



UNITAID

**MID-TERM EVALUATION OF THE “IMPROVING SEVERE MALARIA OUTCOMES”
(ISMO) PROJECT**

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FINAL REPORT

Submitted by:

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ACRONYMS AND ABBREVIATIONS

Acronym	Full description
ACT	Artemisinin-based Combination Therapy
CEPA	Cambridge Economic Policy Associates
CHAI	Clinton Health Access Initiative
HMIS	Health Management Information System
Inj AS	Injectable Artesunate
Ir AS	Intra-rectal Artesunate
ISMO	Improving Severe Malaria Outcomes
KEMSA	Kenya Medical Supplies Authority
M&E	Monitoring and Evaluation
MC	Malaria Consortium
MMV	Medicines for Malaria Venture
MoH	Ministry of Health
MoU	Memorandum of Understanding
MSH	Management Sciences for Health
NDA	National Drug Authority
NMCP	National Malaria Control Program
NMS	National Medical Stores
PFSA	Pharmaceutical Fund and Supply Agency
PMI	US President's Malaria Initiative
PNFP	Private Note for Profit
QoC	Quality of Care
RfP	Request for Proposal
RHB	Regional Health Bureaus
ToR	Terms of Reference
UNICEF	United Nations Children's Fund
US FDA	United States Food and Drug Administration
WHO	World Health Organization
WHO GMP	WHO Good Manufacturing Practises
WHO PQ	WHO Prequalification Programme
WHO TDR	WHO Special Programme for Research and Training in Tropical Diseases

EXECUTIVE SUMMARY

Introduction to the ISMO project

The “Improving Severe Malaria Outcomes” (ISMO) project aims to increase the uptake and create a stable market for Injectable Artesunate (Inj AS) for the treatment of severe malaria and make available Intra-rectal Artesunate (Ir AS) for pre-referral treatment. The project is being implemented by a consortium of Medicines for Malaria Venture (MMV), Clinton Health Access Initiative (CHAI) and Malaria Consortium (MC), over a period of three years from June 2013 to 2016 and with a budget of US\$34m (the majority of which is for the procurement of Inj AS). The main components of the project include: procurement and delivery, updating of treatment guidelines and training for Inj AS in six countries: Cameroon, Ethiopia (two regions), Kenya, Malawi, Nigeria (13 states) and Uganda; as well as acceleration of the prequalification of a second Inj AS product and at least two Ir AS products.

Evaluation objectives and methods

CEPA’s mid-term review of the project, conducted over the period August to November 2015, aims to assess grant performance and consider project achievements, issues and lessons learned, to inform any required changes in the project. We have employed a mixed-methods approach for the evaluation including a desk-based review of documents and data, consultations with project stakeholders (i.e. UNITAID, implementing partners, pharmaceutical companies, the Global Fund, etc.) and country visits to Kenya and Uganda.

Evaluation findings and conclusions

The ISMO project is highly relevant in relation to the needs for improved severe malaria treatment in countries and directly aligned with UNITAID’s mission and mandate, with an effective approach that tackles both demand and supply side issues of the Inj AS market, and emphasises UNITAID’s unique role in the global architecture to engage with manufacturers and help bring them to market.

Project progress and performance to date has been mixed, with some key challenges and issues, but also important achievements. In summary:

- The procurement of Inj AS has not gone as per plan, with initial delays in signing of country Memorandum of Understandings (MoUs) and a protracted price negotiation with Guilin resulting in the first procurements being concluded seven months later than planned. The final agreed price of US\$ 1.42 was higher than expected, but the lowest price paid to date by any donor.
- Unexpected challenges with the selected generic supplier (IPCA), have resulted in a two year delay in dossier submission to WHO (expected in December 2015). While MMV’s support to IPCA has been well received, the issuing of US FDA import

restrictions on select IPCA plants has distracted the manufacturer from progressing its work on Inj AS (exacerbating the challenging price negotiations with Guilin).

These delays have somewhat reduced the project's intended catalytic effect through Inj AS procurements, as the project brought commodities to countries from September 2014 only, at a time when other donors had also started procuring significant volumes of Inj AS (although timing of UNITAID procurements relative to other funders has varied by country).¹ Reduced demand for ISMO project funded procurements in countries in the face of other donors has implied that only 46% of the procurement budget will be spent by project close.

As such, important lessons learned from the project include the need to have adopted a pre-agreed pricing agreement and/ or more strategic approach (e.g. through pooled procurements²) with Guilin at the start of the project. It is difficult to comment if this would have resulted in a lower price, but it would have avoided a lengthy price negotiation during project implementation and consequent transaction costs. Another key lesson is to have considered supporting more than one generic supplier for Inj AS (to help balance risks).

Other issues have been an inadequately defined logframe (which has impeded effective monitoring of results) and some inefficiencies with regards to project procurement arrangements. While the initial lack of clarity of roles and responsibilities with Missionpharma have been resolved and Missionpharma appears to be performing as per plan, there have been unwarranted procurement related costs in Kenya due to poor procurement planning and management.

Notwithstanding these challenges, the project has worked well and made good progress in a number of areas:

- The project has been catalytic in supporting demand generation in its focus countries through its delivery of much-needed trainings, advocacy and policy support. Notably, all planned trainings under the project have been completed/ exceeded targets (except for Cameroon). While the need for supporting supervisions cannot be undermined, feedback has suggested that the trainings have succeeded in improving Inj AS uptake and health worker practice. Other in-country support being provided by CHAI and MC towards advocacy, policy development, quantification, procurement planning and M&E (specifically reviewed in Kenya and Uganda) are also viewed as very useful.
- The work towards supporting the pre-qualification of two manufacturers for Ir AS (Cipla and Strides Arcolab), who are expected to make their submission in December 2015 (which is only slightly later than the Q3 2015 submission anticipated in the

¹ The project's relevance and impact may have also been enhanced had it started earlier, more closely in line with the WHO revision of treatment guidelines in April 2011.

² While pooled procurement was employed in the project, it was only planned for during the course of the project when price declines were not being achieved.

project plan), has progressed well, and is set to be one of the key legacies of the project. The planned market research activities have been completed in a timely manner, though some operational research pieces are still being delayed by ongoing ethical review processes.

- Current data indicate that the project goal of increasing the proportion of severe malaria cases treated by Inj AS is being achieved in Kenya, Uganda and the three states of Nigeria supported by the Malaria Consortium. However, the opposite trend has been observed in Ethiopia, primarily caused by facility level stock-outs related to structural distribution problems. Anecdotal evidence collected in the evaluation indicates a high level of satisfaction with Inj AS both by health workers and patients. However, challenges were also reported relating to over-use of Inj AS for non-severe malaria cases.
- There is considerable potential for primarily the Global Fund to assume the costs of procuring Inj AS in the six ISMO countries once UNITAID support has ended, although there are risks associated with managing the timing of completion of UNITAID funding and commencement of the next round of Global Fund support.

Recommendations

Given the timing of this evaluation, with only six-seven months until project close, our main recommendation is for UNITAID and MMV to discuss and agree a clearly defined no-cost extension for the project – given the imminent dossier submission for WHO prequalification by IPCA and thereby the potential to manage a competitive procurement for Inj AS and work towards the project objective of improving the market conditions for Inj AS.

We understand that MMV is currently in discussion with UNITAID on an extension request and advise that:

- (i) the primary focus of extension period activities is to ensure the necessary technical and facilitating support is provided to IPCA;
- (ii) the project considers providing some support to a second generic manufacturer, not only to balance any further risks for the IPCA submission, but also to set in motion the longer term objectives of broader competition;
- (iii) efforts be made to encourage greater country ownership and a country-specific approach adopted to determine effective transition planning and extension support;
- (iv) a clear and strategic plan is developed in terms of specific types of in-country support and countries to be extended/ added; and
- (v) a clearly defined results framework is set up for the project extension.

Other recommendations for the remaining life of the project are as follows:

- Explore the possibility of expanded pooled procurement and further price negotiation for the planned 2016 procurement.
- Focus on fast-tracking the prequalification process for Ir AS and explore new support to encourage demand creation for the product.
- Consider and disseminate key country-level learnings and best practice.
- Emphasise donor coordination of procurement and delivery of Inj AS; and ensure adequate emphasis is placed on improving M&E systems for data on the need for and use of Inj AS (also relevant for the extension period, if approved).

Finally, broader recommendations to support improved UNITAID project planning and support are as follows:

- Explore the potential for expedited proposal development, review and approval processes to ensure that UNITAID's role in impacting commodity market dynamics is more catalytic and accelerated.
- Consider whether project timeframes may be extended from three to five years to allow for more realistic timelines for market-shaping activities.
- Ensure that projects have quality logframes or results frameworks, with clearly defined indicators that are "SMART", with baselines, interim milestones and final targets as well as detailed risk matrices and mitigation strategies.
- Consider if more simplified project implementation structures can be attained, with clear linkages between roles, responsibility and monitoring.
- Consider the experience gained across multiple projects in engaging with monopolistic suppliers and draw lessons for effective approaches to deliver results. Specifically, based on this project's experience, it is recommended that UNITAID aims to engage early with monopolistic suppliers and ascertain some agreement on pricing and supply in advance; as well as plan to support more than one supplier to bring their product to market; however these approaches need to be assessed carefully for specific commodity market contexts and products.

1. INTRODUCTION AND EVALUATION APPROACH

Cambridge Economic Policy Associates (CEPA) has been appointed by UNITAID to undertake a mid-term evaluation of the “Improving Severe Malaria Outcomes” (ISMO) project, under UNITAID’s long-term agreement on evaluations with CEPA. This report presents our evaluation findings, conclusions and recommendations.

In the introduction section, we provide a brief description of the UNITAID ISMO project (Section 1.1), the evaluation framework and methodology (Section 1.2) and structure of the report (Section 1.3).

1.1. Background to the ISMO project

In December 2012, the UNITAID Board approved the ISMO project, which aims to improve the outcomes for severe malaria through increased uptake and creation of a stable market for Injectable Artesunate (Inj AS) and availability of Intra-rectal Artesunate (Ir AS) for pre-referral treatment. The project was launched in response to limited Inj AS and Ir AS uptake despite a revision of the World Health Organization (WHO) guidelines in April 2011 recommending the use of Inj AS for treating severe malaria and Ir AS for pre-referral treatment of severe malaria in children.³

The project goals, outcomes and outputs are presented in Table 1.1.

Table 1.1: Project goals, outcomes and outputs

Injectable Artesunate	
Goal	To reduce case fatality rates for severe malaria (subsequently revised to: [to increase the] proportion of severe malaria cases treated by Inj AS/Quinine)
Outcome	Creation of a stable market for quality assured Inj AS
Outputs	<ol style="list-style-type: none">1. Increased use of (appropriately used) Inj AS for severe malaria2. Generic manufacturers producing quality assured Inj AS3. Other global donors/funders commit to funding procurement of Inj AS4. Procurement planning for stabilization of the market for Inj AS
Intra-rectal Artesunate	
Goal	Access to life saving quality assured Ir AS for pre-referral treatment for severe malaria
Outcome	Affordable quality assured Ir AS on the market
Outputs	<ol style="list-style-type: none">1. Securing of Prequalification of Ir AS2. Optimise use of Ir AS in low resource settings

The project is to be implemented over a period of three years from June 2013 to 2016, with a budget of US\$34m for several market-shaping activities including acceleration of the

³ World Health Organization Guidelines for the treatment of malaria, 2nd edition – Rev. 1 (2011).

prequalification of a second Inj AS product and at least two Ir AS products as well as procurement and delivery, updating of treatment guidelines and development and delivery of training materials for Inj AS in six countries (Cameroon, Ethiopia (two regions), Kenya, Malawi, Nigeria (13 states only) and Uganda).

A consortium of Medicines for Malaria Venture (MMV), Clinton Health Access Initiative (CHAI) and Malaria Consortium (MC) developed the project proposal and were mandated for project implementation. MMV is the lead implementer, while CHAI and MC are responsible for in-country activities. Missionpharma was selected as procurement agent for Inj AS.

MMV is currently consolidating documentation for the submission of a no-cost extension for the project, to be discussed and agreed with the UNITAID Malaria Team.

1.2. Evaluation framework and methodology

As per the Terms of Reference (ToR) and discussions with the UNITAID Secretariat, the aim of the evaluation is to assess grant performance to date and consider project achievements, issues and lessons learned, to inform any required changes in the project.

We have structured the evaluation framework to consider the following four dimensions for the Inj AS and Ir AS project components, presented in Figure 1.2 over page:

- **Relevance:** the extent of alignment of the project objectives and design with UNITAID's mission and strategic objectives as well as country needs.
- **Efficiency and effectiveness:** whether the project activities have been conducted in an efficient and effective manner in terms of performance against plans.
- **Results:** whether the project is on track to achieve its intended public health and market impact targets.
- **Sustainability:** the potential for sustainability after the completion of UNITAID funding.

Within each dimension we have structured specific evaluation questions for the Inj AS project component that capture the overarching issues relevant for this mid-term evaluation. For the Ir AS project component, we have structured one overarching question that seeks to assess the progress to date against plans.

Our analysis across these evaluation questions forms the basis for the evaluation conclusions, lessons learned and recommendations presented in Section 7.

Figure 1.2: Evaluation framework

Evaluation dimension	Relevance	Efficiency & Effectiveness	Results	Sustainability
Injectable Artesunate	1. Are the project objectives and design aligned with and contribute towards UNITAID’s mission/ strategic objectives and country needs?	2. To what extent has the project been implemented in an efficient manner, in terms of timelines, budget management and roles and management by project partners? 3. Are procurement and supply arrangements consistent with plans and have they worked well in practice? 4. Has health worker training been effective in increasing appropriate use of Inj AS? How effective has the project’s in-country support been and what have been the key challenges?	5. Is the project on track to achieve the intended public health and market impact ?	6. To what extent are project activities likely to be sustained after UNITAID funding has come to an end?
Intrarectal Artesunate	7. To what extent is the project on track to achieve its goal of promoting access to life-saving quality-assured intra-rectal artesunate for pre-referral treatment of severe malaria?			
Evaluation conclusions, lessons learned and recommendations				

We have employed a **mixed-methods approach** for the evaluation including desk-based review of the project documents and the broader literature on severe malaria; consultations with project partners, pharmaceutical companies and donors supporting procurement of severe malaria treatments (e.g. the US President’s Malaria Initiative (PMI), the Global Fund); country field visits to Kenya and Uganda; and select quantitative analysis of the project budget and reported results.

