Progress and impact focus on Senegal accessed 10/11/11 at

[http://www.mmv.org/sites/default/files/uploads/docs/publications/RBM\\_progress\\_and\\_impact\\_series4.pdf](http://www.mmv.org/sites/default/files/uploads/docs/publications/RBM_progress_and_impact_series4.pdf)

<sup>9</sup> Revue de performance du PNLP Mars 2011, accessed 23/1/12 at

<http://www.rbm.who.int/countryaction/aideMemoire/Benin-The-malaria-program-performance-review-2011.pdf>

<sup>10</sup> Source Enquete démographique et de santé et à indicateurs multiples (EDSBF-MICS IV) 2010 – Preliminary report

<http://www.measuredhs.com/pubs/pdf/PR9/PR9.pdf> accessed on 13/12/11

<sup>11</sup> Enquête sur la prévalence de l’Anémie et de la Parasitémie palustre chez les enfants (EA&P) au Mali 2010 ; Kléon Traoré et al, accessed 14/08/11 at <http://www.measuredhs.com/pubs/pdf/FR245/FR245.pdf>

<sup>12</sup> ACT Watch, Household Survey Report (Baseline), 2009, accessed 23/1/12 at

<http://www.actwatch.info/downloads/results/Benin%20Household%20Baseline,%20ACTwatch%2012-09.pdf>

<sup>13</sup> Objectifs du millénaire pour le développement, 2010, accessed 2/1/12 at

[http://www.undp.org/africa/documents/mdg/gabon\\_september2010.pdf](http://www.undp.org/africa/documents/mdg/gabon_september2010.pdf)

<sup>14</sup> ACT Watch “The private commercial sector distribution chain for antimalarial drugs in Benin”, 2009, accessed on 23/1/12 at <http://www.actwatch.info/downloads/results/Rapid%20assessment%20of%20private%20AM%20distribution%20chain%20-%20Benin%20November%202009.pdf>

<sup>15</sup> Source Enquete nationale sur le paludisme 2008-2009

[http://www.measuredhs.com/pubs/pdf/MIS5/MIS5\[revised30Sep2009\].pdf](http://www.measuredhs.com/pubs/pdf/MIS5/MIS5[revised30Sep2009].pdf) accessed 10/11/11

<sup>16</sup> ACT Watch Outlet Survey 2009, accessed on January 23, 2012 @

<http://www.actwatch.info/downloads/results/Benin%20OS2%20Report%20-2009.pdf>

O'Connell et al found comparable results in a survey in five sub-Saharan Africa countries, where non artemisinin monotherapies were widely available in over 95% of outlets compared to less than 25% carrying first line quality assured ACTs; ACTs accounted for less than 25% of the total antimalarial sold<sup>17</sup>.

**In addition, many children with fever receive a treatment already stored in the home as a leftover from prior administrations: 45% in Senegal<sup>13</sup> and 30% in Benin<sup>10</sup>.**

**Most antimalarials available on the market don't comply with international recommendations with regards to quality:** for instance 37% of the ACT and SP samples failed in Cameroon in 2008<sup>18</sup>, and over 40% in Senegal<sup>19,20</sup>. In K O'Connell's survey, quality-assured ACT volumes represented less than 6% of the total market share in the private sector. In M. Ramharter's survey, only 2 among 15 different paediatric ACTs were WHO pre-qualified<sup>21</sup>. All authors of these surveys stress the **need to improve the quality of currently marketed paediatric ACTs as a public health priority, along with strengthening the registration process and post market surveillance.**

**In the formal private sector,** many different products are sold, from multiple manufacturers and of varying quality; many don't follow national policies and syrups and suspensions are largely used. The IMS Health<sup>22</sup> data below show the consolidated average annual sales in volume in ten francophone Africa countries in 2010 in the regulated private market<sup>23</sup>:

API (in 000)	Total (%)	WHO pre-qualified products <sup>24</sup> (%)	Lead product
AL	5,374 (45%)	Approximately 1,500 (28%) Coartem® 1171 Lumet® 200 Artefan® 140 Lumartem® 38	Coartem® 1171
SP	2,501 (21%)	-	Maloxine® 863
ASAQ	1,402 (12%)	Total 598 (43%) Coarsucam® 531 (only FDC) Larimal® 47 Falcimon kit® 20	Camoquin Plus® 557
DHA-PQ	907 (8%)	-	Malacur® 517
AS-SP	738 (6%)	-	Coarinate® 719
ASMQ	646 (5%)	516 (approximately 80% = adult form)	Artequin® 646
AQ	372 (3%)	-	Camoquin® 332
<b>TOTAL</b>	<b>11,940</b>	<b>2615 (22%)</b>	

<sup>17</sup> Kathryn A O'Connell et al, *Malaria Journal* 2011, **10**:326, Accessed 15/2/12 at <http://www.malariajournal.com/content/10/1/326>

<sup>18</sup> Survey of the quality of selected antimalarial medicines circulating in six countries of sub-Saharan Africa, January 2001, at [http://www.who.int/medicines/publications/WHO\\_QAMSA\\_report.pdf](http://www.who.int/medicines/publications/WHO_QAMSA_report.pdf) Accessed 08/8/11

<sup>19</sup> Source Plan stratégique nationale 2011-15 <http://www.pnlp.sn/administration/Upload/documents/1306327775.pdf> accessed 3/11/11

<sup>20</sup> Source PMI MOP accessed 10/11/11 at [http://pmi.gov/countries/mops/fy11/senegal\\_mop-fy11.pdf](http://pmi.gov/countries/mops/fy11/senegal_mop-fy11.pdf)

<sup>21</sup> Michael Ramharter et al, The use of paediatric artemisinin combinations in sub-Saharan Africa, *Malaria Journal* 2011, **10**:365 accessed on 12/2/12 at <http://www.malariajournal.com/content/pdf/1475-2875-10-365.pdf>

<sup>22</sup> IMS Health website:

<http://www.imshealth.com/portal/site/ims/menuitem.ec35b98806417dab41d84b903208c22a/?vgnnextoid=913bc9e28f44f210VgnVCM10000071812ca2RCRD&vgnnextfmt=default>

<sup>23</sup> Source: Consolidated IMS Health data for Benin, Burkina Faso, Cameroon, Congo, Ivory Coast, Gabon, Guinea, Mali, Senegal, Togo in 2010.

<sup>24</sup> List of WHO pre-qualified products - Those only include ACTs - by API and manufacturer accessed on 12/2/12 at <http://apps.who.int/prequal/>





Frequently used antimalarials in francophone Africa

It is not possible to specifically identify treatments sold for children, as many people crush adult tablets for paediatric use. However, according to RBM, forecast demand by age/weight bands indicates that paediatric forms should constitute approximately 60% of the demand, with 70% for AL and 25% for ASAQ<sup>25</sup>. Moreover, the IMS data above includes SP used as preventive treatment for pregnant women. ACTs represent 76% of the sales registered by wholesalers in 2010 (formal private sector); AL and ASAQ, the two ACTs on national

policies in francophone Africa, constitute 57% of these sales. AQ monotherapy has a 3% share, with

high variability between countries; it is especially high in Mali with 199,000 units for a 1,390,000 unit market (14% market share), and Benin, with 58,000 units for a 1,239,000 unit market (nearly 5% MS). **WHO pre-qualified products** total approximately 22% of these products sold in the regulated private sector.

**Syrup and suspensions, none of them WHO-prequalified, are largely used in francophone Africa, with predominance of the following:**

1. **Coartem<sup>®</sup>, Dafa's AL suspension**, with 478,000 units or 4% of the total market, including adult and paediatric antimalarials. It is the lead liquid-based product, with main markets in Ivory Coast, Cameroon and Mali,
2. **Camoquin Plus<sup>®</sup>, Pfizer's AS solid form +AQ suspension**, with 452,000 units or 4% MS, with its main market in Ivory Coast,
3. **Bimalaril<sup>®</sup>, Medical Pharma's AL suspension**, with 381,000 units or 3% MS, with main market in Ivory Coast,
4. **Camoquin<sup>®</sup>, Pfizer's AQ syrup**, with 299,000 units or 2,5% MS, with main markets in Mali and Benin.

**Although solid paediatric formulations are rapidly being adopted according to interviewees, syrups and suspensions are still a favoured formulation for children.**

<sup>25</sup> Source RBM-WHO ROUND TABLE ON ACT SUPPLY, 2011, accessed on 15/2/12 at [http://www.rollbackmalaria.org/partnership/wg/wg\\_procurementsupply/docs/RBM-WHO-Round-Table-on-ACT-Supply.pdf](http://www.rollbackmalaria.org/partnership/wg/wg_procurementsupply/docs/RBM-WHO-Round-Table-on-ACT-Supply.pdf)

### III. KEY BARRIERS TO THE USE OF RECOMMENDED QUALITY ASSURED SOLID PAEDIATRIC ACTs & LEVERS OF CHANGE

The following seven barriers have been assessed:



#### A. Policy - National Essential Medicines List: From evidence to policy

The policy / National Essential Medicines List (NEML) constitutes a low barrier to access to recommended quality assured solid paediatric ACTs for non-complicated malaria.

Malaria policies are in place, linked to National Essential Medicines List (NEML) and Standard Treatment Guidelines (STG). These policies also stipulate free or subsidized ACTs for all patients or for children under 5.

However, the paediatric dosages of ASAQ Fixed-Dose Combination (FDC) are not indicated on the NEML and/or the local malaria protocol in 3 out of 6 countries, and in 2 of them, reference is made to the loose AS+AQ combination and not the FDC. AL liquid formulations are on the NEML or the local malaria protocol for use in the public sector in 3 and eventually in 4 countries, whereas the solid paediatric AL formulation is only referenced in 2 countries.

In addition, there are often discrepancies between the NEML and the local malaria protocol. Rational use of paediatric antimalarials may be improved with a broader dissemination of both the updated NEML and the local malaria protocol. Moreover, while artesunate monotherapies are banned in these countries, AQ and SP monotherapies may still be used for the treatment of non-complicated *P. falciparum* malaria.

The following table summarizes the policy, NEML and national protocol with regards to ACTs:

	Benin	Burkina Faso	Cameroon	Gabon	Mali	Senegal
1 <sup>st</sup> line malaria national policy	AL	ASAQ-AL <sup>26</sup>	ASAQ	ASAQ	AL <sup>27</sup>	AL-ASAQ
Free/subsidized 1 <sup>st</sup> line ACT (Date of origin)	Free <5 <sup>28</sup> (05/11)	Subsidized (2005)	Free <5 (02/11)	Free for all (2003)	Free <5	Free for all (05/10)
Diagnostic confirmation policy Diagnostic free of charge?	For all NO	For all NO	For >5yo Free<5	For >5yo No	For all Yes	For all YES
ASAQ: all FDC dosage forms on the NEML	YES	YES	YES	NO	NO	NO
Liquid AL formulation on NEML / local protocol	NO	NO	YES	NO but AS-L <sup>29</sup>	YES	NO (yes 2012?)
Dispersible AL on NEML	NO	YES	NO	NO	YES	NO

### A1. Standard Treatment Guidelines

ASAQ is first line treatment for non-complicated malaria in Cameroon and Gabon, while AL is first line in Benin and Mali, and both are first line in Burkina Faso and Senegal. In countries where ASAQ is first line, AL is indicated as second line; and vice versa in the other countries. This treatment is free of charge for children under 5 or for all, excepted in Burkina where patients need to co-pay a small fee. This is theoretically in effect in the public sector as well as the faith-based organizations integrated into the public sector. However, implementation of the free policy sometimes proves difficult particularly in Cameroon and Benin. Diagnostic confirmation is theoretically required for all patients in Benin, Burkina, Mali, and Senegal or in patients over 5 years old in Cameroon and Gabon. Yet it is not always done –with a varying frequency between countries- and the ACT may still be provided without diagnostic confirmation in all countries except Senegal. The National Insurance Scheme, such as the CNAMGS “Caisse Nationale d’Assurance Maladie et de Garantie Sociale” in Gabon, or RAMU in Benin may be a good lever to rationalize ACT and RDT use; the CNAMGS Director expressed his desire to promote RDT use, provided adequate stocks of RDTs are available. Artesunate (AS) monotherapy is banned in all six countries; however other monotherapies such as AQ or SP for therapeutic use are not.

### A2. National Essential Medicines List and local national malaria protocol










The National Essential Medicines List (NEML) is defined by a consultative or permanent commission, and in principle is revised every 2 to 3 years. It is the reference for the central pharmacy procurement, and the basis for the elaboration of national treatment protocols. Revised NEMLs can reinforce WHO’s preference for FDC vs loose combination ACTs, and can also reinforce relevant paediatric dosage forms consistent with the national malaria policy treatments. While the NEML was updated in 2011 in Burkina to include both ASAQ FDC in all dosage forms and Dispersible AL, the NEMLs in other countries still need to be updated in order to support broader use of child-friendly quality medicines:

<sup>26</sup> Only ASAQ is subsidized

<sup>27</sup> Interviewees indicated a switch from ASAQ to AL in 2011

<sup>28</sup> Free for children under 5

<sup>29</sup> Artesunate Lumefantrine instead of Artemether Lumefantrine

Country	Situation	Comments
Benin	AL:  Only adult tablets are available in the public sector.	Adult tablets are crushed for use in children. The AL solid paediatric formulation is not mentioned in the NEML nor in the local protocol.
Burkina Faso	AL:  Although AL dispersible appears on the NEML, it is not on the national protocol where only adult tablets are mentioned.	There is a lack of consistency between both documents.
Came- roon	ASAQ: All ASAQ FDC 4 dosage forms are on the NEML. The loose combination is mentioned in addition to the FDC with a mention “clear preference for the FDC when it is available”.	
	AL:  Liquid formulation of AL is indicated in the NEML and the national protocol –with a warning about a 1-week stability once reconstituted; no solid paediatric formulation is mentioned. Various AL tablets are on the central pharmacy procurement list for adults and an AL suspension is procured for children, the latter with government funding.	AL liquid formulation on the NEML is a significant barrier to quality assured children’s treatment as no liquid formulation is pre-qualified by WHO. No quality assured solid paediatric AL formulation is procured by the central pharmacy as it is not on the NEML, and the NMCP is waiting for a WHO recommendation to act.
Gabon	ASAQ  Only the dosage “Artesunate 50mg + Amodiaquine 153 mg ” is on the NEML. ASAQ is 1 <sup>st</sup> line policy treatment, and the central pharmacy updated its procurement list to get ASAQ FDC in all 4 dosage forms.	This dosage refers to the co-blistered and not the fixed dose combination (FDC) , and moreover, no paediatric dosage is indicated. Yet, WHO recommends fixed-dose combinations as “highly preferable to the loose individual medicines co-blistered or co-dispensed” <sup>30</sup> . A ministerial decree allows the central pharmacy to procure ASAQ FDC.
	AL:  Artesunate (AS)-L tablets are on the NEML instead of AL; it is not WHO pre-qualified. Only adult AL tablets are on the national protocol.	The central pharmacy updated its procurement list to be able to get AL tablets and suspension for children. There is a lack of consistency between the two documents.
Mali	ASAQ:  Only the dosage 100/270mg is indicated, i.e. the adult dosage form of the FDC; paediatric dosages are not mentioned.	However ASAQ paediatric dosages are mentioned on the national protocol, and procured by the central pharmacy as needed.
	AL:  Liquid formulation of AL is on the NEML and the national protocol, no solid paediatric formulation.	
Senegal	ASAQ:  Only the dosage “Artesunate 50mg + Amodiaquine 153 mg ” is on the NEML. The reference product mentioned in Senegal is Falcimon®, a Cipla AS+AQ kit.	This dosage refers to the loose and not the fixed dose combination (FDC) , and moreover, no paediatric dosage is indicated. However, a ministerial decree allows the central pharmacy to procure ASAQ FDC.
	AL:  Only adult tablets are on the NEML	A ministerial decree allows the central pharmacy to distribute AL Dispersible; however the NMCP indicated being ready to add AL suspension to the NEML.

<sup>30</sup> WHO guidelines for the treatment of malaria, accessed 12/1/12 at [http://whqlibdoc.who.int/publications/2010/9789241547925\\_eng.pdf](http://whqlibdoc.who.int/publications/2010/9789241547925_eng.pdf)

**National malaria protocols exist in each country and in general, are clear and specific; yet several need to be updated for consistency with the NEML.** Moreover, both policy documents would benefit from further and broader dissemination. For instance in Gabon, the pharmacists association, the distributors and the national insurance organization indicated that they did not have the NEML nor the local malaria protocol, which constitutes a barrier to the rational use of antimalarials. Less than 25% of the structures managing patients had the local protocol in Cameroon in 2008<sup>31, 32</sup> and only 13,5% of the facilities had latest version of the NEML in Senegal in 2009<sup>33</sup>.

### A3. Levers of change for consideration

<p><b>1. UPDATE OF THE NEML AND/OR NATIONAL PROTOCOL VIA A CONSENSUS TECHNICAL WORKSHOP</b></p>
<p>With the NMCP, NMRA, WHO and other stakeholders, to provide the existing evidence to the Ministry of Health (MOH) in order to update NEMLs and:</p> <ul style="list-style-type: none"> <li>- Include relevant solid Fixed Dose Combinations with all paediatric dosage forms,</li> <li>- Include other quality assured products as references in order to increase their visibility,</li> <li>- Provide sufficient specifications to allow for safe procurement,</li> <li>- Remove non quality assured products such as liquid paediatric formulations,</li> <li>- Ensure entire consistency between the NEML and the STG.</li> </ul> <p>This work will be based upon scientific evidence and the latest WHO model formulary for children.</p>
<p><b>2. BROAD DISSEMINATION OF NEML AND LOCAL PROTOCOL</b></p>
<p>This dissemination should target health professionals in public and private sectors, via professional associations, with the support of NMCP focal points. This dissemination may require a consensus meeting for professional associations support. Distributors should be incentivized to disseminate these documents to private sector pharmacists.</p>
<p><b>3. POSSIBLE ROLE(S) FOR MMV:</b></p>
<ul style="list-style-type: none"> <li>- Bundle relevant scientific information that clearly shows advantages of quality assured paediatric formulations. Leverage ongoing phase IV effectiveness studies (e.g. INDEPTH/INESS) in order to draw out paediatric specific evidence.</li> <li>- Facilitate the dissemination of that scientific information at national, regional and international levels, in close partnership with RBM and WHO headquarters and African regional office.</li> <li>- Facilitate the set up or strengthening of a national case management working group focusing on children's treatment, under the leadership of the MOH and with WHO and UNICEF support.</li> <li>- Participate in national workshops to update the NEML and national protocols, under the leadership of the NMCP, with WHO (EML) and champions identified in each country.</li> </ul>

<sup>31</sup> CARTOGRAPHIE ET EVALUATION APPROFONDIE DES SYSTEMES D'APPROVISIONNEMENT ET DE DISTRIBUTION DES MEDICAMENTS ET AUTRES PRODUITS DE SANTE AU CAMEROUN, 2008, Accessed 2/10/11 at <http://apps.who.int/medicinedocs/documents/s17824fr/s17824fr.pdf>

<sup>32</sup> Source ANALYSE SITUATIONNELLE MISE EN ŒUVRE POLITIQUE PHARMACEUTIQUE NATIONALE 1<sup>e</sup> GENERATION, Sept 2008, Accessed 2/10/11 at <http://www.who.int/medicines/areas/coordination/cameroonevaluation08.pdf>

<sup>33</sup> Source CARTOGRAPHIE ET EVALUATION APPROFONDIE DES SYSTEMES D'APPROVISIONNEMENT ET DE DISTRIBUTION DES MEDICAMENTS ESSENTIELS ET AUTRES PRODUITS DE SANTE AU SENEGAL, 08/2009- Accessed 10/11/11 at <http://apps.who.int/medicinedocs/documents/s17561fr/s17561fr.pdf>

## B. Regulatory: From policies to regulations

**Regulatory aspects may constitute a barrier to access to recommended quality assured solid paediatric ACTs for non-complicated malaria.**

Even where national pharmaceutical policies exist, and recommended quality assured solid paediatric ACTs have a marketing authorization, the private sector is complex with many antimalarials registered, from multiple manufacturers, often not in line with the national malaria policy and with varying quality. For instance, in many of the countries, private pharmacies are authorized to market the following legally registered products: AQ and SP monotherapies for the treatment of non-complicated *P. falciparum* malaria, 2-day ACT treatments, and multiple syrups and suspensions to treat children's malaria. Several generics of AL dispersible are now available, but none is quality assured and there is not adequate information on the stability of these formulations. Separately, non-authorized drugs of poor quality are sold by street vendors in the sizeable informal private market.

### B1. Appropriate regulatory standards

A national pharmaceutical policy exists in each of the six countries, with a National Medicines Regulatory Agency (NMRA) responsible for the elaboration, implementation and control of the pharmaceutical directives, health products approval, coordination of pharmaceutical supply, quality assurance and (in some countries) pharmacovigilance<sup>34</sup>. A 2010 WHO assessment of NMRA in 26 sub-Saharan African countries, although not specifically assessing any specific country NMRA, concluded that regulatory structures for medicines do exist and the main regulatory functions are addressed; however, "on the whole, countries did not have the capacity to control the quality, safety and efficacy of the medicines circulating"<sup>35</sup>.