1.3. Structure of the report

The report is structured as follows:

- Sections 2-5 present the findings on the Inj AS component of the project across the four evaluation dimensions of relevance, efficiency and effectiveness, results and sustainability;
- Section 6 presents the findings on the Ir AS component of the project; and
- Section 7 concludes with the key lessons learned from project implementation to date and provides recommendations.

The report is supported by the following annexes: Annex 1 presents the evaluation methods and limitations in more detail; Annex 2 provides a bibliography; Annex 3 presents a list of global stakeholders consulted and the interview guide; Annex 4 provides a list of country stakeholders consulted and the interview guide used; Annex 5 presents a brief assessment of the availability of severe malaria job aides in the three facilities visited in Kenya and Uganda; and Annex 6 gives further detail on Inj AS procurement across the ISMO countries.

2. INJ AS EVALUATION DIMENSION 1: RELEVANCE

The starting point for our assessment is to consider the relevance and alignment of the project with UNITAID's mission and strategic objectives as well as country needs. Our evaluation question is as follows:

Q1: Are the project objectives and design aligned with and contribute towards UNITAID's mission/ strategic objectives and country needs?

We consider:

- The suitability of the project objectives in relation to UNITAID's mission and strategic objectives as well as country needs; and
- Whether the project design/ plan is rational, in relation to the intended objectives and UNITAID's mandate in the global architecture.

2.1. Suitability of project objectives

The project goal is to improve the outcome of severe malaria through increased uptake of Inj AS and access to Ir AS for pre-referral treatment, which is directly aligned with UNITAID's mission to *"contribute to scale-up access to treatment for HIV/AIDS, malaria and TB..."* and one of the strategic goals of its 2013-16 Strategy, namely Strategic Goal 4 to *"increase access to artemisinin-based combination therapies (ACTs) and emerging medicines...that will improve the treatment of malaria"*.⁴ Given the importance of these commodities in improving the outcomes for severe malaria, all stakeholders consulted unanimously noted the high relevance of the project objectives.⁵

The project goal is also directly relevant to country needs given the estimated severe malaria and overall malaria burden, with the project plan estimating the following:⁶

- Up to 8 million of the total of 216 million cases of malaria each year are severe malaria cases (i.e. almost 4%), with approximately 655,000 deaths from malaria being mainly attributable to untreated severe malaria and failed quinine treatments.
- The six project countries of Cameroon, Ethiopia, Kenya, Malawi, Nigeria and Uganda reported 1.9 million cases of severe malaria (World Malaria Report, 2011), with approximately 250,000 severe malaria deaths in these countries in 2010 (World Malaria Report, 2012).

Further, Table 2.1 highlights the overall malaria burden in these countries. While the six project countries are not the top malaria burden countries in Africa, their disease incidence

⁴ UNITAID (2013), UNITAID Strategy for 2013-2016, April 2013: p.14

⁵ Dondorp et al., Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *Lancet* 2010;376:1647-57.

⁶ UNITAID-MMV (2013), Project Plan 1a (Inj AS): p.7

is significant and we understand that country selection was also based on a number of other factors (e.g. willingness to expedite Inj AS scale-up, existing relationships with implementing partners, etc.) which are sensible factors to consider to ensure that project design indeed contributes to achievement of the intended objectives.

Table 2.1: Estimated malaria burden in 2012 (rank within Sub-Saharan Africa in parentheses)

Country	Cases	Cases per 100,000 people
Nigeria	48,000,000 (1)	27,647 (8)
Uganda	8,900,000 (3)	16,626 (20)
Malawi	4,400,000 (10)	26,890 (12)
Ethiopia	4,200,000 (11)	4,463 (36)
Cameroon	3,700,000 (16)	23,683 (29)
Kenya	3,500,000 (17)	7,891 (32)
Sub-Saharan Africa	164,720,760 (44% in ISMO countries)	18,858

Source: WHO Global Health Observatory Data Repository

2.2. Adequacy of project design/ plan

In addition to the public health problem being targeted by the project, in line with UNITAID’s mandate and comparative advantage in facilitating improved markets for health commodities, the project design is relevant in terms of:

- **A unique focus on bringing in additional suppliers for Inj AS.** While several donors are providing support for malaria treatment (e.g. the Global Fund, PMI), no other partner works directly with manufacturers to bring products to the market. The current monopolistic market for Inj AS presents a key challenge and stakeholders have emphasised that UNITAID funding through the ISMO project has a unique and critical role to play in delivering a sustainable and affordable supply of Inj AS.
- **Complementary demand creation activities to encourage market expansion, not being emphasised by other donors.** The project has been designed to tackle both supply and demand side challenges with the Inj AS market, which is an effective approach to ensuring increased uptake and access. In most of the countries supported, Inj AS was already being procured by country governments or other donors (albeit in limited quantities), but outdated treatment guidelines, lack of training, poor quantification capacity, amongst other issues had limited the extent of Inj AS uptake. The focus on training provided by the ISMO project, as well as other country-level support (e.g. for improved quantification, advocacy, etc.) serves to support demand growth. More generally, stakeholders have commented on the importance of this *demand creation* role of the ISMO project, which is different from the role of the Global Fund for example, which *responds* to country demand.

As such therefore, the project has been well-designed to play a unique and catalytic role to improve access and uptake of severe malaria treatments and thereby improve severe malaria outcomes. However, our review as well as consultation feedback also suggests some weaknesses with the project design and planning, as follows:

Potential lack of a strategic approach to engaging with Guilin

While engaging with a monopolistic supplier is challenging (and we understand that all project partners have made considerable efforts to this effect), we question whether a pre-determined and more strategic approach to engaging with Guilin may have been more useful and contributed to positive results (also with the benefit of hindsight following the experience with two years of project implementation). This may have included, for example, a pre-agreed pricing agreement with Guilin (until there is competition from the other suppliers) or a consideration of options for pooled procurement with other large buyers. On the former example, our discussions with Guilin indicate that they would have preferred to be involved during the initial project discussions and reach a pricing agreement for the project as a whole at the outset. It is difficult to comment on whether this may or may not have resulted in a lower price for Inj AS, however this would have reduced transaction costs related to delayed procurements during the life of the project. On the latter example, while pooled procurement was employed in the project, it was only planned for during the course of the project when price declines were not being achieved.

All of this bears considerable significance given the “moral hazard” situation created by UNITAID’s commitment to purchase certain volumes under the project which, while affording higher predictability to Guilin, also weakens UNITAID’s bargaining position in the face of a sole supplier. Guilin’s incentive to exercise its market power was particularly strong given the project’s intention to encourage greater competition in the Inj AS market.

More “risk prone” approach by targeting one generic supplier for Inj AS

We understand that MMV undertook a due diligence of several potential Inj AS manufacturers at the start of the project, assessing their capacity to make a dossier submission for WHO prequalification within the project timelines. IPCA was selected as the most likely candidate, but has since run into several challenges. Equally, other manufacturers that were not selected have progressed (and also become more relevant given the delays with IPCA). This reflects the dynamic environment for product development and the evolving market context.

While project implementers are convinced that IPCA will be the manufacturer most likely to first present a product for WHO prequalification, our consultations have raised the issue as to whether it would have been beneficial to work with another supplier in addition to IPCA, possibly with an option to provide more technical support than was available in the IPCA collaboration. More recently, we understand that MMV is looking to sign an MoU with Mylan.

Weak project logframe

While there are several technical challenges with measuring the public health impact of the project (which resulted in a change of the project goal from a reduction in the case fatality rates for severe malaria on account of poor data availability), our review suggests a number of weaknesses in the project logframe including:

- The logframe has not been set up as a logical flow of activities to outputs, outcomes and finally impacts. There is a mix of output and outcome indicators accorded to the four project outputs – e.g. the indicator for Output 4 on procurement planning is on stock outs, which is at the outcome rather than output level.
- The list of defined indicators does not appear to be comprehensive in relation to the project activities. For example, our country visits highlighted a number of key activities being worked on by CHAI and MC (such as work on guidelines and policy developments), but these are not adequately reflected in the logframe which includes indicators related to training activities alone (Indicators O1.1 and O1.2).
- A number of activities and outputs do not have an associated target to be achieved under the project (e.g. Indicator 3.2 on percentage of annual forecasted funding needed for Inj AS that is committed for 2017 in targeted countries), including mid-term targets to enable an assessment of project progress, or do not have a clearly defined baseline (e.g. Indicator P.2 on the median Inj AS price paid annually has a 20% end of project reduction target against UNICEF and Global Fund reference prices, but it is not clear which exact reference price is to be used; also because the prices forecasted under the project budget (US\$ 1.26-1.00 per 60mg vial) are substantially lower than the targeted reduction).

These weaknesses have impacted the ability to effectively measure the progress made by the project (not only for this evaluation, but also for ongoing project management) and have resulted in varying expectations on key “success parameters” relating to the project.

Summary findings:

- The ISMO project goal is highly relevant and aligned with UNITAID’s mission/objectives and country needs, given the burden of severe malaria and the potential for Inj AS and Ir AS to improve treatment outcomes.
- The project is well-designed to meet its intended objectives by focusing on both demand and supply side issues in the Inj AS market. The project design also reinforces UNITAID’s comparative advantage in the global architecture by focusing on bringing in additional suppliers for Inj AS.
- However, there are some key weaknesses with project planning that have impacted on its ability to meet intended objectives, including (i) the lack of a pre-determined and strategic approach to engaging with Guilin; (ii) working with only a single generic manufacturer for Inj AS; and (iii) an inadequately defined project logframe.

3. INJ AS EVALUATION DIMENSION 2: EFFICIENCY AND EFFECTIVENESS

Under the second evaluation dimension, we examine whether project implementation has been efficient and effective to date, by considering the following key aspects:

- timeliness, budget management and delivery against roles and responsibilities of project partners (Section 3.1);
- planned versus actual procurement and supply arrangements (Section 3.2); and
- efficacy of in-country training and other support to encourage uptake of Inj AS (Section 3.3).

3.1. Timeliness, budget management and partner roles

Our evaluation question is as follows:

Q2: To what extent has the project been implemented in an efficient manner, in terms of timelines, budget management and roles and management by project partners?

3.1.1. Timeliness

Following the WHO recommendation for the use of Inj AS in April 2011, the project was developed by the implementing partners around mid-2012 and approved in December 2012 by the UNITAID Board. Thereafter, the project commenced in June 2013 and the first procurements took place in June 2014 (discussed further below). As such, stakeholders have commented that the project would have been more relevant to country needs and desire to roll out Inj AS if it had “more closely followed the heels” of the WHO recommendation for use of Inj AS in 2011.

Following project commencement, there have been a number of key delays from the project plan, as follows:

- **Delays in signing country Memorandums of Understanding (MoUs).** Only two countries (Uganda and Cameroon) signed MoUs for the project in 2013, as planned.⁷ MoUs for Kenya, Ethiopia, Nigeria and Malawi were signed in January, February, April and November 2014 respectively.⁸ The process took longer than expected due to the number of stakeholders involved, degree of legal complexity, and the structure of the Ministry of Health in some countries. For example, the process for Malawi was delayed until an agreement could be reached with the National Malaria

⁷ 2013 Annual Report, p.7

⁸ 2014 Annual Report, p.11

Control Program (NMCP) to integrate the country's multiple parallel supply chains into one integrated national operation.⁹

- **Delays in procurement.** A lengthy price negotiation has implied that the first procurement under the project took place in June 2014 as compared to the planned Q3 of 2013. The delay was also on account of the timelag in signing country MoUs as described above. This is discussed in more detail in Section 3.2 below.
- **Delays in procurement approvals.** According to current rules, every order issued under the project has to be approved by UNITAID, which adds to the timeline for procurement. We understand that UNITAID is currently reviewing its administrative processes to enhance efficiency for all their projects in the future.
- **Country-specific delays during project implementation.** For example: in Kenya, the roll out of training and data collection was slowed down by the need to communicate and seek approval from county level health departments; in Uganda, the importation of commodities was delayed by around three weeks while Missionpharma was registered to hold stock of Inj AS with the Ugandan National Drug Authority (NDA) and a further delay of around one week was incurred as SPEDAG (Missionpharma's local clearing agent) was not pre-appointed on the Ugandan Revenue Authorities Customs System, which National Medical Stores (NMS) require for all suppliers.
- **Delays in bringing a second supplier for Inj AS to the market.** Issues with the selected generic supplier for Inj AS has implied that its submission for WHO-prequalification, planned for end 2013, has not yet taken place (currently estimated to be in December 2015). This is also discussed in more detail in Section 3.2 below.