A marketing authorization is required for every product. Manufacturers must submit in each country, and in most cases, countries have slightly different requirements. This is a bottleneck for manufacturers and is also costly as they must prepare multiple technical dossiers and submit to multiple plant inspections; however there are an increasing number of harmonization initiatives to reduce this bottleneck by arranging joint reviews among stringent regulatory authorities and NMRAs from developing countries. These initiatives accelerate registrations for eligible medicines while improving regulatory capability<sup>36</sup>.

### B2. Relevant products licensed

**Quality assured solid paediatric ACT formulations consistent with the national malaria policy have a marketing authorization in all six countries:**

- ASAQ: Sanofi-Aventis' Coarsucam® in 4 dosage forms, or ASAQ Winthrop in its generic packaging, including 3 paediatric ones,

<sup>34</sup> For additional information, please refer to the WHO « évaluation approfondie des systèmes d'approvisionnement et de distribution des médicaments et autres produits de santé » for several of these countries

<sup>35</sup> Assessment of medicines regulatory systems in sub Saharan African countries", WHO, 2010 accessed on 25/11/11 at [http://www.who.int/healthsystems/Assessment26African\\_countries.pdf](http://www.who.int/healthsystems/Assessment26African_countries.pdf)

<sup>36</sup> WHO PQ assessment training accessed on 12/2/12 at [http://apps.who.int/prequal/info\\_press/pq\\_news\\_28September2011\\_AssessmentTraining.htm](http://apps.who.int/prequal/info_press/pq_news_28September2011_AssessmentTraining.htm)

- AL: Novartis' Coartem®-Dispersible.

**In addition, dispersible AL generics from Ajanta - Artefan® Dispersible -, EGR Pharma - Cofantrine® Dispersible - and Imex Health - Lufanter® Dispersible - have recently been granted a marketing authorization in some or all of those countries,** yet none is WHO pre-qualified at this time. Mepha's paediatric formulation of ASMQ, paediatric Artequin®, is also available in these countries, although the formulation is not WHO pre-qualified. For DHA-PQP, Salvat's Malacur®, Holley Cotec's Duocotecxin®, and Odyfarm's Artecom® are available as adult and liquid paediatric formulations, and Artecom Dispersible® is available in some countries; none of these is prequalified. In addition, several FDCs of ASAQ have a marketing authorization in some countries.

**In addition to these ACTs, the formal private sector is complex with many antimalarials registered, from multiple manufacturers, often not in line with the national malaria policy. Over 150 antimalarials were registered in 2008 in Burkina, Mali and Senegal, and over 90 in Benin and Cameroon. While Artesunate monotherapies have been banned, paediatric suspension of AQ monotherapy is a favourite antimalarial in the formal private sector in Mali and Benin. Fighting monotherapy use has been identified as a priority in some countries, given the threat of resistance triggered by such treatments.**

The 2010 WHO malaria guidelines states that "ACTs should be used" and "The continued use of artemisinins or any of the partner medicines, such as monotherapies, can compromise the value of ACTs by selecting for drug resistance"<sup>28</sup>. All monotherapies are theoretically banned for therapeutic use in Burkina and Gabon; they are, however, still sold in Gabon. The market also includes multiple syrup and suspension formulations for children, and 2-day ACT treatments, except in Burkina where less than 3-day ACT treatments are banned. In addition, many antimalarials available on the market do not comply with international recommendations with regards to quality.

**Moreover, illegal drugs of poor quality are sold by street vendors in all six countries,** including chloroquine and monotherapies.

### B3. Levers of change

<p><b>1. STRONGER ENFORCEMENT OF REGULATIONS &amp; CONTROL MEASURES IN THE PRIVATE SECTOR</b></p> <p>Enforcement of national regulatory authorizations must be addressed in the private sector to ensure the use of <u>antimalarials consistent with the national malaria policy and preferably</u></p> <ul style="list-style-type: none"> <li>- <u>in harmony with the WHO recommendations, i.e. WHO guidelines for malaria treatment and the model list of essential medicines for children</u><sup>37</sup></li> <li>- <u>and with prioritization of quality assured products.</u></li> </ul> <p>"Technical homologation" workshops are necessary under the NMRA leadership, and with the NMCP, the WHO and key national malaria stakeholders.</p>
<p><b>2. RESTRICTION OF MONOTHERAPIES USE TO THEIR INDICATIONS, SO THEY ARE NO LONGER USED FOR TREATMENT OF P FALCIPARUM NON-COMPLICATED MALARIA; STRONG ENFORCEMENT, ALONG WITH PHASING IN RELEVANT PRODUCTS (SEE BELOW)</b></p>
<p>Nationally, these measures should be considered:</p>

<sup>37</sup> Accessed on 12/2/12 at [http://whqlibdoc.who.int/hq/2011/a95054\\_eng.pdf](http://whqlibdoc.who.int/hq/2011/a95054_eng.pdf)

- A consensus workshop where existing evidence is presented, under the leadership of the NMRA, with strong WHO support, and with all actors,
- Recommendations communicated to the MOH for decree (or law),
- Increased MOH pressure against all monotherapies used for treatment of *P falciparum* non complicated malaria,
- Sensitization of prescribers, pharmacists, distributors and communities in parallel.

Regionally – Internationally, these options could be considered:

- WHO clarification
- ALMA and UEMOA may be engaged along with WHO,
- Manufacturers, particularly large multinational corporations, should stop production of all monotherapies for treatment of non-complicated *p falciparum* malaria, including Amodiaquine syrups (e.g. Camoquin and Camoquin Plus by Pfizer.)

### 3. PRIORITIZATION OF QUALITY ASSURED PRODUCTS



Driver of change

**In the private sector, few are aware of the varying quality of the treatments.** A visible logo could be considered to indicate the international quality assured status, (i.e. eligibility for procurement by the GFATM, thus potentially becoming a strong positive driver for prioritization of quality assured products in the market, hence providing a commercial advantage.) This is a similar concept as used by the AMFm (the Green Leaf), although with a larger application as it is not solely for GFATM procured products but for all quality assured products.

### 4. ENGAGEMENT OF NATIONAL AND OTHER HEALTH INSURANCES: KEY INFLUENCERS OF THE RATIONAL USE OF ANTIMALARIALS AND RDTs IN THE PRIVATE SECTOR VIA THEIR REIMBURSEMENT POLICY,



Driver of change

For countries where national insurance schemes are gaining momentum, approved formularies could help reinforce the prioritization of quality-assured paediatric medicines. Close collaboration and on-going communication with institutions such as the CNAMGS in Gabon or RAMU in Benin on national and international paediatric treatment policies is important.

### 5. COMMUNITY SENSITIZATION AGAINST SELF-MEDICATION (SEE G BELOW)

### 6. HOW MMV MAY FACILITATE RATIONAL USE OF RECOMMENDED QUALITY ASSURED SOLID PAEDIATRIC ACTs:

- Bundle relevant scientific information to facilitate regulatory market rationalization , including evidence/rationale to restrict the use of non-AS monotherapies to their indications , reinforcing WHO directives.
- Participate in national workshops, i.e. EML and/or procurement workshops, to rationalize antimalarials in the private sector and restrict the use of non-AS monotherapies and non 3-day ACT therapy, under the leadership of the NMRA, with NMCP, WHO, key stakeholders and champions identified in each country, including national insurance representatives.
- Pursue exploratory discussions regarding the possibility of product labelling or tagging that distinguishes their international quality status, particularly for products in the private market.
- Facilitate the engagement of manufacturers to seek WHO pre-qualification and to stop production of all monotherapies for treatment of non-complicated *p falciparum* malaria.

## C. Manufacturing & Supply: Consistent quality supply

**The lack of adequate and constant supplies can constitute a barrier to access to recommended quality assured solid paediatric treatments for non-complicated malaria.**



**In most countries, procurement and distribution systems are in place; however stockouts of ACTs and RDTs in the public health centres are a key barrier to access, due to a combination of structural and financial issues. ASAQ procured in the public sector is most often in the form of paediatric FDC quality assured dosages. AL is often used in the public sector in the form of crushed adult tablets (often procured with GFATM funding) or suspension (procured with government funding), whereas PMI procures Dispersible tablets. In the private sector, many treatments are procured, not necessarily following the recommendations and of varying quality. Dispersible AL paediatric formulations, although recent, are achieving acceptance in countries where they are commercialized, and often are sold more frequently than the same product in a liquid formulation. Faith based organizations often procure their own drugs outside of the central pharmacy and/or receive donations that are not necessarily consistent with the national policy.**

**Novartis' Coartem®-Dispersible is the only WHO-prequalified AL paediatric formulation, and it suffered from inconsistent availability in the last half of 2011. Sanofi Aventis was the only ASAQ FDC manufacturer pre-qualified for public sector tenders, which constituted a supply risk; however IPCA's ASAQ FDC has been WHO pre-qualified after completion of that study. Moreover, international demand for ACTs has been increasing significantly, in part thanks to AMFm orders – but looking towards 2012-2013, it has been difficult for manufacturers to get reliable demand forecasts, given (in part) uncertainties about the continuation of the AMFm. As such, many manufacturers don't want to invest in additional expansion of capacity based on forecasts that may not be reliable.**

### **C1. Procurement and Supply chain functionality**

**Procurement and distribution systems of varying reliability are in place in the public, faith-based and private sectors. In general, government central pharmacies are responsible for procurement, storage and distribution of essential medicines, primarily generics, to the population at lowest costs. These central pharmacies often supply the public sector, as well as those faith-based organizations integrated into the public health system. Moreover, they may also supply the private sector in some cases, such as:**

- In Burkina, the CAMEG supplies generics to the private sector, including subsidized ACTs in private pharmacies –although they are difficult to find. Similarly, in Cameroon, the CENAME is supposed to provide ASAQ to the private pharmacies, although in practice this is not happening very reliably.
- In Senegal and Benin, the central pharmacy distributes essential medicines to private pharmacies, but this does not include antimalarials at this time.
- In Gabon, the OPN does not distribute generics to the private sector.

**The central pharmacy theoretically procures antimalarials based upon the NEML, although the NEML needs to be updated and thus is not the basis for procurement in some countries. For instance, ASAQ is 1<sup>st</sup> line ACT in Gabon where the co blister AS+AQ figures on the NEML, but ASAQ FDC is procured. In Senegal, although the NEML is not updated, AL has a special authorization to be on the PNA procurement list.**

In the public sector, the following ACTs are procured by central pharmacies<sup>38</sup>:

National Policy	ASAQ 1 <sup>st</sup> line treatment	AL 1 <sup>st</sup> line treatment
<b>ASAQ procured</b>		
ASAQ FDC	Burkina, Cameroon, Gabon	Benin, Mali, and Senegal as 2 <sup>nd</sup> line ACT
Suspension	Burkina (CAMEG funding for private sector use)	
<b>AL procured</b>		
Dispersible	Possibly Burkina in 2012 (CAMEG own funding)	Mali & Senegal (PMI –CIDA funding) Possibly Benin 2012 (PMI funding)
Non dispersible for children’s use		Benin (GFATM funding)
Suspension	Cameroon, Gabon (gov. funding)	Senegal (government funding, 2009)

**Stocks outs of ACTs and RDTs in the public health centres are a key barrier to access to recommended quality assured solid paediatric ACTs.** Several countries acknowledged that in addition to structural and financial issues, there is insufficient coordination between the NMCP, the central pharmacy, partners and donors, leading to inefficiencies and stock outs. In response, several countries have set up coordination mechanisms to strengthen ACT demand forecast and supply: Burkina and Senegal have set up coordination commissions, and Benin has a case management working group under the NMCP leadership that addresses some of these concerns.

**In addition, global demand for the few quality assured paediatric ACTs is increasing significantly, and it is difficult to obtain reliable demand forecasts, in large part because of a lack of reliable data in-country regarding consolidated public and private sector demand. That constitutes a key barrier as manufacturers don’t want to invest in additional capacity on the basis of forecasts that may not be sufficiently reliable.**

**In the public sector, there are often distribution issues leading to frequent stock out beyond regional pharmaceutical depots. These are related to a combination of financial and structural issues, including inaccuracy of demand forecasts, non-optimal procurement, stock management and distribution planning.** The central pharmacy generally distributes down to the regional level - with the exception of Mali where it is compulsory for the central pharmacy to go down to the district level, and Gabon where the process is different from other countries. The peripheral health centres then come to get supply at the regional or district level. As there are often underlying financial constraints, stockouts often lead to the sales of non-recommended medicines in order to generate revenues.

**In some countries, larger faith-based organizations are integrated into the public system, and access the same essential medicines as the public sector, via the central pharmacy, although these faith-based organizations often experience more stockouts than the public sector;** this was the case in Benin, Burkina, Cameroon and Senegal. In other countries like Gabon, faith-based organizations

<sup>38</sup> Source interviewees and GFATM <http://www.theglobalfund.org/en/procurement/pqr/> accessed on 09/02/12

are not able to access essential drugs via the central pharmacy. Faith-based organizations often procure drugs via IDA, Medeor, or Pharmapro; these organizations also receive donations that are not necessarily consistent with the malaria policy, and they may have insufficient knowledge of national policy. WHO has developed guidelines to assist with donations and to support increased quality<sup>39</sup>. Information and sensitization of their procurement departments may be an important tool for improved rational use of antimalarials.

**In the formal private sector, the following solid paediatric ACT are available in some or all of the countries:**

AL	Status
Artefan® Disp, Ajanta	Recently registered, not available during the survey
Coartem®-Disp, Novartis	Referenced, but not available from the manufacturer during the survey
Cofantrine® Disp, EGR Pharma	Recently commercialized in some countries
Lonart® Disp, GVS Lab	Not available in francophone Africa during the survey
Lufanter® Disp, Imex Health	Recently commercialized in some countries
ASAQ	
Coarsucam®, Sanofi Aventis	Available in all six countries + as ASAQ Winthrop in Burkina
ASMQ	
Artequin® pediatrique, Mepha	Available in all six countries

**Only two of these solid paediatric ACTs are WHO pre-qualified (green highlight): Sanofi-Aventis's ASAQ FDC and Novartis' Coartem® Dispersible.** Sanofi-Aventis was the only ASAQ FDC manufacturer pre-qualified for public sector tenders, which represented a supply risk given the large demand for the product –*IPCA's ASAQ FDC has been WHO pre-qualified after the completion of that study.* . Sanofi-Aventis is currently developing plans to have two manufacturing sites in order to ensure diversified production capability; in addition, DNDi is facilitating the development of another quality assured ASAQ FDC production site. Similarly, although there are WHO pre-qualified generics of AL, Novartis' Coartem®-Dispersible is the only pre-qualified paediatric formulation and it was not available from the manufacturer over the past several months. The arrival of AL dispersible generics is recent, and none is WHO pre-qualified. It is interesting to note that Ajanta's Artefan®, Imex Health's Lufanter® and EGR Pharma's Cofantrine® also exist in a liquid formulation, by the same manufacturer and **paediatric AL Dispersible generics, although recent, have been rapidly adopted and are now sold more than the same product in liquid formulations.** For instance, in Benin, dispersible from the Imex group (Cofantrine® and Lufanter®) is sold ten times more than the liquid formulations of these products, and over 2 to 3 times more in Gabon.

**In addition, as noted above, many antimalarials are sold in the private sector to be used by children, , that are not aligned with national malaria policy nor WHO guidance, such as AQ or SP monotherapies and ACTs of less than 3-day treatment duration.**

**In the private sector, there are a handful of main distributors who import and supply medicines to the registered pharmacies.** The supply chain is functional, but normally only in larger cities.

<sup>39</sup> WHO 2010 revised guideline for medicines donation accessed 12/2/12 at [http://whqlibdoc.who.int/publications/2011/9789241501989\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241501989_eng.pdf)

## C2. Products available at health facility level

**In the public sector**, all interviewees referred to the unreliable availability of ACTs and RDTs as the primary barrier to access to treatment. **As documented widely in many other studies in Africa, stockouts of ACTs and RDT are indeed a crippling problem in the public sector, leading patients to procure alternative treatments in the public health centre or in the private sector.** When there is no ACT in the required dosage form, a prescriber in the public sector may charge to inject quinine or write a prescription for the patient to purchase an ACT treatment at a nearby pharmacy at a high cost. In the 2010 Gabon NMCP evaluation, 10 out of 25 primary health centres experienced ACT stockouts from three to sixteen months during the last five years<sup>11</sup>; in addition, RDTs are not available anywhere. In Benin<sup>40</sup>, Burkina<sup>41</sup>, Cameroon<sup>29</sup> and Mali<sup>42</sup>, the availability of ACTs in the public sector was estimated at around 70 to 75%. In Senegal, there were significant and repeated stock out in some centres and overstocking in others in the recent past; this is attributable in part to a new procurement code and in part to a strike of health centres personnel.

**Private sector retailers rarely cited stockout concerns**, as lead times are short and products can be sourced from multiple wholesalers –with the exception of Coartem®-Disp in the second half of 2011. Pharmacists stock products based upon demand, influenced by prescribers’ and pharmacists’ habits, as well as by guidance from pharmaceutical representatives and consumer preferences – which are not always aligned with quality assured products. Distributors and pharmacists generally welcome solid ACT formulations, as they are easier to stock and transport.


## C3. Levers of change

<b>1. STRENGTHENING OF THE SUPPLY CHAIN: THE LEADING REQUEST FROM ALL 6 COUNTRIES</b>
Extensive training is planned by partners, with focus on capacity building, monitoring of use and planning for timely supply despite a long procurement process.
<b>2. AVAILABILITY AND USE OF RDT</b>
In addition to structural and financial supply issues, demand for ACTs is increased as RDTs are not sufficiently used, hence availability and use of RDT may be a key lever of change. PMI is supporting some activities aiming to increase RDT use in the three countries they support: Benin, Mali and Senegal.
<b>3. BOLSTERING ACT COORDINATION</b>
Mechanisms should be encouraged and best practices emulated to facilitate communication and coordination among stakeholders involved in ACT policy, supply and financing. Necessary players include the NMCP, NMRA, central pharmacies, donors, professional associations and experts. There are some leading examples from countries such as Kenya which can be studied.
<b>4. RELIABLE DEMAND FORECASTS SHOULD BE ENCOURAGED.</b>

<sup>40</sup> PMI MOP FY2012 Accessed 23/1/12at [http://www.pmi.gov/countries/mops/fy12/benin\\_mop\\_fy12.pdf](http://www.pmi.gov/countries/mops/fy12/benin_mop_fy12.pdf)

<sup>41</sup> Source Swiss TPH

<sup>42</sup> Analyse de la situation de base de l’approvisionnement en médicaments antipaludiques et TDR au Mali, Emmanuel Nfor et al, 2009, USAIS, SPS, PPM

<p>These will help facilitate production planning and alignment of donor funding of realistic demand, which requires, among other elements, proper monitoring of past consumption.</p>
<p><b>5. QUALITY ASSURED PAEDIATRIC ASAQ AND AL GENERICS</b></p>
<p>A second ASAQ FDC manufacturing site, and additional paediatric AL generics, both WHO pre-qualified, are critical. For ASAQ FDC, if Sanofi Aventis successfully manages two active sites from late 2012 onwards, this will be helpful, alongside DNDi's efforts to facilitate the development of a new ASAQ manufacturing site –It is to note however that IPCA's ASAQ FDC has recently been pre-qualified by WHO, after the completion of that study-.</p>
<p><b>6. ENGAGEMENT OF THE PRIVATE SECTOR DISTRIBUTORS AND PHARMACISTS TO INCREASE COVERAGE WITH RECOMMENDED QUALITY ASSURED PAEDIATRIC ACTS</b></p>
<p>This could help displace poor quality medicines sold in the informal sector:</p> <ul style="list-style-type: none"> <li>○ <u>Nationally</u>: the engagement of the private sector is key and is a component of the Senegal and Benin malaria strategic plans,</li> <li>○ <u>Internationally</u>: Distributors, wholesalers - i.e. Laborex, Mission Pharma, Ubipharm, Planete Pharma, IDA-, and central procurement departments (or those of faith-based organizations) have a strong logistical and financial incentive to favour solid formulations, and could become important drivers for such formulations. Their sensitization to quality assured solid ACTs may improve ACT rational use.</li> </ul> 
<p><b>7. HOW MMV MAY HELP ADDRESS SUPPLY CHAIN ISSUES TO INCREASE ACCESS TO QUALITY PAEDIATRIC ACTS:</b></p>
<ul style="list-style-type: none"> <li>○ Document and disseminate MMV's current stock management pilot initiatives in E. Africa;</li> <li>○ Encourage national ACT coordination mechanisms;</li> <li>○ Encourage manufacturing partners to work with accurate forecasts to meet demand for paediatric ACTs</li> <li>○ Through partners, seek engagement with private sector distributors and sellers to facilitate their sensitization. This can include international initiatives targeting distributors, wholesalers and faith-based organization procurement departments. The objective is to encourage them to embrace the use of quality assured paediatric formulations.</li> </ul>

## D. Financing : Quality assured paediatric ACTs affordable for all involved

**Financing flows within countries constitute a barrier to quality assured solid paediatric treatments for non-complicated malaria.**

**ACTs are theoretically free or subsidized with a small patient co-payment in the public sector, yet financing free products represents a significant challenge for the health centre and/or the central pharmacy, often leading to stocks out. This in turn requires patients to procure medicines elsewhere at a higher cost.**

**In the private sector, antimalarials runs from 5 francs CFA (franc de la Communauté Financière Africaine – 1€ = 656 FCFA) in the “informal” market to up to 6000CFA. Liquid paediatric formulations as well as DHA-PQP and AS + MQ regardless of their formulation are generally the most expensive antimalarials used for children. Encouragingly, relatively new dispersible AL formulations are up to 4 times less expensive than the same product in liquid formulation, given**

their lower costs of manufacture, transport and storage – this may be a strong driver of future uptake.