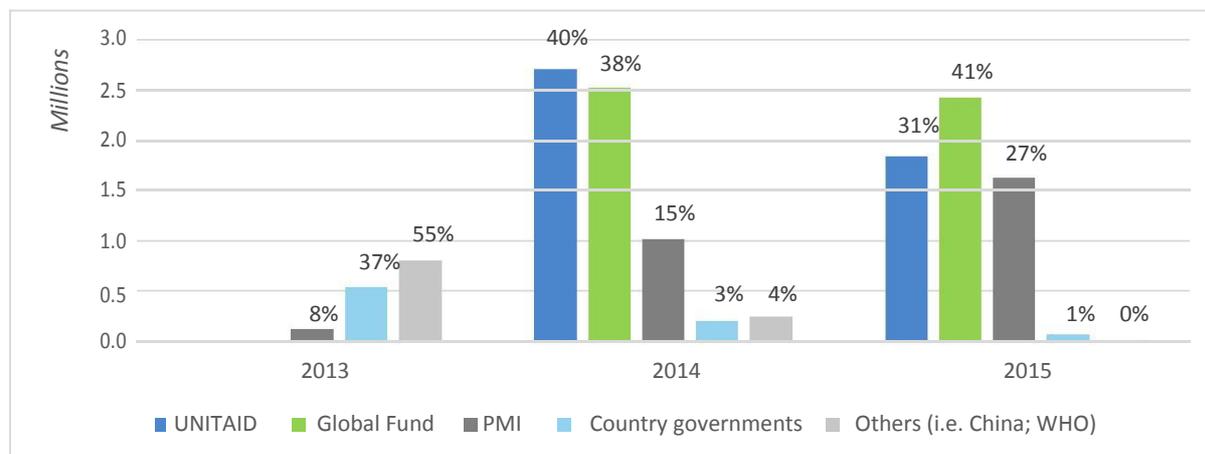
As such, there has been a key delay in the project getting off the ground, followed by a number of delays during implementation – particularly the delays in procurement and supplier expansion for Inj AS. Although it may not have been possible to anticipate many of the delays during the project planning phase (and we note that most of the above delays were not anticipated under the 'Risk Assessment and Management' section of the project plan), timelines have generally been optimistic. In particular, the expectation of rapidly introducing a second prequalified Inj AS manufacturer may not have been realistic. The time allocated for project start-up and signing of MoUs may also have been insufficient.

The procurement delay in particular has somewhat detracted from the potential relevance of the project in some countries where other donors had already been procuring Inj AS before the ISMO project had started. For example, Figure 3.1 shows that by the time UNITAID commodities were procured for the project countries in 2014, the Global Fund and PMI were also procuring significant volumes of Inj AS, thereby reducing the relevance of

⁹ This also delayed UNITAID's first delivery by a quarter, although the impact of the delay was mitigated by a donation from PMI in Q2 2014. (2014 Semi-Annual Report, p.30)

UNITAID’s intended catalytic role through procurement. This is not to suggest that the project as whole has not been catalytic – indeed, there is good evidence to suggest that the project has played a catalytic role as described further in Sections 3 and 6.

Figure 3.1: Inj AS vials procured in ISMO project countries by funder



The experience has varied by country – e.g. in Uganda, the Global Fund and PMI starting procuring Inj AS in 2014, before the ISMO project (where procurement was postponed as it was not needed immediately), but in contrast, ISMO played more of a “front runner” catalytic role in Kenya. Annex 6 provides further details on Inj AS procurement by year, funder and country.

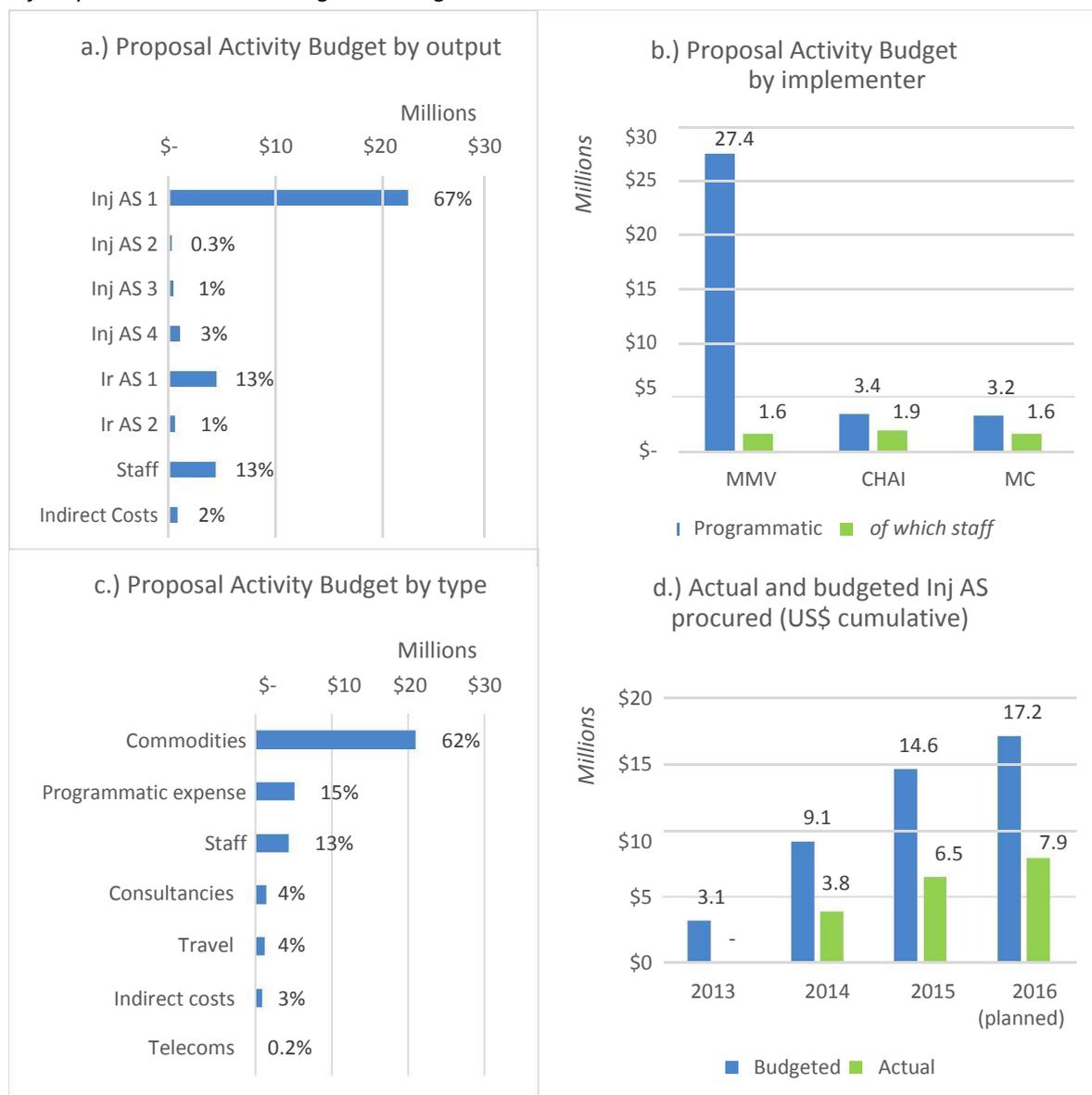
3.1.2. Budget management

Due to delays in the project procurement, the budget is considerably underspent to date. As per Figure 3.2 over page:

- The total budget of the project is US\$ 34m, majority of which (US\$ 21m) is earmarked for Inj AS procurement channelled through MMV.
- However, due to procurement delays, the project is significantly underspent against the original procurement plan. As of 15th September 2015, MMV has placed orders worth US\$ 6,457,000: representing 38% of the project’s procurement budget.¹⁰ The underspend is expected to persist until the end of the project, by which point only 46% of the procurement budget is anticipated to be spent.

¹⁰ It should be noted that the difference between planned and actual procurement is even greater when measured in number of vials, since price per vial has been higher than anticipated under the budget. Only 4,547,416 of the 15,099,944 budgeted vials have been bought to date (30%).

Figure 3.2: ISMO budget analysis by (a) output¹¹; (b) implementer; (c) expense type; and (d) actual Inj AS procurement values against budget



Source: (a) – (c): Project budget; (d): MMV Procurement Analysis – September 2015

3.1.3. Roles and management by project partners

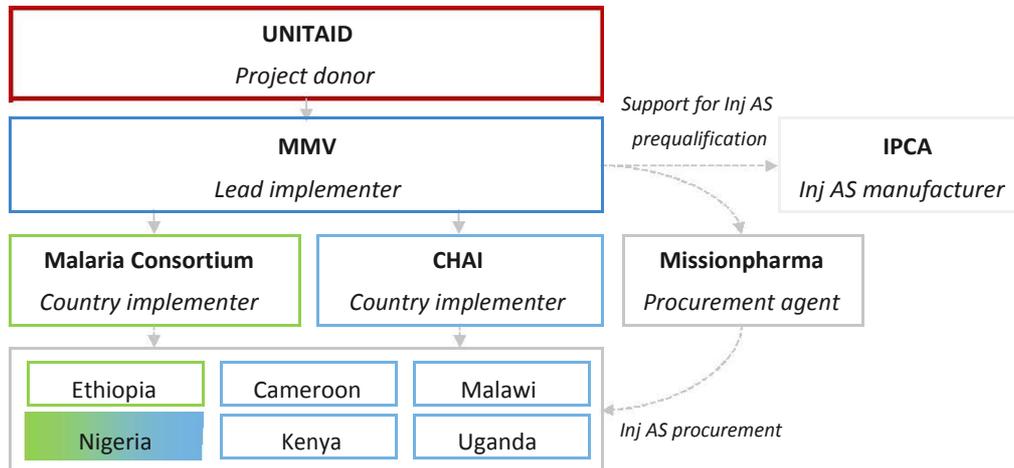
Figure 3.3 below sets out the main project partners for the Inj AS component of the project. In particular:

- MMV is the lead implementer tasked with delivering the overall project and responsible for coordinating country implementation partners, working directly to promote the prequalification of a second Inj AS supplier through support to IPCA and providing Inj AS to the six implementation countries via its procurement agent Missionpharma.

¹¹ See Section 1.1 for a description of each output.

- Responsibility for in-country activities is split between the two country implementers, based on their existing networks. Malaria Consortium is the implementer for 2 regions in Ethiopia, and 3 states in Nigeria, whereas CHAI is the lead implementer for 10 Nigerian states, as well as Cameroon, Kenya, Malawi, and Uganda.

Figure 3.3: Inj AS project partners



At the outset we note that the project organisational structure with three implementing partners is complex, and would inevitably create some issues with management and coordination. While the three partners have their specific roles, it may be questioned whether MMV is best placed to lead the project’s country-level activities (given their limited direct involvement). Further, while the allocation of countries between CHAI and MC based on presence/ experience is rationale, we understand that both organisations generally work independently in their focus countries/ regions. Specifically in Uganda, where both organisations are present, we understand that they have not been in regular contact on the project. There were some initial issues in terms of defining roles and responsibilities in the Uganda work plan, and some tasks originally allocated to MC have since been undertaken by CHAI (e.g. stock management monitoring; health worker assessments; and kit reviews).

Notwithstanding this, our consultations have suggested that project management and delivery is working well. All manufacturers involved in the project have expressed a high degree of satisfaction with the collaboration and support provided by MMV; and both CHAI and the Malaria Consortium are recognised, reputable and well-functioning organisations with strong country presence. There has been strong support of their work at the country level (based on feedback in Kenya and Uganda).

Summary findings:

- Delays in “getting started” as well as in planned procurements under the project have somewhat reduced the project’s intended catalytic “frontrunner” role, with other donors funding Inj AS procurements in many project countries. As a result, the project has spent far less than budgeted and is not expected to exhaust the budget before project end. Some of the delays (e.g. IPCA dossier submission to WHO PQ) may also be on account of ambitious timelines.
- The project organisational structure is complex, although general feedback on management and delivery has been positive.

3.2. Procurement and supply

Our evaluation question is as follows:

Q3: Are procurement and supply arrangements consistent with plans and have they worked well in practice?

In the following section we consider how the project has performed with respect to procurement and supply arrangements as compared to the project plan, and whether these have worked well in practice. We structure our analysis by considering:

- how the volume and price of Inj AS procurements undertaken so far have compared to the project plan (Section 3.2.1);
- what progress has been made towards introducing a second WHO-prequalified Inj AS manufacturer (Section 3.2.2);
- whether selection and performance of Missionpharma as the project’s procurement agent has been efficient and effective (Section 3.2.3);
- whether procurement has been effectively coordinated with other donors (Section 3.2.4); and
- how the project has supported in-country procurement management (Section 3.2.5).