## D1. Pricing system

In the public and integrated faith-based sectors, ACTs are free for children under 5 and may be free for all, with the exception of Burkina where they are subsidized with a small patient co-payment. Treatment prices are supposed to be posted in public health centres, but rarely are. The free medical consultation and free ASAQ for children under 5 in Cameroon is theoretically available in the private sector; however the reimbursement modalities are not clear and the private sector most often does not adhere to this policy.

In the private sector, medicines prices are set and the retail price of antimalarials runs from 5CFA in the informal private market to up to nearly 6 000CFA in private pharmacies. Liquid formulations are generally the most expensive, along with DHA-PQP and AS + MQ regardless of their formulation (see the most expensive products highlighted in red in the table below). The solid formulation of a given product is priced 2,5 to 4 times less than its liquid formulation. Examples of private sector prices are indicated in the table below. (Wholesalers' prices (PGHT) are listed in € in 2010 per IMS Health; retail prices (PP) in CFA were reported by distributors during interviews in 2011-12<sup>43</sup>. (656 CFA = 1 Euro)

AL	Products	Liquid formulation PGHT in € [PP in CFA]	Solid formulation PGHT in € [PP in CFA]
Suspension – 60ml	Coartesiane® - Dafra	3,24 – 3,43 [4085-4500]	
	Lufanter® - Imex Health	2,95 – 3,00 [≅ 3800]	
	Cofantrine® - EGR Pharma	2,84 – 3,15 [≅ 3400]	
	Artefan® - Ajanta	1,96 – 3,33 [≅ 2450]	
	Lonart® - GVS Lab	2,75 – 2,84	
Non Disp. - 6 tab. 20/120	Various manufacturers		0,50 – 2,28
	Coartem® Novartis		0,97
Disp. tablets	Coartem® Novartis (pack of 36)		[1150 – 1300]
	Artefan® Disp Ajanta		[1000]
	Lufanter® Disp Imex Health		[940]
	Cofantrine® Disp – EGR Pharma		[950-1000]
ASAQ			
FDC	Coarsucam® - Sanofi Aventis		
	25/67,5		1,62 – 1,93
	50/135		1,78 – 2,12
	100/270 – 3 tablets		2,02 – 2,38
	100/270 – 6 tablets		2,83 – 3,33
Susp. – 60ml	Camoquin Plus® - Pfizer	2,30 [1900-2850]	
DHA-PQ			
Tablets	Artecom® Odypharm <sup>44</sup> (+trim)		3,50

<sup>43</sup> 1€ = 656 CFA on 09/02/11

<sup>44</sup> 8 tablets - adult

AL	Products	Liquid formulation PGHT in € [PP in CFA]	Solid formulation PGHT in € [PP in CFA]
	Duocotecxin® - Beijing Cotec <sup>45</sup>		4,00
Susp. – 60ml	Malacur® - Salvat	3,00 [3480-3750]	
ASMQ			
Granules	Artequin® pediatrique		3,00 [3400- 4100]
AQ			
Suspension	Camoquin® - Pfizer	1,53 [1900]	

Pharmacists have a substitution right in most countries in order to provide patients with a cheaper generic, but this is rarely done. In all these countries, many crush adult tablets for children in order to get the lowest priced ACT.

## D2. Affordable to payer

As noted, while in theory in the public sector, ACTs are free for children under 5 (except small co-pay in Burkina), in reality, the following barriers impede access to quality assured affordable paediatric ACTs:

- **Barrier to the patient:** ACTs that are theoretically free /subsidized are not always available, thus patients have to procure a treatment at a cost either in the health centre or at a nearby pharmacy. Financing thus remains a barrier to access for many. Moreover, in most countries patients have to pay for other medicines and/or consultative services. Senegal attempts to ensure that treatment made available through Home Based Management (HBM) is free and Senegalese laws seek to protect free care and treatment for patients who can prove inability to pay. Overall, cost of care represents a significant barrier for many in those countries, with patients financing between 19% of their care in Senegal<sup>46, 47</sup> to 37% in Burkina<sup>48</sup> and up to 60% in Cameroon in 2007<sup>29</sup>. While national insurance schemes are starting to be developed in some countries, such as the CNAMGS in Gabon, coverage levels vary: 60% in Gabon, 20% of Senegal, and 5% of Mali. There are plans to develop and strengthen such insurance health schemes in Benin and Cameroon<sup>49</sup>.
- **Barrier to the central pharmacies and health centres as they function on a cost recovery system, because of a lack of margin on free products (with the exception of Gabon.)** When a product is free, there is no margin to support its management and distribution, hence free products are not a priority for the transporter, and the system is not sustainable. As mentioned by an interviewee: “Free ACTs get picked up whenever there is some room left in the car or on the bike.” For such free products, a planning phase allowing for specific funding for transport and storage are critical. In Senegal, health centres are to receive a subsidy, but

<sup>45</sup> 8 tablets - adult

<sup>46</sup> Source Rapid assessment of private sector\_USAID\_March 2009 accessed 10/11/11

[http://www.shopsproject.org/sites/default/files/resources/5272\\_file\\_FINAL\\_Senegal\\_Assessment\\_rev.pdf](http://www.shopsproject.org/sites/default/files/resources/5272_file_FINAL_Senegal_Assessment_rev.pdf)

<sup>47</sup> Source Plan stratégique national 2011-15 <http://www.pnlp.sn/administration/Upload/documents/1306327775.pdf> accessed 3/11/11

<sup>48</sup> Source CARTOGRAPHIE DES SYSTEMES D'APPROVISIONNEMENT ET DE DISTRIBUTION DES MEDICAMENTS ET AUTRES PRODUITS DE SANTE AU BURKINA FASO 2010, accessed on 25/11/11 at <http://apps.who.int/medicinedocs/documents/s18637fr/s18637fr.pdf>

<sup>49</sup> Source PLAN NATIONAL DE DEVELOPPEMENT SANITAIRE (PNDS) 2011-2015, Cameroun, Accessed 14/2/12 at [dev.cdss.dros-minsante-cameroun.org/download/file/fid/3464](http://dev.cdss.dros-minsante-cameroun.org/download/file/fid/3464)

- interviewees indicated that health centres generally don't get it, leading them to recover those costs via a higher margin on other drugs. In Benin, health centres should be reimbursed for dispensing ACTs, provided that they managed the case properly, but it is too early to tell whether this system will function properly. Practically, care is not yet free for children under 5. Countries may ask the GFATM for funding for transport, generally down to the regional level, but these requests are often missing, and this funding is not available for peripheral health centres. In Cameroon and Benin for instance, the free policy was suddenly announced by the president of the country and implemented in 2011. Gabon is planning to switch to a cost recovery system, abandoning an allocated budget system for transport.
- **Barrier to the health centres because of a lack of margin on free consultations, as in Cameroon for children under 5.** They may try to recover their loss on free consultations via a supplementary margin on adults' clinic price.

### D3. Levers of change

<b>1. A CROSS-SUBSIDY MARGIN</b>
Cross-subsidies on which stipulated margins are applied to other products could increase adherence to the free ACT programme by allowing: <ul style="list-style-type: none"> <li>○ Margin on the management and transport of the drugs, all the way to the periphery,</li> <li>○ Margin for the public health centres that run free clinics,</li> <li>○ A clear compensation scheme for faith-based and other private sector organizations so that they can participate in the programme</li> </ul>
<b>2. NATIONAL INSURANCE SCHEMES</b>
These can decrease out of pocket costs on health care, with strong support from donors including the World Bank (WB). In addition, national insurances could become a key potential lever to improve rational use of antimalarials via their reimbursement policy, including ACTs and RDTs.
<b>3. HOW MMV MAY FACILITATE RATIONAL USE OF RECOMMENDED QUALITY ASSURED SOLID PAEDIATRIC ACTS:</b>
<ul style="list-style-type: none"> <li>○ Continue to work with manufacturers to develop quality assured paediatric generics as a priority focus area.</li> </ul>

### E. Health Professionals: from policy to practice

**Lack of demand by professionals constitutes a barrier to access to recommended quality assured solid paediatric treatments for non-complicated malaria.**

**Although public sector prescribers generally follow national policy, they may still prescribe a non-first line policy treatment if first line ACTs are not available. In the private sector, health professionals often don't follow therapeutic guidelines, for various reasons related to established practice patterns, conflicting sources of information with a strong influence by commercial representatives, and in some cases financial incentives. In addition, pharmacists and faith-based organizations may not have adequate information to make strong recommendations for quality medicines. All providers, including pharmacists, may benefit from further sensitization and information on the international recommendations, national policy, use of RDT, quality assurance,**



quality assured paediatric treatments and the importance of dispensing advice and pharmacovigilance (PV) when the latter becomes in effect.

## E1. Health professionals aware, trained and available

Most interviewees noted that in the public sector, health professionals (HP) are informed and generally follow the policy if ACTs are available, but RDTs are not yet widely used. In some instances, however, if ACTs are not available, they may falsely document a severe malaria case in order to be able to prescribe another available antimalarial – typically quinine – and patients often accept injected antimalarials because of lingering (erroneous) perceptions of the superior efficacy of injected medicines. Alternatively, if ACTs are not available, HPs may prescribe an ACT only available (at high cost) in the private sector.