3.2.1. Planned versus actual procurement

Planned procurement

Under output 1 of the project plan (increased use of Inj AS for severe malaria), 15,099,944 60mg vials were budgeted to be delivered across the six ISMO countries. The project budget forecast a price of US\$ 1.26 per vial in the first year of the project, which would then drop to US\$ 1.20, US\$ 1.08 and US\$ 1.00 over the following three years as production from a second WHO-prequalified manufacturer became available. The overall commodity budget totalled US\$ 17,154,836 (excluding shipping and other costs).¹² The project plan proposed that the

¹² MMV Procurement Analysis – September 2015

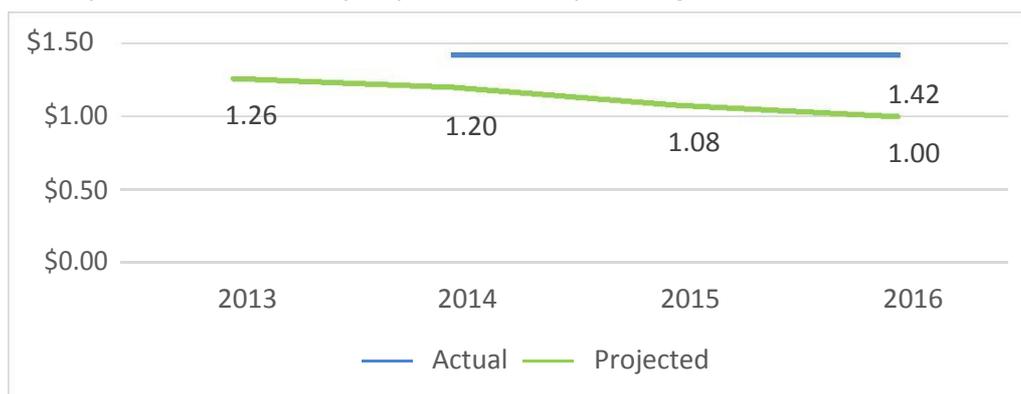
first round of procurement should commence at the end of Q3 2013, with deliveries arriving in each of ISMO country by the end of the year.¹³

Actual procurement to date

Procurement of Inj AS to date has not followed the plan described above. Actual procurement has deviated from initial plans in the following respects:

- Price.** During initial negotiations with Guilin, Missionpharma negotiated a price of US\$ 1.45. The proposed price substantially exceeded what had been expected and was rejected by UNITAID.¹⁴ In an attempt to secure price reductions by leveraging larger volumes, project partners approached the Global Fund and jointly continued negotiations with Guilin from February 2014. A final price of US\$ 1.42 was agreed in June, after a delay of 4 months. The agreed price is not substantially lower than the original agreed price, and is not likely to fall during the remaining project timeframe as projected in initial forecasts (Figure 3.4). In fact our consultations with Guilin indicated that they did not view the price of US\$ 1.42 as fixed for the remaining period of the project, especially if they might need to expand their supply capacity to meet increasing demand (in the face of a second WHO-prequalified supplier not being present in the market as yet). On the other hand, the price is a 22.4% reduction relative to the UNICEF Supply Catalogue price of US\$ 1.83: surpassing the 20% target laid down in the project logframe (though this target is not clearly defined in terms of a specific benchmark price).¹⁵ The price is also the lowest achieved to date, with PMI reporting to have paid between US\$ 1.50 and US\$ 2.50 per 60mg vial.¹⁶

Figure 3.4: Projections and actual Inj AS price achieved per 60mg vial



Source: CEPA analysis

¹³ UNITAID-MMV (2013), Project Plan 1a (Inj AS): p.19

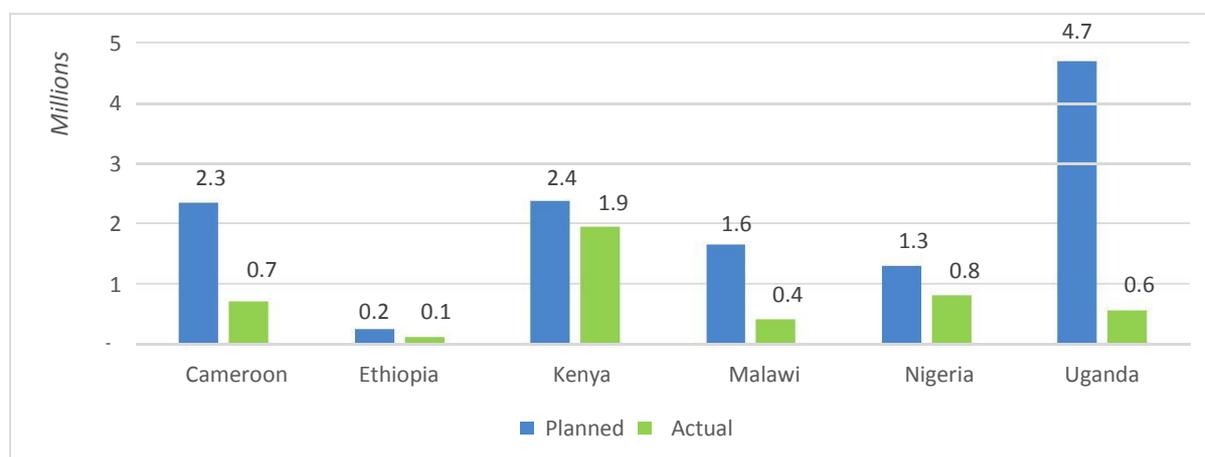
¹⁴ We understand from UNITAID that the quality of the price negotiations could not be ascertained as there was no report on the price negotiation process. Further, there was no attempt to coordinate with other large buyers such as the Global Fund.

¹⁵ 2014 Annual Report, p.10

¹⁶ 2014 Annual Report – Supporting spreadsheet, indicator O3.1

- **Timing.** Following delays in signing country MoUs (lasting from November 2013 – February 2014)¹⁷ and prolonged price negotiations with Guilin (February to May 2014), the first order was placed in June 2014. The very first deliveries to Kenya and Nigeria, which were treated as “emergency orders”, arrived in September and October respectively. Overall, the first procurement was delayed by 7 months.¹⁸
- **Quantities.** 4,547,416 vials have been delivered by the project to-date. This amounts to just 30% of the total quantity budgeted.
- **Distribution by country.** By the time that Inj AS started arriving in-country, commodity needs had developed differently to what was foreseen. The distribution of Inj AS deliveries was altered as a result. In Uganda, for example, the first delivery was postponed until July 2015 as other donors had already committed to meeting Uganda’s need until that time. In Kenya, a delivery of 518,223 vials was redirected from Cameroon so as to keep trust with country stakeholders (made possible by an over-quantification in Cameroon). By the end of 2015, therefore, some countries will have received close to the amounts initially expected, whereas others will have had far less than planned: as illustrated in Figure 3.5, Uganda, for instance, will only have received 12% of the anticipated quantity by end-2015, though Kenya will have received 82% of expected deliveries. Although these changes are partially the result of project delays, they also reflect the extent to which other donors have supported Inj AS procurement in each country (and by extension, the extent to which UNITAID’s support has been required).

Figure 3.5: Planned and actual Inj AS vials procured (Jun 2013- Sept 15) – by project country



Source: MMV Procurement Analysis – September 2015

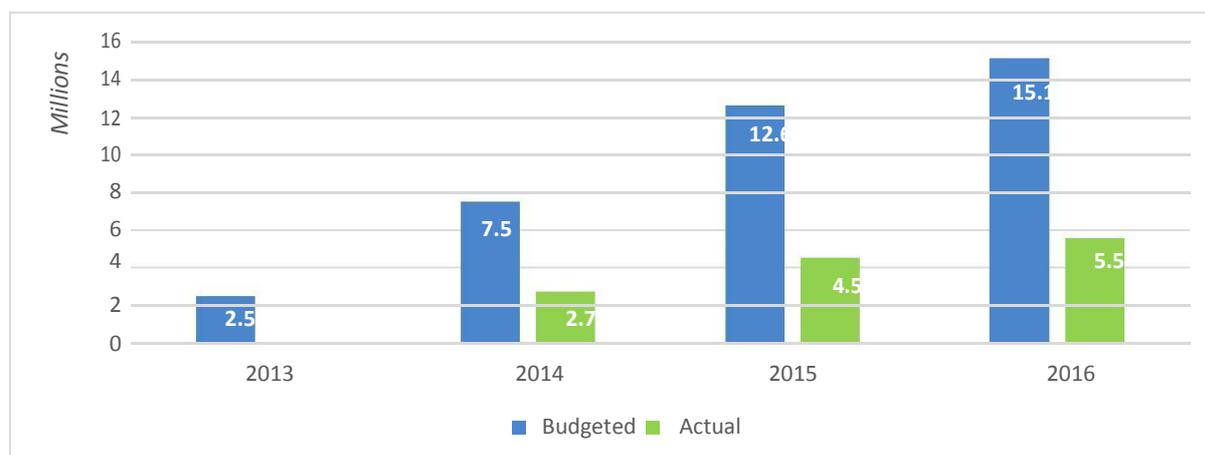
¹⁷ Signature of the MoU for Malawi was postponed until parallel distribution challenges had been resolved in November 2014, though the text of the agreement had been finalised in February. The 2014 Annual Report does not include the months between February and November in its assessment of “delays caused by MoU signatures”.

¹⁸ 2014 Annual Report, p.18

Future expectations

The full quantity budgeted across the three years of the project is not expected to be delivered before project-end. By mid-2016, only 5,547,416 vials are forecast to have been purchased – 37% of the budgeted total (Figure 3.6).

Figure 3.6: Actual and budgeted Inj AS vials procured through UNITAID funding (cumulative)



Source: MMV Procurement Analysis – September 2015

Summary review of project procurement and implications

As described, there has been a substantial deviation from the project plan in terms of procurements under the project. There have been several implications and increased transaction costs as a result of this, including:

- Reduced relevance of UNITAID’s catalytic procurement role in encouraging country uptake of Inj AS, in the face of other donors funding some of the early procurements.
- A decline in project credibility with country governments, given signed MoUs that indicated agreed higher volumes and earlier timings of availability of Inj AS.
- Need to re-train health workers in Nigeria due to mismatched timing of procurement and training.

Price negotiations under the project have however afforded the lowest price for the product to date.

With the benefit of hindsight, one may question the added value of the extended price negotiations with Guilin, especially given the result of a marginal decline from the first agreed price. As discussed in Section 2.2, it may have been preferable to have a more strategic approach with Guilin from the outset of the project.

3.2.2. Introduction of a second WHO-prequalified Inj AS manufacturer

Submission of a second Inj AS dossier for WHO-prequalification has been a key target of the ISMO project, as listed in the project logframe. During May 2013, when the project plan was

being written, dossier submission from IPCA – the most promising manufacturer – was expected before the end of 2013, with approval anticipated by the second half of 2014.¹⁹ However, IPCA is now expected to submit a dossier in December 2015. Submission was delayed by the following events:

- **United States Food and Drug Administration (US FDA) import warning.** The FDA issued an import alert against an IPCA plant in January 2015: citing serious data falsification identified during an inspection in July 2014.²⁰ In March 2015, two more plants were added to the import alert list following further investigations.²¹ Health Canada also banned 50 IPCA products in 2014 in light of the FDA’s findings. As a result, IPCA voluntarily ceased exports to the US market and had to redeploy internal resources to manage the issue.
- **Factory pre-qualification.** IPCA have been constructing a new factory for the production of Inj AS. Construction generated some delays in the Inj AS development stage, and will require a further delay after the Inj AS product is prequalified as the factory is audited. The audit process would normally take 6-8 months, but we understand that an inspection slot has been reserved for Q2 2016 and so the process should be completed in three months.
- **Solubility issues.** Inj AS takes the form of a vial of powder and two diluents. IPCA’s product had a tendency to not dissolve completely, or to precipitate out of the solution over time. This technical problem needed to be resolved before generating stability data.²²

As a result, the market has been dominated by a monopolistic supplier for much longer than anticipated, with consequent impacts on prices being secured for the product (as discussed in the previous section).

Although progress has been much slower than initially anticipated, our consultations have indicated that MMV’s support to IPCA has been effective and well received. IPCA clearly indicated that their timelines would have been further delayed without MMV’s support. In particular, the following assistance was noted as having helped expedite submission:

- **General support.** MMV has provided ongoing technical assistance to IPCA to help align their product and factory with WHO specifications, and have organised meetings between WHO Good Manufacturing Practises (WHO GMP) and IPCA as required.

¹⁹ ISMO Project Plan 1a (Inj AS), p.40

²⁰ <http://www.ipcalabs.com/pdf/Ipca-Voluntary-Stoppage-of-Shipment-to-US-consequent-to-US-FDA-inspection.pdf>

²¹ http://assets.fiercemarkets.net/public/Ipca_Laboratories_Ltd_250315.pdf

²² 2014 Annual Report, p.14

- **Stability data.** 6 month stability data is usually required before a product is submitted for WHO pre-qualification. However, WHO has agreed to accept IPCA's submission with just 3 months' data as a result of MMV's intervention.
- **US FDA import warning.** Following the US FDA's import warning, MMV provided a consultant to perform a mock-audit ahead of the joint audit by WHO GMP; Australian Therapeutic Goods Administration (TGA); and US FDA.
- **Factory pre-qualification.** Owing to MMV's support, WHO agreed to conduct a quick visit to IPCA's Inj AS plant in the event that they pre-qualify their product. IPCA hopes that this will significantly reduce the usual 6-8 month waiting time.

Our discussions with IPCA indicate that if they submit their dossier in December 2015 and prequalification is expedited by WHO with MMV's support, then commodities could be ready for the donor market in September 2016 – following a WHO audit of IPCA's production facilities. As such, the second prequalified manufacturer of Inj AS is highly unlikely to enter the market before project-end in June 2016.

Procurement management and performance

During the first and second procurement rounds, some issues were faced in the coordination between Missionpharma and project partners (e.g. lack of clarity in roles and responsibility for price negotiation, arranging supporting documentation such as import duty waivers, etc.). These issues were broached in a formal correspondence from MMV dated 16th December 2014, to which Missionpharma responded by requesting a meeting to align expectation levels and improve collaboration.

Both MMV and Missionpharma report that responsibilities are much clearer following their meeting, and that coordination has improved during the third round of procurement. Both parties have agreed to hold bi-annual meetings to continue to review and improve coordination for the remainder of the project. Following this meeting, MMV reported that Missionpharma had *“considerably improved their level of services (cost estimates on time, daily follow-up, weekly updates, response time to MMV requests)”*.²⁵ As such, it may be concluded that the selection of Missionpharma was reasonable and has not caused any major issues for project performance.

However, we found that the decision to remove in-country support from Missionpharma’s contract in exchange for a reduced fee has created substantial difficulties for implementing partners in Kenya. Our analysis of import waiver processes in Kenya suggests that has raised rather than lowered overall project costs.

²⁵ MMV (2015), ISMO project updates for UNITAID

3.2.4. Donor coordination

Donor coordination of procurements is an ongoing challenge for all health sectors, exacerbated by poor quantification capacity in countries. We understand that substantial efforts have been made towards ensuring coordination of the UNITAID project with other donor procurements, however invariably there have been some issues and “last minute” revisions to align with country needs and requirements. For example, in Uganda, early commitments from the Global Fund and PMI made UNITAID deliveries in 2014 unnecessary, and the NMCP asked the project team to postpone its delivery until 2015 (reflecting good coordination). However, UNITAID had already placed the order and the batch in question was nearing completion, and in this event, the batch was transferred to another buyer (reflecting the challenges with management).

The existence of multiple donors also poses challenges for country management as well as for Guilin in managing its orders.

3.2.5. In-country procurement management

We examine two key aspects: (i) capacity for quantification and support provided by the project to this effect; and (ii) the situation with respect to stock outs. Our focus has been on Kenya and Uganda, where we have conducted a more detailed review through the country visit.