In the private sector, prescribers are expected to follow national policy, yet they may often prescribe an alternative, and syrups and suspensions for children are widely used. There is generally a lack of information on essential medicines and insufficient dissemination of policy documents. However, recently, solid formulations such as AL dispersible are becoming known and easily accepted by HP. In Gabon and Benin, AL Dispersible treatments are among the primary antimalarials sold today and the dispersible formulations are rapidly replacing the liquid ones. As previously noted, 2-5 % still prescribe AQ monotherapy to treat non-complicated malaria in the formal private sector in any given country – mainly Pfizer's Camoquin®-- and in Mali this figure is up to 14%.

**When prescribers recommended a non-policy antimalarial, it was due to one of the following reasons:**

- Lack of information on policy and recommendations,
- Preferences and habits.
- Poor previous experience, in particular with AQ,
- Lack of time to provide dispensing advice (particularly in the case of ASAQ, which is not flavour-masked.) Many interviewees indicated that with good dispensing training, and particularly in well run and supervised programmes, adherence to ASAQ therapy is excellent. In the absence of dispensing advice, syrups or other known paediatric formulations appear easier to prescribe than solid paediatric formulations, since the latter is a new concept.
- Influence by commercial representatives, who are often a key source of information, specifically in the private sector,
- In some cases, financial incentives impact HP judgement.

Michael Ramharther has documented similar findings in his study, particularly regarding the role of medical sales representatives and manufacturers advertising<sup>50</sup>. Medical representatives were cited as the 2<sup>nd</sup> source of information by professionals<sup>5</sup>.

**Scientific information, sensitization and supervision of health workers, with focus and involvement of private sector providers, is a priority and key to increasing universal access to malaria program interventions. Moreover, coordination among partners via systematic training meetings under the NMCP leadership is also viewed as a priority. Technical working groups would strengthen the focus on children's malaria treatment and coordinate advocacy and sensitization. Additional**

<sup>50</sup> M Ramharther et al, accessed 12/2/12 at

[http://www.mmv.org/sites/default/files/uploads/docs/events/ASTMH2010/1\\_Michael\\_Ramharther.pdf](http://www.mmv.org/sites/default/files/uploads/docs/events/ASTMH2010/1_Michael_Ramharther.pdf)

**partners may include civil society representatives along with Ministries of Families, as activated women (mothers) may help accelerate rational use of antimalarials via community sensitization.**

**In addition, in the private sector, pharmacists often have an advising role as families are trying to save money and time by consulting directly at the pharmacy, and yet most of pharmacists' scientific information is coming from the pharmaceutical companies themselves.** As a key actor to promote rational use of medicines, pharmacists could be further enlisted in national health initiatives designed to give them evidence-based scientific information instead of leaving this space to representatives from the pharma industry. Furthermore, pharmacists may play a larger role in the future to provide diagnosis for malaria, and could follow an algorithm prepared by the "physicians' association" whereby if patients test positive for uncomplicated malaria, they would prescribe an ACT under a mechanism of "collective prescriptions" such as in Quebec (<http://www.espaceitss.ca/20-fiches-thematiques/les-ordonnances-collectives-s-outiller-autrement.html?pageEnCours=2>)<sup>51</sup>. They would be included into the public health system instead of having a prescription right by "derogation" today. Pharmacists could officially prescribe antimalarials as they do with ARVs in some countries (but financing mechanisms would need to be defined.)

National College of Pharmacists ("ordre des pharmaciens") are positive about such involvement of private sector pharmacists, provided they are involved in design discussions, and receive support to set up these initiatives. A pilot could be performed in some pharmacies, bolstered with communication from the Ministry of Health.

There is one caveat in terms of access for the poorest patients: most pharmacists are in larger cities, and thus not in areas where major gaps impact health care coverage and medicines supply in rural areas of Africa. There is on average 1 pharmacist per 10.000 inhabitants in this part of Africa vs. 5 pharmacists per 10.000 inhabitants in Europe<sup>52</sup>.

In Gabon, a model of engaging pharmacists has recently been reviewed. It requires a strict supervision of pharmacists in alignment with the physicians' association, and hinges on an agreement with the "ordre des médecins". In Senegal and Benin, malaria training financing for pharmacists was requested, with the aim to integrate pharmacists into the malaria programme.

**Faith-based organizations play an important role in health care in most of these countries. In faith-based organizations integrated with the public sector, training of health professionals (HP) should occur as part of district training programs.** However, it is often difficult for the faith-based organizations HP to attend lengthy public sector trainings. Most major faith-based organizations organize yearly national training seminars with all HPs as well as monthly regional trainings. In general, they are not sufficiently informed about quality assured paediatric formulations, and have indicated they would welcome timely and accurate information.

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<sup>51</sup> Pr Diane Lamarre, president, Quebec « Ordre des pharmaciens » and pharmacists without borders: «As there is a lack of physicians in Quebec and many people don't have a general practitioner, in order to improve the health system efficiency and build upon the quality of relationship of communities with their pharmacist, the "collective prescription" initiative was started in 2002. It aims at extending the responsibilities of pharmacists, while keeping the physicians at the center of the initiative. These collective prescriptions are in place for hypertension, diabetes, anticoagulants, first-quarter pregnancy nausea." The process is as follows: Two or three-page algorithms have been designed by physicians so that pharmacists may initiate, follow up treatment or refer to the physicians on the basis of specific symptoms.

<sup>52</sup> WHO 2010 health statistics, accessed 2/1/12 at [http://www.who.int/whosis/whostat/FR\\_WHS10\\_Full.pdf](http://www.who.int/whosis/whostat/FR_WHS10_Full.pdf)

## E2. Levers of change

<p><b>1. INFORMATION, EDUCATION &amp; SENSITIZATION OF HPS REGARDING NATIONAL AND INTERNATIONAL GUIDANCE ON THE USE OF QUALITY ASSURED ACTs AND RDTs IN THE CORRECT CASE MANAGEMENT OF UNCOMPLICATED MALARIA IN CHILDREN.</b></p>
<p>Reinforcement of knowledge for all sectors and all HP categories, including faith-based organizations, pharmacists, distributors, health insurances professionals, should be encouraged under the direction of the Ministry of Health.</p> <p><u>Regionally</u>, under WHO leadership, with UNICEF and RBM, the following focal points could be engaged:</p> <ul style="list-style-type: none"> <li>- Western and central Africa health organizations (OOAS, OCEAC: Dr Victoire Benao ), a commission specifically working on malaria may be proposed.</li> <li>- Paediatricians organizations: the regional network “Sub Saharan Francophone Africa paediatrician” &amp; the UNAPSA, “Union des Société et Associations de Pédiatres d’Afrique”, headed by Dr Paul Koki, Cameroon,</li> <li>- Pharmacists: the CIOFP Conférence Internationale des Ordres de Pharmaciens Francophones organizes an Inter-African forum each June. <b>Dr Toukourou, Benin pharmacists’ association president, is also deputy head of the sub-Saharan Africa section of the CIOFP. The next meeting could focus on priority paediatric antimalarials, i.e. recommended and quality assured.</b> The <u>ACAME</u>, the African Association of Central Pharmacies, is also a key stakeholder in this endeavour.</li> <li>- ALMA: key for sensitization of political leaders.</li> </ul>
<p><b>2. FURTHER INVOLVEMENT OF PHARMACISTS REGARDING PATIENT CARE</b></p>
<p>Involvement of pharmacists should remain a priority. Taking into account the key role of pharmacists in advising patients, they may be licensed to engage further by administering RDTs and orienting patients on malaria treatment and follow up, based upon an algorithm prepared by the physicians association (“ordre des médecins”) under a mechanism of “collective prescriptions”. A pilot could be conducted in some pharmacies, in parallel with MOH communication. <b>PMI, as a strong supporter of private sector initiatives, could be approached to discuss such a pilot.</b></p>
<p><b>3. HOW MMV MAY FACILITATE BETTER KNOWLEDGE AMONGST HPs:</b></p>
<ul style="list-style-type: none"> <li>- Facilitate sensitization at international, regional and national levels.</li> <li>- Consider highlighting and disseminating evidence about experiments where pharmacists are officially involved in patient’s care under a mechanism of “collective prescription”.</li> </ul>

## F. Monitoring & Evaluation

**Monitoring constitutes a barrier to access to recommended quality assured solid paediatric treatments for non-complicated malaria.**

**There is insufficient monitoring of cases, policy implementation, and supply consumption in the field. In addition, pharmacovigilance is nascent and slowly is becoming a priority. There were repeated requests for support to help improve supply monitoring.**

**Monitoring of cases, of policy implementation and of ACT consumption in the field are critical both in the public and private sectors. Monitoring of prescriptions is basically non-existent in the latter. In the public sector, NMCPs do track the use of donor-funded malaria medicines, in addition to tracking by the central pharmacy for all essential medicines supply.**


As noted above, ACT coordination committees are either in place or being set up, to strengthen coordination between partners.

**Prescriptions monitoring.** In Senegal, the NMCP has set up quarterly meetings with each district to review cases and case management indicators in the public sector (including volume of cases tested, cases confirmed, and ACTs dispensed). ACTs are theoretically only provided on the basis of a positive RDT. Monitoring and evaluation is becoming a priority for all countries, and partners, particularly PMI, are supporting the development of supervision and monitoring /evaluation, along with capacity building. **There is basically no monitoring of prescriptions in the private sector; in some cases where national insurance may play a larger role in the future, functional monitoring of systems may become more viable.**

**Pharmacovigilance (PV) is nascent, with few adverse event notifications in most countries. In Senegal, PV has been developed with ACTs in 2007 under the NMCP’s leadership, and slowly extended to other diseases in the public sector. The goal is to transition accountability to the National Poison Control Center under the NMRA’s authority.**

**Support to facilitate supply availability via monitoring appeared as a key area for consideration by MMV.**

Levers of Change.

<b>1. MONITORING OF CASES AND PRESCRIPTIONS TO IMPROVE CASE MANAGEMENT TRACKING IN PUBLIC SECTOR.</b>
This will complement the work to strengthen capacity on supply chain management, which is a main focus for several partners’ work, including PMI and the GFATM. Strengthening the case management working group, under the leadership of the NMCP, may be a key lever to increase ACT availability, rational use and coordination between partners.
<b>2. SUPERVISION OF PRESCRIPTIONS IN THE PRIVATE SECTOR</b>
<div style="display: flex; align-items: flex-start;">  <div> <p>Improving supervision in this area can help monitor adherence to guidelines, along with private sector sensitization.</p> <p>National Insurance Schemes may become a lever of change in this area, and communication with these institutions is recommended.</p> </div> </div>
<b>3. STRENGTHENING OF A PERMANENT AND REGULAR PHARMACOVIGILANCE SYSTEM</b>
WHO AND THE GFATM, among others, are focusing on this critical area – it is a long-term proposition, and will require significant investment, training, and supervision to create functional national PV systems that work across both public and private sectors.
<b>4. HOW MMV MAY SUPPORT IMPROVED MONITORING AND EVALUATION:</b>
<p>Advocate for the development of effective PV systems.</p> <p>Encourage the work of ACT coordination committees to increase coordination between</p>

partners, involving key stakeholders, including national insurance representatives.