Quantification

Project partners have noted serious quantification challenges in all countries. For example, in Kenya severe malaria cases and Inj AS usage is not reliably reported in the Health Management Information System (HMIS) due to the inconsistency of facilities' in-patient reporting. Consequently, the quantification of Inj AS needs has been based on estimates of disease burden and past consumption rates of quinine and (more recently) Inj AS. A second technique recommended by the Roll Back Malaria Partnership based on a percentage of the number of uncomplicated malaria cases reported in the country has also been used to generate comparator estimates, though this technique tends to give much higher numbers than the consumption approach (as much as three times higher). Although 5% is the proportion suggested by Roll Back Malaria, Kenya's quantification committee have considered 3% to be more realistic.

Current quantification methods are recognised as being imperfect, but have been satisfactory in generating national estimates of need in the absence of better information. The distribution of Inj AS in Kenya is also based on national-level assessments of each facilities' need, which is supported by CHAI. Kenya operates a "smart-push" system to allocate Inj AS between facilities based on stock-checks and communication with county-level pharmacists. Given that allocations are based on consumption estimates, which are informed by previous allocations, there is a risk that some facilities may be chronically under-supplied.

These quantification challenges underline the importance of supporting country data systems, which the ISMO project has been doing through two channels:

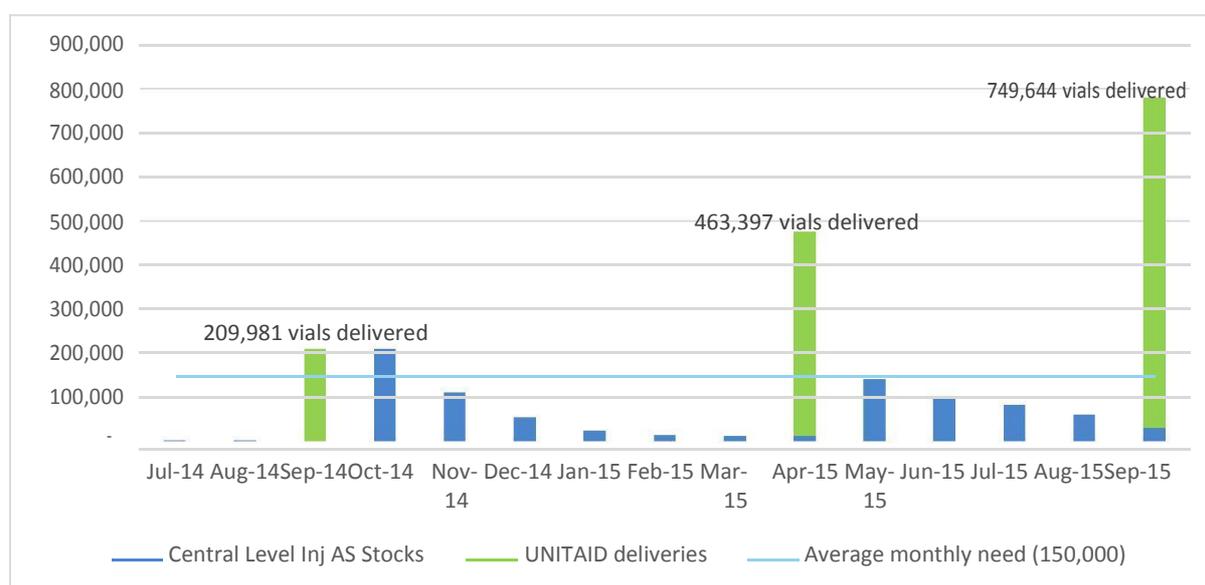
1. Approximately 30 representative facilities are being selected in most of the ISMO project countries for monitoring and evaluation activities. A HMIS contact within each facility is being supported to report accurate Inj AS usage and stock-levels, and malaria-related mortality. If successful, this practice will be used as a pilot for future additions to HMIS data modules.
2. In Kenya and Uganda, CHAI has collaborated towards developing a national in-patient Quality of Care (QoC) survey which includes a severe malaria management module to strengthen reporting of stock and consumption of Inj AS, as well as health worker proficiency at treating severe malaria. The survey will be integrated with HMIS systems in the long-term.

As such, there are key challenges with regards to quantification, however the project is playing an important supporting role to facilitate improvements.

Stock-outs

Field visits have highlighted that country experiences of managing stock levels of Inj AS have differed. In Kenya, as shown in Figure 3.7 below, following the relatively small first consignment in September 2014, there were significant stock outs at the national level until the next consignment was received in May 2015. During this time widespread shortages were reported at the health facility level. There was additional evidence that country distribution mechanism led to further stock outs at some facilities, particular higher level facilities, and required a redistribution of stock within some counties.

Figure 3.7: Inj AS stock levels at the Kenya Medical Stores Agency (KEMSA) over time



Source: CEPA analysis of KEMSA stock level data

Uganda has not had an issue with stock outs at the national level since Inj AS was introduced in 2014 on account of several donors supporting procurements. Some short-term stock outs have been observed at the health facility level due to an epidemic in the northern part of the country, where the distribution mechanism was not able to adjust for such a rapid increase in the use of Inj AS. These issues were however rectified in a short space of time.

From the information available to the evaluation team we can observe that Nigeria and Ethiopia have both experienced stock-outs at the facility level due to distribution problems. In Ethiopia distribution was disrupted by the structural shift from the Regional Health Bureaus (RHB) distribution channel to the central Pharmaceutical Fund and Supply Agency (PFSA). Malaria Consortium has been supporting the transition by providing regular stock update data to the PFSA using the M&E data it collects. In Nigeria, health worker strikes from November 2014 to January 2015 obstructed the distribution of Inj AS to facilities.

Summary findings:

- Project procurements have been lower than planned, delayed largely on account of lengthy price negotiations, and secured for a higher than expected price. These issues have entailed transaction costs and detracted from the project's intended catalytic role. However, this price is the lowest being paid by any donor to date.
- Dossier submission for WHO-prequalification of a second Inj AS product is expected in December 2015, almost two years later than anticipated – implying the lack of competition in the market to date. However MMV support for IPCA has been much valued by the manufacturer.
- Initial procurement management problems within the project (in relation to roles and responsibilities of Missionpharma) have been overcome, though some inefficiencies are apparent, specifically with regards to managing in-country delivery in Kenya.
- Donor coordination on procurements is an ongoing challenge, although project implementers have made efforts to support coordination.
- The project has engaged closely with in-country quantification processes, and is contributing to long-term improvements in data availability (although challenges remain). Some stock-outs have been reported at county-level.

3.3. Health worker training and other in-country support

Q4: Has health worker training been effective in increasing appropriate use of Inj AS? How effective has the project's in-country support been and what have been the key challenges?

A number of key activities have been implemented under the project to encourage increased uptake of appropriately used Inj AS for severe malaria, including:

- Design and implementation of severe malaria case management trainings; and
- Other activities aimed at creating and supporting the “enabling environment” for Inj AS uptake including advocacy amongst key stakeholders and developing a strategy for roll-out at the facility level.

We consider the progress made under each of these below as well as other broader challenges that have impacted Inj AS uptake in countries.

Health worker training

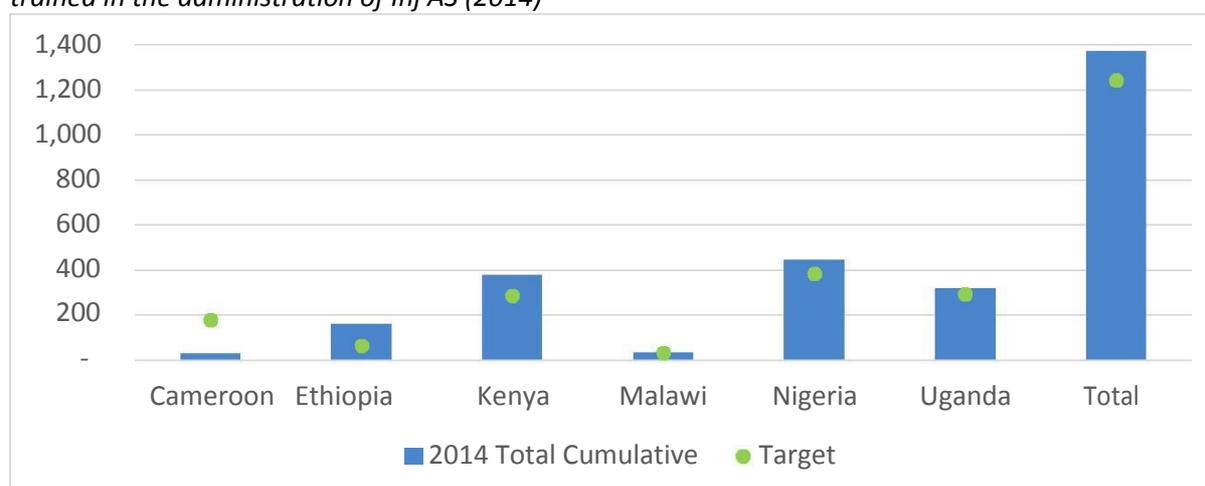
Substantial progress has been made in terms of designing and implementing health worker trainings in the use of Inj AS as part of training for severe malaria case management. In particular:

- Training modules have been designed and developed in collaboration with country NMCPs. All six countries now have case management training materials aligned with the WHO guidelines on administration of Inj AS, including on dosing specifications for pregnant women and children under 20kg. We understand from MMV that

training materials have also been used outside of the six ISMO project countries in Namibia, South Africa, Zambia, DRC and Cape Verde.

- Trainings have been delivered through a Training of Trainers approach, and have exceeded the project target of reaching 1,243 health facilities with at least one health worker trained. By the end of 2014, the number of health facilities with at least one health worker trained had reached 1,371: 13% higher than the target. Some further trainings were conducted in 2015 – mostly in Cameroon where training only commenced in September 2014 after the MoH made the decision to postpone roll-out until the first (Global Fund) delivery in August²⁶ – so the final result will be higher still. The number of facilities trained by the end of 2014 is presented by country in Figure 3.8.

Figure 3.8: Number of secondary and tertiary health facilities with at least one health worker trained in the administration of Inj AS (2014)



Source: 2014 Annual Report (supporting excel)

We have examined the experience with health worker trainings in Kenya and Uganda in more detail through our country visits during the course of this evaluation. Our main findings are as follows:

- **There has been comprehensive support from CHAI in the design and delivery of the trainings, with positive results.** In Kenya and Uganda, CHAI has supported trainings through (i) curriculum development; (ii) planning and delivery of training to region-level trainers (typically Ministry of Health (MoH)/ NMCP staff); (iii) supervising trainings being delivered at the region and health facility level; and (iv) follow up supervision of health workers in administering Inj AS at the facility level (though less so in Kenya where counties assume this responsibility). CHAI's support has also included the production and distribution of job aides. We present our findings from

²⁶ 2014 Semi-Annual Report, p.13

site visits in Kenya and Uganda on the availability of these aides to health workers in Annex 5.

- **The Training of Trainers approach has been cost-effective, though not always delivered to a high standard.** The Training of Trainers approach was reported to have been very effective in reaching large numbers of workers from a broad range of facilities within a limited budget. There is evidence to suggest that trainings have succeeded in improving Inj AS uptake and health worker practice (Box 3.2). However, our facility visits found evidence that some trainings had been cut short to focus on re-constitution of Inj AS while excluding the other aspects of the approved training curriculum (as supported by CHAI), including: epidemiology, diagnosis, follow up, communication with patients, stock needs and data compilation. The extent to which this has occurred is unknown. Country stakeholders generally agreed that, while a more rigorous approach to training may have been more effective, the chosen method was the best choice subject to time and budget constraints.

Box 3.2: Effectiveness of severe malaria management training in Uganda

Between May and July 2014, CHAI coordinated trainings on severe malaria management using Inj AS at 352 health facilities in Uganda, reaching 1,914 health workers. Between December 2014 and March 2015 CHAI coordinated support supervisions and mentorship in all the 352 facilities. During these follow-up visits the CHAI and NMCP teams administered health worker tests on the management of severe malaria, including how to properly administer Inj AS. Results indicate that the training was effective in increasing health worker knowledge of severe malaria management: average test scores increased from 42% to 69% after training.

There is also some evidence that transmission of training within facilities has been taking place. Health workers who had not received training themselves, but whose colleagues had been trained still scored higher than the baseline pre-training average (61% vs 42%): though some improvements over time may have occurred in the absence of training as health workers became more familiar with using Inj AS.

Source: CHAI (2015): Report on the Severe Malaria Support Supervision for the HC IVs and Hospitals (based on survey findings).

- **There is a recognised need for greater supervision of health workers following training sessions to ensure that Inj AS is being properly administered.** This is linked to the finding in both Kenya and Uganda that Inj AS is being widely misused for uncomplicated cases of malaria. This appears to have occurred for a number of reasons, including:²⁷
 - clinician's preference for showing results as quickly as possible (and using Inj AS as opposed to other treatments to achieve this);

²⁷ The incentives are however thought to be different in the private sector, where there is a preference to continue treatment with quinine, which requires patients to stay for longer periods in hospital and therefore incur higher charges.

- uncertainty on the diagnosis of severe malaria and a preference to over-subscribe treatment for these cases with Inj AS rather than under-subscribe treatment with Artemisinin-based Combination Therapies (ACTs), particularly as the risks of under-subscribing treatment could be fatal;
 - unavailability of ACTs, where Inj AS has been used as an alternative treatment;
 - widespread use of Inj AS in times of epidemic as health workers seek to control the disease using the most effective mechanisms available; and
 - patient demand for Inj AS, stemming from the view that an injection is more effective than tablets.
- **Trainings were started prematurely in some countries.** Feedback from our in-country interviews suggested that training activities had been timed well to coincide with the roll-out of Inj AS in Kenya and Uganda (though in Uganda trainings supported roll-out of Inj AS provided by the Global Fund rather than the ISMO project itself). Even though trainings in Uganda preceded the first ISMO delivery, Inj AS supplies provided by the Global Fund had already reached most facilities. However, as noted in the 2014 ISMO Annual Report, trainings in Nigeria started in 2013 before any significant volumes of Inj AS had arrived. By the time of the first ISMO delivery in September 2014 additional refresher courses were required.

Despite some of the challenges noted above, there was unanimous feedback during our country visits that health worker trainings provided by the project have been much valued and regarded as highly catalytic in supporting the uptake of Inj AS.

Other in-country support

Aside from the aforementioned support for training material development and delivery, CHAI has been an active member of the various technical working groups concerned with severe malaria and case management of malaria.

In Kenya this has included attending the monthly meetings of the Malaria Case Management Technical Working Group (comprised of KEMSA, Management Sciences for Health (MSH), HMIS and PMI) and its Drugs Management Sub-Committee. In Uganda, this has included attending meetings of five technical working groups in case management, Monitoring and Evaluation (M&E), Behaviour Change Communication (BCC), malaria and pregnancy, and vector control. CHAI's inputs across these groups has been focused on quantification, forecasting and procurement planning of Inj AS needs, but has also allowed CHAI to facilitate discussions with other donors operating in malaria (particularly PMI) to fill gaps in country need. CHAI's involvement in these groups is thought to have aided collaboration between stakeholders, and has been well received by the Kenyan and Ugandan NMCP units.

CHAI is also engaging through the Technical Working Groups to advocate for and push forward plans for a QoC survey focusing on inpatient care in Kenya. The survey would allow cases, treatments and patient outcomes for inpatients to be monitored and reported: including for severe malaria. Current inpatient reporting rates through HMIS are typically very low: around 12%, so a bi-annual survey would provide valuable information to allow the country to more accurately monitor inpatient health services. This activity has again been conducted alongside the Kenyan NMCP, and CHAI's support has been widely appreciated.

As such, CHAI's support to the NMCP units and malaria technical working groups in the planning, delivery and supervision of trainings, as well as in the quantification, forecasting and procurement planning of Inj AS needs has been extremely useful and widely appreciated by country stakeholders. CHAI is also making efforts to support countries incorporate Inj AS into their regular supervision schedules, and improve quantification and M&E through improved country data collection mechanisms, however, these aspects remain as key challenges to the effective uptake and proper administration of Inj AS in future.

Summary findings:

- Planned trainings under the project have been delivered in all countries except Cameroon, with the number of trainings exceeding targets in some countries.
- Trainings have been generally successful in reaching a large number of health workers, and formal and anecdotal evidence suggests that they have been effective in improving Inj AS uptake and health worker practice, though the quality of training has been variable. However misuse and overuse of Inj AS is an issue. Continued follow-up supervision of health workers is necessary to ensure that Inj AS is being properly administered.
- The project is currently supporting country data systems via its M&E activities and assistance in the development of in-patient QoC surveys in Kenya and Uganda. Support to quantification and coordination committees has been effective and well received. However both of these aspects are key challenges at the country level.
- The overall “demand creation” work of the project in countries has been much valued and is viewed as highly catalytic in supporting uptake of Inj AS.

4. INJ AS EVALUATION DIMENSION 3: RESULTS

Our evaluation question is as follows:

Q5: Is the project on track to achieve the intended public health and market impact?

The project plan outlines the public health and market impact related goals and targets, as presented in the table below.

Table 4.1: Project public health and market impacts

Project goal (public health impact)	To increase the proportion of severe malaria cases treated by Inj AS/Quinine
Project outcome (market impact)	Creation of a stable market for quality assured Inj AS

We consider the progress made on each in turn below.

4.1. Public health impact

At the outset we note the challenges in measuring the public health impact of the project to date – not only due to the standard issues with time lags between project activities and impacts and the issues with “attribution” to UNITAID funding given the role of a number of other stakeholders in facilitating project results (e.g. country governments, other donors, etc.) – but also because of the challenges with data collection. As such, the project goal (relating to public health impact) of “reduce case fatality rates for severe malaria” was changed to “proportion of severe malaria cases treated by Inj AS/ quinine in the previous month” in 2014.

However, it is difficult for this evaluation to present and assess the progress to date as data on the revised goal has also not been available and has not been reported on to date (i.e. as of the 2014 Annual Report which has been made available to this evaluation).

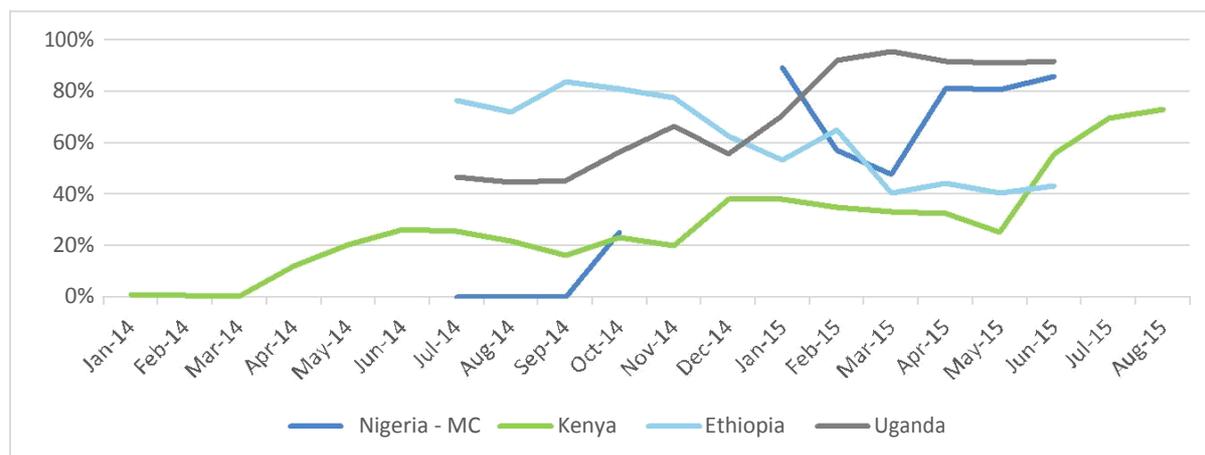
During our country visits to Kenya and Uganda, we have been able to access some data on the revised project goal for four of the six project countries, as presented in Figure 4.2 below.²⁸ As can be seen from the figure:

- There have been improvements in increasing the proportion of treatments using Inj AS as compared to quinine, most notably in Uganda and Nigeria (data for 3 states only), but also in Kenya. Note that data for Nigeria is not available during November and December 2014 due to health worker strikes.
- However, the opposite trend has been observed in Ethiopia. Although early deliveries from PMI had elevated Inj AS usage in Ethiopia to around 80% by mid-2014, the proportion of severe malaria cases treated with Inj AS fell to around 40% in

²⁸ Data is not yet available for Cameroon or Malawi.

March to June 2015.²⁹ The reversal in Ethiopia reflects facility-level stock-outs caused by a structural shift in procurement channel from RHB to the central PFSA. We understand that the Malaria Consortium team has been working with PFSA and RHB to improve the transition and reduce stock outs by reporting low stock levels identified during the monitoring and support supervision period to PFSA.

Figure 4.2: Percentage of severe malaria cases treated with Inj AS



Source: Kenya – CHAI estimates based on HMIS commodities dispensed, for endemic and epidemic-prone regions only; Ethiopia, Nigeria, Uganda – MC estimates derived from 30 facilities per country

In-country feedback strongly supported the view that these results have been driven at least partly by the ISMO project. Even in countries where only a small amount of commodities have been delivered, stakeholders emphasised the importance of severe malaria management trainings in increasing usage and demand for Inj AS at facility level. In Kenya, for example, early procurements made by the Government were reported to have been under-used to the point that their shelf-life was almost exhausted because health workers had not yet been trained to use Inj AS.

The above notwithstanding, we note that the public health impact of the ISMO project has not been as large as intended by this stage of project implementation, primarily due to procurement delays. These delays also imply that the project’s public health impact will not be as large as intended, given that the budgeted procurements will not be completed by the end of the project.

No reliable data on the outcomes of patients treated with Inj AS under the project is available, though the clinical studies which provided motivation for the project indicate that artesunate is significantly more effective than quinine at reducing mortality. Dorndorp et al. (2010) found that children treated with artesunate as part of the AQUAMAT clinical trial had 22.5% lower mortality than those treated with quinine, while the SEAQUAMAT study group

²⁹ Most severe malaria cases not treated with Inj AS receive quinine. This is the case even when quinine is no longer procured and supplied to facilities by national level systems, since facilities and regional governments are able to buy quinine directly from private suppliers. During Inj AS stock-outs, patients may also be asked to buy quinine themselves.

(2005) reported 34.7% lower mortality.^{30,31} Both studies also reported that quinine was associated with higher rates of hypoglycaemia. No significant differences in recovery times were observed. Therefore, we should expect that the project has improved patient outcomes through increased use of Inj AS, though quantifying this impact is not possible without reliable data.

Finally, Box 4.1 provides some qualitative information on “broader” public health impacts in terms of reduced time for treatment, etc., based on (mostly anecdotal) feedback received during country visits.

Box 4.1: Anecdotal information on broader public health impacts

Implementers and health workers interviewed during country visits gave highly positive feedback on the use of Inj AS. For example, the Head Clinician of a hospital in Uganda reported that artesunate “had done wonders” in improving patient outcomes. Broader feedback suggested that Inj AS is improving patient outcomes in the following ways:

- **Recovery times.** The most commonly reported advantage over quinine was the speed of patient improvement. Unconscious patients have been reported to become ambulatory within an hour of being administered with artesunate.
- **Burden on staff.** Artesunate requires less monitoring than quinine when being administered intravenously – reducing the burden on health workers’ time. It can also be given instantly as an intra-muscular injection when intravenous delivery is not an option and also as a pre-referral treatment.
- **In-patient stay duration.** Since artesunate requires little surveillance, some health workers have reported that their patients are able to travel home between doses (administered once every 12 hours – whereas quinine is administered every 8 hours) rather than be admitted as an in-patient.
- **Cost.** Patients are sometimes able to avoid hospital admittance (and the associated charges) and treatment with artesunate also typically requires fewer consumables as well as less health worker attention. This reduces the costs borne by facilities and patient charges. Stakeholders were divided on whether these benefits alone compensate for the commodity price differential to quinine.
- **Satisfaction with Inj AS.** Stakeholder consultations and anecdotal evidence almost all confirm that Inj AS is a superior product to quinine for the treatment of severe malaria. Partners confirm that staff acceptance of the drug is high and receives an extremely good reception by both health workers and patients.

³⁰ Dondorp et al. (2010), Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial

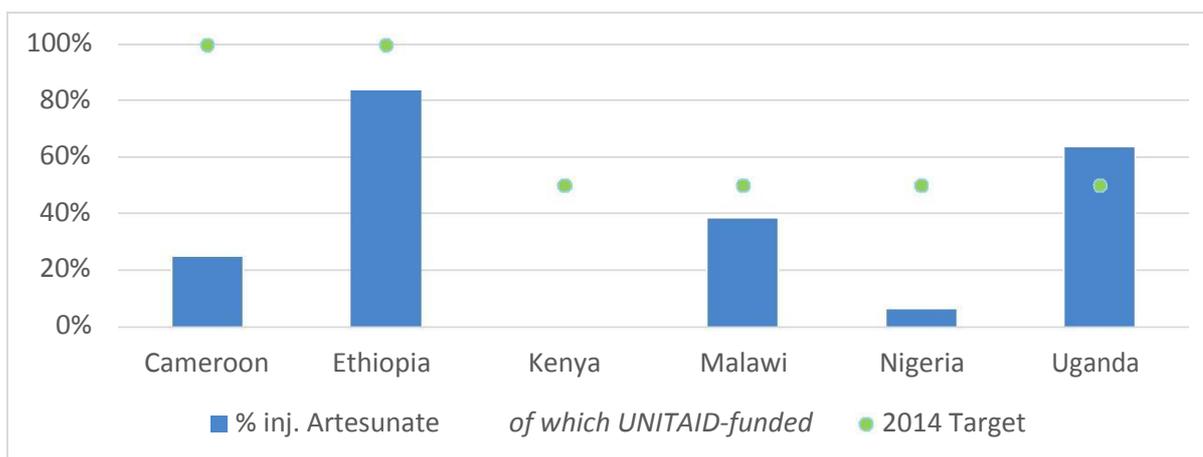
³¹ South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group (2005), Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial

4.2. Market impact

As noted previously, the intended market impact of the project is represented by the project outcome of “creation of a stable market for quality assured Inj AS”. As per the logframe, this is measured by two key indicators:

- *Percentage reduction in median price of prequalified Inj AS* – As noted in Section 3.2, the reduction in price has not been as much as anticipated, but it is the lowest price being made amongst the major buyers (PMI, UNICEF).
- *Percentage of annual severe malaria treatments procured for the public sector that are Inj AS in the targeted countries* – The target for this indicator is 90% by 2016 and there have been some improvements to date from 16% in 2013 to 62% in 2014 (Figure 4.3 provides the details by country). However it is noted that only some of these procurements are through UNITAID support.

Figure 4.3: Percentage of annual severe malaria treatments procured for the public sector that are Inj AS, 2014



As such, there has been some progress towards the intended market impact of the project, although it is difficult to reach a clear conclusion without a clear definition of the price-related indicator and lack of a mid-term milestone on percentage of public procurements on Inj AS.

More generally, the creation of a “stable market” is critically dependant on the second supplier for Inj AS coming into the market, where we note that the project is considerably delayed from plans. However we note that this is highly likely to be achieved in the coming months (with dossier submission in December 2015 and availability for procurement by September 2016), thereby implying that the project is near achievement of its intended market impact.

Summary findings:

- The project has demonstrated progress towards its revised goal of increasing the proportion of severe malaria cases treated by Inj AS/Quinine in Kenya, Nigeria and Uganda (and thus potential public health impact). In Ethiopia severe distribution obstacles have reversed strong early progress. Results for Cameroon and Malawi have not been available to the evaluation team.
- In terms of market impact, delays in procurement and IPCA product prequalification have implied that the planned impact is not as much and as soon as intended (and will not be achieved by project end in June 2016). However with IPCA prequalification submission planned for in the coming months, the potential for achieving the intended market impact over a slightly longer timeframe is high.