## G. Acceptability by communities

**Demand by consumers is a barrier to access to recommended quality assured solid paediatric treatments for non-complicated malaria. Addressing consumer acceptance could be a key driver to increase the use of quality paediatric ACTs.**

Many caregivers are used to using antimalarial treatments stored at home or purchased from informal vendors to treat children with fever. Chloroquine is still frequently sold in the informal sector. Community sensitization can help diminish tendencies to self-medicate, and to promote the rational use of quality products.

Crushing adult tablets for children both in the public sector and in the private sector is still widely practiced, in part because it is perceived to be a cheaper alternative than buying paediatric syrups. Dispensing training may help rectify this tendency, since quality dispersible medicines for children are less costly than syrups and comparable in price to quality adult ACTs. Healthcare professionals should be sensitized to the importance of this dispensing training, and in addition, community workers, HBM agents and pharmacists may become good promoters for correct dispensing information.

### G1. Community awareness of diseases, treatments & timing to seek care

**Most interviewees agreed that sensitizing communities is a good opportunity to drive change in consumption patterns.** Care givers are willing to use quality paediatric treatments as evidenced in Home Based Management (HBM) programmes, even more so when positive results are readily detected.

Price is an important driver for community acceptance, as is ease of use. Although communities may initially have biases in favour of liquid formulations, they can readily accept a solid paediatric formulation when proper dispensing instructions are shared with them. Moreover, interviewees indicated that effervescent formulations have a strong positive image, which should facilitate the use of solid child friendly formulations; to the contrary, the crushed tablet is perceived as the “treatment of the poor”. All interviewees agreed that households generally have access to plastic containers suitable for dissolving the soluble or dispersible pill.

**Dispensing training is paramount. Since health professionals may be hard pressed to find the time to explain first-time use, the role of pharmacists and community healthworkers could be key. In each village, health agents or “badienou gokh” (community mammas) such as in Senegal are highly respected and close to the communities, and can reinforce correct dosing with soluble paediatric formulations.** Even with ASAQ (not flavour masked), after proper instructions on how to administer with sweet tasting food to mask the taste, children and mothers were said to easily accept the treatment.




**Self-medication, traditional healers, and the informal drug market are major issues in all six countries.** Mothers often go directly to the “ambulant” (mobile street drug seller) because of a combination of

financial constraints, long wait times at health centres, and stockouts of ACTs in the public health centre drive them to seek alternatives. Reinforcement of **community sensitization is key to promote rational use of quality products.**

## G2. Patient access to care via HBM

**Home Based Management (HBM) may be an efficient complement to primary health centres, and HBM or/and pharmacists may have a major role to expand access to relevant care and quality medicines.** Preliminary data show that HBM can dramatically decrease patient reliance on informal market vendors. In a meeting in Mali with mothers, *relais* and other HP in the context of PNLP/ PSI CCM programme, all pointed to the following clear benefits of the programme: better and faster access to care, effective treatment for approximately a third of the previous price (1000 to 1500 vs 4500 CFA previously), and far fewer cases of severe malaria needing referral to the CSCOMs. Mothers were specific in relaying positive comments about the treatment and did not express any concern about the solid formulation after they were shown a first administration. HBM is a priority for several partners including UNICEF, GFATM and PMI, and its harmonization and expansion within the health system are critical.

## G3. Levers of change

1. COMMUNITY SENSITIZATION IS PARAMOUNT	
 <p>Driver of change</p>	<ul style="list-style-type: none"> <li>NMCPs have generally been very open to considering various means to sensitize and inform, in partnership with grassroots NGOs (including TV spots in local language, educational “causeries” (chats) in the village or church, radio spots using famous actors and musicians, religious leaders, clubs against malaria in schools. )</li> <li>Under the NMCP leadership, potential partners may include <b>Women’s Community Based Management Organizations (CBOs), Faith-based organizations and churches heads, village heads, the Ministry of Families, GFATM, WHO, PSI, and other civil society organizations and grassroots NGOs.</b></li> <li><b>Women from the communities may be empowered to take the leadership of the campaigns.</b></li> </ul>
2. DISPENSING TRAINING	
Sensitization of HPs on the importance of dispensing training, along with the availability of referrals from pharmacists, HBM agents and/or “community mammas” to reinforce that dispensing training. Visuals support materials can help, and manufacturers should be encouraged to develop these dispensing education tools.	
3. STRENGTHENING & COORDINATION OF HOME-BASED MANAGEMENT PROGRAMMES	
These are a priority for GFATM, PMI, and UNICEF among other partners.	
4. HOW MMV MAY FACILITATE RATIONAL USE OF RECOMMENDED QUALITY ASSURED SOLID PAEDIATRIC ACTS:	
<ul style="list-style-type: none"> <li>Encourage partners engaged in community sensitization work.</li> <li>Work with pharma partners to ensure adequate dosing and dispensing instructions are developed, with appropriate visual materials.</li> </ul>	

## IV. WHAT CAN MMV DO NOW?

MMV should consider the following areas where it may directly or indirectly be able to support faster and broader adoption of WHO-recommended quality assured paediatric ACTs, with primary focus on international level activities and indirect facilitation of national level activities.

### A. Priorities

- I. Advocate for recommended quality assured paediatric ACTs with a three- pronged focus on**
- Recommended ACTs and their rational use, including RDT use, the importance of dispensing training, and pharmacovigilance (PV).
  - The quality of paediatric medicines and quality assurance,
  - Restrict the use of non AS-monotherapies to their indications, i.e. NOT for treatment of non-complicated *P. falciparum* malaria, and phase out non 3-day ACT therapy.

Such advocacy has the following objectives:

Barrier	Objective of the interventions
NEML and/or local protocol refer to ACTs that are not FDC or not quality assured, and do not stipulate market withdrawal of non-artemisinin monotherapies for therapeutic use.	To facilitate the update of the policy and policy documents (NEML & local protocol), including a phase out of ALL monotherapies for treatment of non-complicated <i>P. falciparum</i> malaria with restriction of the use of non AS monotherapies to their indications.
HPs not sensitized to recommendations regarding the quality of medicines.	To sensitize HP on recommendations, including use of RDTs, monotherapies, quality, paediatric formulations.

### II. Facilitate the availability & prioritization of quality assured paediatric ACTs

Such prioritization has the following objectives:

Barrier	Objective of the interventions
Quality assured products are not recognized as such by most HP and pharmacists	To increase the visibility of quality assured ACTs, so they may get a commercial advantage
Most paediatric ACTs are not quality assured	To encourage more manufacturers to seek WHO pre-qualification for paediatric-designed medications
Insufficient sensitization to the concept of quality and quality assurance of paediatric antimalarials	Increase awareness on issues regarding poor quality treatments and on benefits of quality assurance

### III. Facilitate a better alignment of the antimalarials used with national guidelines and WHO recommendations

This has the following objectives:

Barrier	Objective of the interventions
In many countries, only chloroquine and AS oral monotherapies are banned	To encourage the restriction of the use of non AS-monotherapies to their indications and the phasing out of their use for treatment of non-complicated <i>P. falciparum</i> malaria, at international and national levels, and facilitate the switch to recommended products
AQ and SP monotherapies are largely used for treatment, including in children	To phase out those monotherapies for therapeutic use

### IV. Advocate for the creation or strengthening of functional national PV systems

This has the following objectives:

Barrier	Objective of the interventions
There is minimal if any information on the safety of antimalarials once they are marketed.	To facilitate the set up or strengthening of a functional PV system in country.

### V. Contribute to strengthening the supply chain

This has the following objectives:

Barrier	Objective of the interventions
Stock outs are a major issue in all six countries, in part related to insufficient stock management	To strengthen stock management capacity, including consumption monitoring mechanisms
Pharmacists have an important counselling role yet they struggle with little scientific information and no official prescribing role.	To engage pharmacists as an additional official point of entry into the health system.

## B. Proposed interventions

According to Brenda Waning, Boston University, the analysis of the field of paediatric ARVs show that two elements were instrumental to improve the availability of new formulations and reduce prices: sensitization / advocacy and positive business case /financials including clearer descriptions of potential demand. Dialogue was critical with countries to decrease policy barriers and with manufacturers to encourage them to develop quality products<sup>53</sup>.

<sup>53</sup> B. Waning, 2010, Evidence from the ARV field accessed on 15/2/12 at [http://www.mmv.org/sites/default/files/uploads/docs/events/ASTMH2010/2\\_Brenda\\_Waning.pdf](http://www.mmv.org/sites/default/files/uploads/docs/events/ASTMH2010/2_Brenda_Waning.pdf)



## **B1. Sensitize and advocate for recommended quality assured paediatric ACTs**

**This includes a three-pronged focus on: (a) recommendations re: case management and rational use; (b) reinforcing messages re: quality; (c) removing ALL monotherapies and non 3-day ACT therapies for treatment of *P. falciparum* malaria.**

1. **MMV can consider bundling relevant scientific information**, with the goal of reinforcing the public health advocacy from WHO's Better Medicines for Children effort that prioritizes quality-assured paediatric ACTs. National, regional and global data may be used, with focus on efficacy, tolerance, effectiveness, adherence, stability and cost effectiveness of paediatric formulations. A summary of data regarding solid vs liquid formulations with regards to quality assurance would be important. In addition, it will be important to develop a synthesis of arguments to restrict the use of non AS monotherapies to their indications and phase out their use for treatment of uncomplicated *P. falciparum* malaria, as well as clear information on the importance of dispensing information and dosage preparation and on compliance with national treatment guidelines.