5. INJ AS EVALUATION DIMENSION 4: SUSTAINABILITY

A key issue under the evaluation is to examine the potential for sustainability of the project after the UNITAID funding has come to an end. Our evaluation question is as follows:

Q6: To what extent are project activities likely to be sustained after UNITAID funding has come to an end?

We examine:

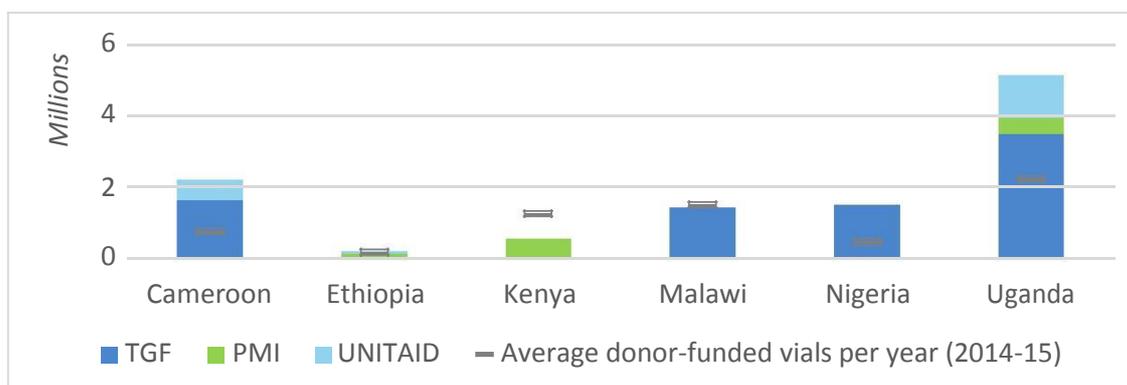
- the potential for sustainability of project results in terms of continued funding for Inj AS in implementation countries (Section 5.1); and
- the sustainability of ISMO training activities (Section 5.2).

5.1. Potential for sustainability of Inj AS procurement

Discussions with global and country level stakeholders on the potential for Inj AS to continue to be funded and used in implementation countries after project-end have suggested the following:

- **Increasing domestic funding for the procurement of Inj AS will be a major challenge** given competing demands of other health and non-health priorities. Some national and regional governments have made small procurements thus far (e.g. Kenya, Nigeria, Uganda), but are not willing to meet their full requirement.
- There is **significant potential for other donors to assume the costs of procuring Inj AS once UNITAID's support ceases, although this varies by country.** Figure 5.1 shows Inj AS quantities committed for 2016 by the Global Fund and PMI, in addition to those currently forecast to be delivered under the ISMO project in the first half of 2016. The chart also shows the average quantities delivered per year across 2014-15 as a rough proxy of country need (although we appreciate this is fairly understated). Based on these forecasts, Cameroon, Nigeria and Uganda in particular appear to have ample funding for Inj AS committed in the near future. Kenya, on the other hand, does not yet have commitments in place to meet its full need in 2016.

Figure 5.1: Forecast Inj AS donor procurement (vials) in 2016 - by country and funder



Source: MMV No-Cost Extension request – October 2015

We provide more detail on these contrasting cases of the potential for sustainability for Kenya and Uganda in Box 5.1 below.

Box 5.1: Potential sustainability of Inj AS funding in Kenya and Uganda

High-risk example - Kenya

Kenya's quantification committee has estimated its total Inj AS need at 1.8 million vials per year and the country's central distribution agency (KEMSA) has 780,000 vials in stock as of September 2015 (i.e. approximately 5 months' consumption). No further UNITAID-funded procurements are planned before the end of the ISMO project.

However, despite PMI's commitment to supply 540,000 vials in January 2016 and expectation to contribute another 540,000 in 2017 (to be confirmed under PMI's next Malaria Operational Plan), there is currently a shortfall in donor funding available to meet Kenya's need from mid-2016 to late 2017. In the event that UNITAID support does end in June 2016, consultations suggested that PMI may scale-up its support by a small amount, and the Government of Kenya could allocate a small amount of its Global Fund counter-funding allocation. However, it is likely that a gap will remain until the country can secure support for Inj AS through the next Global Fund funding cycle (no Inj AS has yet been procured for Kenya via the Global Fund) starting in around mid-2017, when deliveries might be expected to arrive in late 2017 – early 2018.

In the event that donor support for Inj AS does not meet country needs, counties would be responsible for procuring the commodity using their existing health budgets. However, national, county and facility level feedback strongly suggests that many counties will return to procuring quinine and much of the progress of the ISMO project in training health workers and embedding the use of Inj AS at the facility level could be lost.

Low-risk example – Uganda

Uganda's Quantification and Procurement Planning Unit (QPPU) has estimated that 3.8 million vials will be needed in 2016 for public and Private Not for Profit (PNFP) facilities.

Inj AS commitments for 2016 currently exceed this requirement:

- **UNITAID:** MMV forecasts that it will deliver 1,200,000 million vials in the first half of 2016
- **Global Fund:** 3,400,000 vials committed
- **PMI:** 450,000 vials committed to be delivered to PNFP facilities

The supply line for 2016 is therefore in a healthy state, and excess commitments may also cover early 2017. Moreover, although some stakeholders expressed concern that the Government of Uganda would not continue to buy Inj AS after dedicated funding from UNITAID was withdrawn, NMCP representatives suggested that the country would prioritise the procurement of Inj AS through a reallocation of Government and Global Fund budgets if necessary. As such, there is a strong likelihood that the procurement of Inj AS in the country will be sustained following UNITAID's support.

As such:

- **There is a heavy reliance on the Global Fund** to sustain procurement of Inj AS after project-end. PMI, the only other major donor expected to be active in ISMO countries, is only likely to commit relatively small quantities in years to come. PMI is also constrained to only supply PNFPs in Uganda, where public facilities will be highly dependent on the Global Fund.
- **Gaps may occur where Global Fund funding cycles do not align with the end of UNTAID support.** This is especially likely in the case of Kenya, where Global Fund support is not expected to be available until late 2017 (as noted above in Box 5.1).
- **All countries have, or are expected to include Inj AS in their concept notes to the Global Fund.** CHAI and MC have provided technical support to assist NMCPs in Cameroon, Malawi, Uganda, Nigeria, and Ethiopia to include Inj AS in their concept note submissions. In-country consultations have confirmed that Kenya is likely to apply for Inj AS funding after mid-2017.

Overall, there is good potential for sustained funding for Inj AS in the project countries. However, timing the end of UNTAID support to align with Global Fund funding cycles has emerged as a key issue.

In the event that donor funding is not available in the short-term after project-end, some country stakeholders report a risk that countries will revert back to using quinine due to its lower commodity cost: especially in countries where the responsibility for procurement is devolved to the state/county level. This is despite a general recognition that Inj AS is more effective and the total treatment costs (including costs of inpatient duration, commodity and other non-commodity costs) for Inj AS and quinine are similar.³² There is a real risk, therefore, that key project results could be eroded if support is not successfully sustained after project-close.

5.2. Sustainability of ISMO training activities

As noted above, the ISMO project has resulted in the widespread training of health workers in the use of Inj AS as the first line treatment of severe malaria. This has prepared countries to continue to use Inj AS in the short-, medium- and longer-term, but this will be dependent on the continued procurement of Inj AS at the national level so as to ensure that health workers continue to use and remain familiar with its administration. Sustainability will also be dependent on the continued supervision of health workers by countries, a critical requirement to ensure appropriate use of Inj AS. Field visits confirmed that the countries

³²A study of AQUAMAT trial data by Yoel Lubell et al. (2011) found that the mean cost of treating severe malaria was similar for children treated with quinine (US\$ 63.5) and artesunate (US\$ 66.5). It should be noted that artesunate used during the trial cost around US\$ 1.06 per 60mg vial, whereas the ISMO project buys at US\$ 1.42.

are well placed to integrate the supervision of Inj AS into regular supervision of other health services, and there are plans for the ISMO implementing partners to support this process.

Summary findings:

- Plans for transition from ISMO vary from country to country, however there is evidence indicating that countries are increasingly prioritising Inj AS in partner funding applications, notably the Global Fund. Importantly though, Global Fund funding cycles pose a challenge and may create a gap in funding and continuous access to Inj AS if the ISMO project comes to an end in mid-2016.

6. EVALUATION OF IR AS PROJECT COMPONENT

This section focuses on a review of the Ir AS component of the project. We have structured a single comprehensive question to capture the performance on this component:

Q7: To what extent is the project on track to achieve its goal of promoting access to life-saving quality-assured intra-rectal artesunate for pre-referral treatment of severe malaria?

We have assessed the project performance to date with respect to the Ir AS specific goal to promote *“access to life-saving quality-assured intra-rectal artesunate for pre-referral treatment of severe malaria”*. Our assessment focuses on the two outputs defined under the project log-frame. Namely:

1. Whether the project has been instrumental in accelerating the WHO prequalification of an Ir AS product.
2. Whether research activities have generated relevant evidence that will help improve the use of Ir AS in low resource settings.

We consider each of these in turn below.

6.1. Progress towards WHO prequalification of Ir AS

6.1.1. Progress to date

Our review suggests that the project has made good progress towards its intended output of making affordable quality-assured Ir AS available on the market. Two manufacturers (Cipla and Strides Arcolab) were selected for support towards submission of an Ir AS dossier for WHO prequalification. At the time of writing, Cipla has successfully demonstrated bioequivalence against the comparator TDR product, Strides plan to receive bioequivalence read-out before December and both manufacturers are expected to submit their dossiers in December 2015. This is later than the Q3 2015 submission anticipated in the project plan due to early delays with transferring the WHO Special Programme for Research and Training in Tropical Diseases (WHO TDR) dossier to MMV and securing access to data for a comparator product, however the delay is not substantial. Compared to the history of little to no advancements in the previous decade, current progress represents a clear and substantial success.

6.1.2. Role and contribution of MMV

Feedback from manufacturers on MMV’s support has been strongly positive. For example, one stakeholder reported that their partnership with MMV *“has been one of the most refreshing we have been involved in”* and *“the kind of support we got from MMV was amazing”*. Consultation feedback also strongly indicated that MMV’s support to the two manufacturers has been instrumental in accelerating their progress. One manufacturer

estimated that it would have taken another two years to submit a dossier without MMV's support.

The following activities were highlighted as particularly valuable to accelerating Cipla and Strides Arcolab's progress towards prequalification:

- **WHO TDR dossier transfer.** MMV negotiated the transfer of an Ir AS dossier from WHO TDR with a full underlying clinical trial database which has enabled considerable savings in time and money.
- **Securing access to a comparator product.** To avoid having to generate completely new clinical test data, Strides Arcolab and Cipla preferred to demonstrate bioequivalence against the WHO TDR product which underwent clinical tests between 1999 and 2003. As part of this process, it was necessary to test the new products against a comparator capsule, and to demonstrate that the comparator capsule was representative of the product used in WHO TDR's original clinical trials. Securing access to information held by Catalent - the comparator capsule manufacturer, was a key challenge during this process. Catalent was initially unwilling to share necessary manufacturing information as it might wish to sell the information to manufacturers interested in competing with Strides and Cipla. MMV reached an agreement with Catalent in December 2014 – after a 4 month delay.
- **Facilitating WHO collaboration.** Manufacturers reported that a particularly valuable aspect of MMV's technical support has been their ability to arrange meetings with WHO prequalification authorities whenever clarifications on requirements and expectations are needed. Having a partner based in Geneva was noted as particularly helpful. Discussions with WHO facilitated by MMV have indicated that the approval process may be expedited for both Ir AS dossiers.

6.1.3. Potential for impact

The decision to support two manufacturers through prequalification rather than just one has been successful in de-risking this aspect of the ISMO project: if one of the two manufacturers were to experience a major delay, the other would still be able to progress. Furthermore, in the event that both Cipla and Strides Arcolab dossiers pass prequalification, two quality-assured suppliers will be able to sell to the donor-funded market: preventing a monopoly supplier situation. This achievement would have the dual benefits of making quality-assured Ir AS less prone to high monopoly pricing, and long lead-times and stock outs. We further note that pricing agreements put in place as a pre-condition for MMV support should prevent either Cipla or Strides Arcolab from charging in excess of a mutually agreed rate. In this respect the project is currently on track to achieve its goal of making affordable quality-assured Ir AS available on the market.

6.2. Market research progress

Both activities under the market research workstream on potential demand for prequalified Ir AS have been completed: (i) country situation assessments on policy change requirements for country roll-out were carried out by Health-E-Net in 20 high-burden countries; and (ii) an epidemiological modelling of need was conducted by William Davidson Institute of the University of Michigan. Consultations have indicated that, so far, dissemination of results has been limited, though further dissemination is expected closer to the first Ir AS prequalification.

6.3. Operational research progress

In this section we report on the status of the four operational research pieces commissioned under Ir AS Output 2: Implementation research on the interaction of Inj AS with Ir AS in community case management. We note that each research activity is currently being implemented, though some are experiencing substantial delays – mainly due to extended ethical review processes. The following table presents our understanding of the current state of progress for each research piece, as informed by consultation with Malaria Consortium. The assessment of delay is against timelines laid down in the original workplan.

Table 6.1: Operational research progress summary

Research activity	Country	Status (as of early October 2015)	Approx. delay (months)
1. Define the potential interplay between Inj AS and Ir AS for pre-referral treatment of severe malaria in countries	Ethiopia	Analysis and report writing (<i>final draft-stage</i>)	15
	Uganda		
2. Investigate appropriate expectation for intramuscular use of Inj AS as a community-level tool to address severe malaria and assess risks that need to be considered and mitigated if such an approach were to be put forward	Ethiopia	Internal review	12
	Nigeria - MC	Internal review	12
	Uganda	Analysis and report writing - <i>delayed in particular by a request during ethics review to make a full Knowledge-Attitudes-Practice study, when proposal was for Knowledge study only.</i>	12
3. Explore how the presence of Inj As and Ir AS might encourage inappropriate monotherapy use for uncomplicated malaria and estimate how large the potential risk is in order to develop mitigation strategies	Ethiopia	Analysis and report writing	18
	Uganda	Analysis and report writing	18

Research activity	Country	Status (as of early October 2015)	Approx. delay (months)
4. Document experiences and assess best practices in capacity building that appear to be associated with high acceptance and use of Inj AS among hospital-based health worker	Nigeria - MC	Responding to ethics review comments – <i>Research was initially intended to cover all 13 ISMO states, but scope was reduced to the 3 states covered by Malaria Consortium.</i>	12
	Uganda	Awaiting ethics review feedback	12

It is not clear what actions Malaria Consortium could have taken to expedite the ethics review processes responsible for the majority of delays, though this experience underlines the need to incorporate potential ethics review delays into project planning. Malaria Consortium has reported that it has been proceeding with preparatory activities while awaiting ethical review feedback.

Summary findings:

- The project is currently on track to achieve its goal of making affordable quality-assured Ir AS available on the market.
- Support to Cipla and Strides Arcolab has been instrumental in accelerating WHO-prequalification of an Ir AS product. Although progress has been slower than initially anticipated, both manufacturers are currently expecting to submit a dossier in December 2015.
- Market research activities have proceeded largely as planned, though dissemination of results has been limited to-date. Operational research activities have been heavily delayed by ethical review processes.

7. LESSONS LEARNED AND RECOMMENDATIONS

This final section presents lessons learned from the project to date and suggests recommendations going forward.

7.1. Lessons learned

We highlight the following lessons learned based on the experience of the ISMO project thus far:

The project design of supporting both the demand and supply side of the Inj AS market is an effective approach

Global and country-level stakeholders have strongly echoed the importance of the project's demand-creation activities for Inj AS (i.e. updating treatment guidelines, healthworker training, quantification assistance etc.) in tandem with its supply-side intervention (which is a recognised unique focus of UNITAID). This has been viewed as an effective coordinated response to the market challenges impeding increased uptake of Inj AS by countries.

An early and more strategic approach to engaging with Guilin may have yielded more positive results

The project has experienced a protracted price negotiation with Guilin, with consequent transaction costs, also on account of delayed establishment of market competition. Although UNITAID and MMV made strong efforts on price negotiation, Guilin had little incentive to lower its offer after the project's procurement volumes had been committed and market entry from IPCA was expected imminently.

As such, an important lesson is the need for an early discussion with Guilin during proposal development and finalisation, with the possibility of some agreement or understanding on pricing. More generally, a more strategic and pre-planned approach to engaging with Guilin should have been considered, with options such as pooled procurement considered early on. Our discussions with Guilin also indicated that they would have preferred to be involved during the initial project discussions and to have reached a pricing agreement for the project as a whole at the outset.

This lesson has wider implications for UNITAID given that many of the markets where it intervenes have a monopolistic supplier – however, an appropriate approach would be highly contingent on the specifics of each market and product or compound in question.

Supporting more than one Inj AS generic manufacturer may have reduced risks

MMV's support to IPCA has been instrumental in accelerating its progress towards prequalification, yet the decision to support just one manufacturer until recently has left the project highly vulnerable to delays. IPCA is not now expected to be able to supply Inj AS to

the donor-funded market until at least Q3 2016. Supporting a second Inj AS manufacturer from early on in the project may have helped to reduce these risks, although this would also have required greater financial resources.

Given the delays experienced so far, and with the possibility of further delays to come, this may have been a more prudent measure; especially in light of the importance of introducing a new manufacturer to creating a stable market for quality assured Inj AS.

Despite initial concerns, Missionpharma has performed well, although the procurement approach has not necessarily been as cost effective as intended

Initial concerns with the selection of Missionpharma, while possibly justified, have not materialised. Some initial confusion with regards to the division of responsibilities between Missionpharma and project implementers has highlighted the importance of establishing clearly defined roles from the outset: which has now been done.

However, the decision to waive Missionpharma's in-country support has proved costly in Kenya (estimated additional costs of US\$ 54,063.38), where the complexity of the waiver process obliged CHAI to hire a local clearing agent. Although closer communication with in-country implementers could have flagged this obstacle earlier on, we recognise that the problem was technical in nature and particular to Kenya. It should, however, serve as a lesson for procurement activities in Kenya under this and future projects.

Planned timelines have not always been realistic and there is a case for stronger risk/contingency planning

Although project implementation has been delayed by factors which could not all have been necessarily predicted, planned timelines have been optimistic in several areas. More generally, it is questioned whether a three year timeframe for UNITAID projects may be feasible for the types of market shaping activities targeted by the project.

The timeframe for bringing a new Inj AS supplier to the market has been particularly ambitious. It may therefore have been more realistic to set a longer project lifetime including contingency for probable project delays. Longer timelines could also have been anticipated for finalising country and region-level MoUs.

For the Ir AS project component, it is not unusual for ethical review processes to cause significantly delays, with a clear lesson to apply more caution and conservatism while planning project timeframes.

Data challenges pose severe constraints for planning and measurement of results

Due to the inconsistent and incomplete state of in-patient records in the ISMO countries, quantification has been based largely on historic consumption rates. This risks perpetuating situations of over or under supply, and makes it more difficult to react to changing trends in

disease-burden. Poor HMIS data also implies challenges in measuring the public health impact of the use of Inj AS.

The absence of sufficient data to permit confident quantification and monitoring underscores the importance of activities currently being carried out by CHAI in Kenya and Uganda to support nation-wide in-patient Quality of Care surveys.

The potential for sustainability of Inj AS following UNITAID funding varies by country and requires careful planning and coordination

Our review has shown that the potential for sustainability of Inj AS procurements is high, although this varies by country. There are some risks with regard to timing of UNITAID procurements and continuation through Global Fund and PMI funding, which requires effective sustainability planning and coordination.

7.2. Recommendations

Based on the evaluation findings and lessons learned, we provide the following recommendations for the ISMO project going forward.

Given the timeline for this evaluation, with around 6-7 months remaining for project completion, our first recommendation relates to a project extension, focusing on the priority areas and issues to consider for the extension. Thereafter, we provide some additional recommendations for the remaining term of the project as well as broader recommendations for UNITAID project planning and support more generally.

Recommendation 1: UNITAID and MMV should discuss and agree a clearly defined no-cost extension for the project

The delay in IPCA dossier submission for WHO prequalification has so far prevented achievement of the intended market impact relating to stable supply and reduced prices. However IPCA is currently very close to submitting its dossier in December 2015 and, following all necessary approvals, could be ready to supply Inj AS around September 2016.

As such, there is a fairly strong case to extend the project to ensure successful pre-qualification and market entry of IPCA and manage a competitive tender for improved market outcomes, despite the general non-desirability of project extensions. Ongoing support from the UNITAID project would help ensure that these developments are “seen through to the end” and the project is successful in improving market conditions for Inj AS supply. Further, an extension would help to ensure ongoing support for Inj AS procurements in country and better planning for alignment with Global Fund funding rounds.

We note that MMV has submitted a no-cost extension request to UNITAID in mid-October, and we are broadly supportive of their propositions, however make the following specific points for UNITAID’s attention as it looks to review and finalise a no-cost extension:

- First, our view is that the rationale for an extension is predicated primarily on how close IPCA is to dossier submission, and hence the **primary focus of the extension period activities should be to ensure the necessary technical and facilitating support is provided to IPCA** to complete its pre-qualification and make its product available in the market. Consultations with IPCA have not suggested any specific need different from what MMV has been providing thus far, however they have highlighted the value in MMV ensuring that the WHO pre-qualification process itself takes place in a timely manner.
- Second, there **may also be merit in providing some support to a second generic manufacturer**, not only to balance any further risks for the IPCA submission, but also to set in motion the longer term objectives of broader competition.
- Third, careful planning and coordination is required with country governments and other donors to ensure the successful transition of UNITAID funding to other sources. In particular, while UNITAID’s role is not one of a “gap-filler” for other donor funding, given the early stage of uptake of Inj AS, it would be critical to ensure that the funding momentum is not lost for the project countries amidst Global Fund funding cycles. As such, **efforts need to be made to encourage greater country ownership and a country-specific approach is required to determine effective transition planning and extension support.**
- Fourth, in support of the objective of ensuring that Inj AS use is embedded in country policy and health systems, we see merit in continuing the in-country work on advocacy, quantification, trainings, M&E, etc. in the existing six ISMO project countries and possibly extending to other countries as well (e.g. DRC and other states in Nigeria as proposed in the MMV no-cost extension request), however would recommend that **a clear and strategic plan is developed in terms of specific types of support and countries to be extended/ added.** For example, a strategic assessment should be carried out to determine whether it makes sense to provide additional trainings for existing health facilities or to expand to new lower-level health facilities (as was suggested by some consultees in Kenya and Uganda) or to focus on supporting supervision of health workers. There are also some clear gaps in quantification and M&E capacity in countries which, in our view, represent critical areas for further technical assistance and support. Again, a country-specific approach would need to be adopted given varying country contexts and needs. **All planned support should be fully aligned with country national health plans and systems.**
- Finally, we would recommend that an approval for extension is based on **a clearly defined results framework** for the additional period of the project. This would entail:
 - Developing a smaller and more focused results framework that clearly maps intended outputs, outcomes and impacts of the extension activities.

- Identifying measurable indicators (for which data is available or a data collection plan is foreseen) and defining baselines, milestones and end of project targets.

Recommendation 2: Explore the possibility of expanded pooled procurement and further price negotiation for the planned 2016 procurement

The project could explore the possibility of pooling procurement across all key procurement partners including the Global Fund, PMI and UNICEF; and engage with Guilin for accessing reduced prices (possibly even based on some agreement for market sharing once other suppliers are on board – although we caveat this statement strongly as we have not been privy to the cost-based calculations impacting price and have not reviewed possible pricing and market scenarios). In support of an efficient procurement, we would recommend that:

- Planning for the procurement (along with other partners) commences early.
- Partners agree on acceptable pricing levels and roles and responsibilities in advance and do not engage in a lengthy price negotiation process.

Recommendation 3: Emphasise donor coordination of procurement and delivery of Inj AS

There is a case for the project to act as a coordinator for donor procurements, also to ensure the achievement of the sustainability objectives of the project. The project should ensure that there is adequate coordination at the country level and with Global Fund procurement in Geneva.

Recommendation 4: Focus on fast-tracking the prequalification process for Ir AS and explore new support to encourage demand creation for the product

The project has made good progress towards its intended outcome of making affordable quality-assured Ir AS available on the market, with Cipla and Strides Arcolab expected to submit their dossiers in December 2015. As suggested by the manufacturers, we recommend that MMV focus its support in the remaining project period on working with WHO to fast-track the prequalification process. Further, UNITAID may also explore the additional support to encourage uptake of Ir AS (e.g. through supporting training, advocacy and other demand creation activities), though we understand that this may be the subject of a separate project proposal.³³

³³ Although this has not been a focus of our evaluation, it has been noted during consultations in Kenya that the Ir AS roll-out has been the subject of recent Case Management Technical Working Group discussion. Although Ir AS is already recommended under Kenya’s guidelines, uptake has not been prioritised yet as attention is focused on filling the pipeline with Inj AS. The Government of Uganda has already been procuring small quantities of Ir AS and PMI is currently considering procurement support. In the event that Ir AS roll-out is included in a future UNITAID project, therefore, both countries would be receptive to support provided.

Recommendation 5: Ensure adequate emphasis is placed on improving M&E systems for data on the need for and use of Inj AS

Weak country HMIS and other data collection mechanisms has limited reporting under the ISMO project, and on severe malaria, case management and outcomes more generally. This lack of data has hindered both the ISMO project and the NMCP more generally in quantifying Inj AS needs, directing commodities to those areas most in need, and responding to issues where they arise (e.g. where other commodities are used instead of Inj AS or where patient outcomes are below expectations). As such, an important focus for UNITAID support in countries should be to improve M&E systems (e.g. through the QoC survey in Kenya) to ensure that this does not hamper implementation.

We do not have a clear view on whether UNITAID should fund this directly or support the work of other partners, given this is a higher-level strategy question for UNITAID. However we highlight that improved data collection and monitoring bears particular relevance given UNITAID's specific role in commodity market dynamics and the consequent need for better data to support planning and measurement of progress.

Recommendation 6: Consider and disseminate key country-level learnings and best practice.

Given the overall goal to encourage Inj AS uptake across countries, it would be useful to document key learnings and approaches from the six project countries to serve as guidance for other countries.

Recommendation 7: Broader recommendations to support improved UNITAID project planning and support

We provide some recommendations below to support improved UNITAID project planning and support, based on the lessons learned from the experience of the ISMO project design and implementation to date.

- Explore the potential for expedited proposal development, review and approval process to ensure that UNITAID's role in impacting commodity market dynamics is more catalytic and accelerated.
- Consider whether project timeframes may be extended from three to five years to allow for more realistic timelines for market-shaping activities.
- Ensure that projects have quality logframes or results frameworks, with clearly defined indicators that are "SMART", with baselines, interim milestones and final targets as well as detailed risk matrices and mitigation strategies.
- Consider if more simplified project implementation structures can be attained, with clear linkages between roles, responsibility and monitoring.

- Consider the experience gained across multiple projects in engaging with monopolistic suppliers and draw lessons for effective approaches to deliver results. Specifically, based on this project's experience, it is recommended that UNITAID aims to engage early with monopolistic suppliers and ascertain some agreement on pricing and supply in advance; as well as plan to support more than one supplier to bring their product to market (with a clear rationale for partner selection); however these approaches need to be assessed carefully for specific commodity market contexts and products.