### **2. REGIONALLY / INTERNATIONALLY**

**MMV may share information, sensitize and advocate, as follows:**

- a. **Via existing networks, engage regional political leaders, professional associations, in close partnership with WHO, RBM and UNICEF.** These groups may share best practices during their conventions:
  - Health Ministers via ALMA: the African Leaders Malaria Alliance can be a good forum to strengthen senior political will and energize a focus on better medicines for children and on the restriction of the use of non AS monotherapies to their indications.
  - Regulators, via the pharmaceutical departments of UEMOA in Western Africa, OCEAC in central Africa, and with OOAS (West African health organization), where a commission working specifically on malaria could be an option.
  - Paediatricians and nurses, via the regional network "sub-Saharan Francophone Africa paediatricians" and the "Union des Sociétés et Associations de Pédiatres d'Afrique", UNAPSA, under the leadership of Pr Paul Koki from Cameroon. These professional associations are key to disseminate and promote scientific information. Regional PCIM technical coordination, under leadership of Pr Blaise Ayivi, Benin, should also be involved.
  - Pharmacists and international distributors, via the African group of the CIOPF, the "international conference of the francophone pharmacists association", and their inter African forum. The ACAME, the African Association of Central Pharmacies, is a key stakeholder in this endeavour.
  - Faith-based international organizations.
- b. **Organize regional workshop(s), with WHO, RBM and UNICEF**, with the aim to share best practices between networks.
- c. **Facilitate a regional technical working group focus on children's medicines, and particularly antimalarials, under the leadership of WHO and/or UNICEF**, including, in addition to the regional representatives mentioned above, national "champions" who will establish regional priorities, promote best practices and thrive to accelerate access to recommended quality assured paediatric ACTs in their own country.
- d. **Engage multilateral and bilateral donors committed to malaria to support these efforts to prioritize paediatric ACTs that are both recommended and quality assured.**

### **3. NATIONALLY**

**MMV is not positioned to have a direct role in implementation and should instead identify in-country organizations and mechanisms to influence and disseminate information at country level, with the NMCP, WHO, RBM and national “champions”. These players should be encouraged to undertake these areas of work:**

- a. **The set up or strengthening of a national technical case management working group focusing on children’s medicines including malaria, under the leadership of the MOH/NMCP with strong WHO support**, and including NMRA, physicians and pharmacists associations “orders”, researchers, paediatric societies, partners, national insurance representatives. **This group will review relevant evidence for national decision making, and in turn facilitate the following:**
- b. **A national consensus workshop in order to revise the NEML and local protocol and review a timeline for removing all monotherapies and non 3-day ACT therapies for treatment of uncomplicated malaria, under the leadership of the MOH/NMCP, with strong WHO support.** Such workshop will also involve key malaria stakeholders and include national insurance representatives. The recommendations will support the MOH in revising the NEML and treatment protocols.
- c. **A revision of the list of approved/ to be approved antimalarials, under the leadership of the MOH/NMRA.** The expert committee, or national “drug commission”, will in turn provide recommendations on licensing to the NMRA.
- d. **Information, education and sensitization of health professionals in the public, faith-based and private sectors, under the leadership of the NMCP, with strong WHO support. This can leverage RBM resources, researchers, key opinion leaders, central pharmacies and health professional organizations, and should target:**
  - Paediatricians, nurses, midwives and HP who see children, via the national paediatricians scientific society,
  - All physicians and practitioners, via the physicians’ association,
  - Nurses via their association,
  - Pharmacists and distributors, via the national pharmacists association; those will in turn train their employees,
  - Faith-based organizations HP and pharmacists,
  - Health students (physicians, nurses, pharmacists), with the Ministry of Education,
  - National insurance physicians,

The focus of this sensitization should be on the use of quality assured antimalarials and recommended paediatric ACTs.

- e. **Official ceremonies** as a good and recurrent complement to the sensitization training.
- f. **A community sensitization campaign**  
This could be conceived and implemented with NMCP leadership, and with engagement of the Ministry of Women and families, civil society representatives and women-empowerment organizations. The campaign may focus on community education about how to react when a child has fever, on the role of government-recommended treatments for children, and on the difference between quality assured paediatric treatments and other drugs on the market.

## **B2. Facilitate the availability & prioritization of quality assured paediatric ACTs**

1. **Explore the possibility of raising visibility of quality assured ACTs in the private sector -- for instance with a specific logo**, such as “approved by the GFATM”. This increased visibility, in combination with improved regulatory monitoring and sensitization campaigns could offer distributors and sellers a commercial advantage to induce them to prioritize quality assured products. This borrows from a similar strategy used by the AMFm, with a larger application for all quality assured products.

2. **Encourage more manufacturers to seek WHO pre-qualification or a stringent regulatory approval for paediatric specific treatments.** This may be via a supportive facilitation of their regulatory approval processes and/or national registration work. The QUAMED project (<http://www.quamed.org/fr/accueil.aspx>) may be a key partner in that endeavour.
3. Advocate on the international scene for an increased quality of antimalarials in francophone Africa, in parallel to a national level sensitization to quality.

### **B3. Facilitate a better alignment of the antimalarials used with national guidelines and WHO recommendations**

1. Engage WHO and RBM to facilitate a better alignment of the products used with national guidelines and WHO recommendations, via national policies, regulations, recommendations and sensitization.
2. **Activate and maintain the focus of international agencies around enforcing a code of conduct with manufacturers from whom they procure.** Stopping commercialization of all antimalarial monotherapies for therapeutic use of non-complicated malaria with restriction to the products actual indications in a controlled setting should be a contractual condition for a manufacturer to be able to sell other drugs to an international buyer (ex UNICEF, GFATM, GAVI, MSF).
3. **Seek appropriate ways to support the Mali and Benin NMRAs and MOHs** to take action against large use of AQ monotherapy to treat *P. falciparum* non complicated malaria.

### **B4. Set up or strengthen functional national PV system**

1. **Continue to engage with WHO, the GFATM, INESS and other partners regarding the strengthening of national PV systems,** for the collection of safety data on antimalarials initially, to be secondarily extended to other medicines.
2. **Advocate for donors to support** the improvement of PV, and emphasize the increased importance of this at a time when several new quality assured products are entering African markets.

### **B5. Contribute to strengthening the supply chain**

1. **Disseminate the results of current stock management pilot initiatives (e.g. SMS for Life) to help countries analyse new options to strengthen stock management.** It is noteworthy that almost all countries signalled stock management as a key concern for improving access to better medicines for children.
2. **Initiate a pilot project whereby pharmacists are officially involved as an entry point into the health system, under a mechanism of “collective prescription”, to manage cases.** This engagement of pharmacists in reinforcing proper case management (by correctly using RDTs and then dispensing ACTs as needed) could be based on an algorithm prepared by the “ordre des médecins”. A pilot for such an initiative may be performed in select sites, under the guidance of the MOH.

## V. CONCLUSION

This survey identifies main barriers and potential drivers to improve access to quality assured paediatric ACTs in six countries: Benin, Burkina Faso, Cameroon, Gabon, Mali and Senegal. We provide specific recommendations and strategic areas of intervention for consideration by MMV.

These primarily aim to facilitate a better alignment of the antimalarials used with the national guidelines and WHO recommendations and focus on bundling of relevant information, broad multi-level advocacy and sensitization to the concepts of:

- **Recommended ACTs and their rational use, including RDT use, dispensing training, and PV;**
- **Product quality and quality assurance,**
- **The phase out of the use of ALL monotherapies and non 3-day ACT therapy for treatment of non-complicated *P. falciparum* malaria,**

This work ultimately seeks to facilitate policy and regulatory updates, and to create a message impact for HP, pharmacists and community health programs. As described, MMV will need to define its appropriate role vis-à-vis WHO and national partners, depending on the nature of the suggested intervention.

In addition, MMV should contemplate how it can support efforts to increase the visibility and prioritization of quality assured products in the private sector. Given MMV's work with many manufacturers that have elected to step up to the quality hurdle, MMV can explore how to incentivize more manufacturers to seek quality assured status for medicines for children.

MMV advocacy can also be tapped to support a WHO-led messaging effort that seeks to restrict the use of non AS monotherapies to their indications and stamp out non 3-day ACT therapies for treatment of *P. falciparum* malaria. With regards to supply chain improvements, MMV can document its experience with pilot activities to strengthen supply chain management and ensure that countries understand the lessons learned to-date.

Last, MMV may consider how to encourage countries to conduct a pilot whereby pharmacists may be officially enrolled under the MOH and physicians' association control to initiate case management.

## VI. APPENDIX: METHODOLOGY

The current study, commissioned by Medicines for Malaria Ventures (MMV), aims to understand the barriers and potential levers to facilitate the adoption of paediatric ACTs that are both recommended and quality assured, to treat non-complicated malaria in children in francophone Africa. This work is qualitative and based upon secondary and primary research in Benin, Burkina Faso, Cameroon, Gabon, Mali, and Senegal.

Francophone countries have been selected in consultation with the MMV access team based upon a set of selection criteria focused on the western or central Africa region, malaria burden, population, first line ACT treatment, and malaria funding levels, so as to provide a sufficient variety of experiences and allow actionable recommendations.

Primary research involved interviews with decision makers, influencers and key in-country malaria stakeholders representing the following three sectors: 1. Government, 2. NGO/Faith-based organizations/donors and 3. Private sectors. These in-country interviews were organized in partnership with the NMCP and the WHO in each of these 6 countries. In addition, interviews with international experts and organizations were conducted.

<b>Government sector, parastatal organizations and regulatory bodies</b>
<ul style="list-style-type: none"> <li>- Central pharmacy</li> <li>- Medical School – Public Hospital - Researchers</li> <li>- Ministry of Health – “Direction de la santé”</li> <li>- Ministry of Women’s Empowerment and the Family (in Cameroon)</li> <li>- National Insurance</li> <li>- National Malaria Control Programme</li> <li>- National Medicines Regulatory Agency</li> <li>- WHO malaria and essential medicines departments in country office</li> </ul>
<b>NGO – Faith-based organizations – Donors</b>
<ul style="list-style-type: none"> <li>- Catholic, Baptist or Muslim health centres</li> <li>- Civil society organizations</li> <li>- Global Fund /Principal Recipient</li> <li>- Main NGOs and development partners in country: PSI, MSF etc</li> <li>- PMI in Mali, Senegal, Benin</li> <li>- UNICEF</li> </ul>
<b>Private sector</b>
<ul style="list-style-type: none"> <li>- Ordre National des médecins</li> <li>- Ordre National des Pharmaciens</li> <li>- Paediatric Association</li> <li>- Private distributors and wholesalers</li> <li>- Private sector pharmacists association</li> </ul>
<b>International organizations</b>
<ul style="list-style-type: none"> <li>- GFATM</li> <li>- MSF</li> <li>- RBM</li> <li>- WHO EMP and GMP</li> </ul>

Interviews occurred between July 2011 and February 2012. The interview guideline is based upon a WHO EMP framework for the evaluation of access to medicines, with the permission of Drs Suzanne Hill and Gilles Forte. Interviews focus on the following 7 potential barriers to access:

1. Policy
2. Regulatory
3. Manufacturing and supply
4. Financing
5. Demand by health professionals
6. Monitoring & evaluation
7. Acceptability to consumers

**This report constitutes the executive summary of the study and complements six individual country reports. This executive summary, along with the individual country reports, includes the recommendations for MMV based on the overall survey results in the six target countries.**