



UNITAID

**END OF PROJECT EVALUATION OF THE CHAI PAEDIATRIC HIV/AIDS AND
INNOVATION IN PAEDIATRIC MARKET ACCESS (IPMA) PROJECTS**

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Final Report

Prepared by:

Cambridge Economic Policy Associates Ltd



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EXECUTIVE SUMMARY

Background

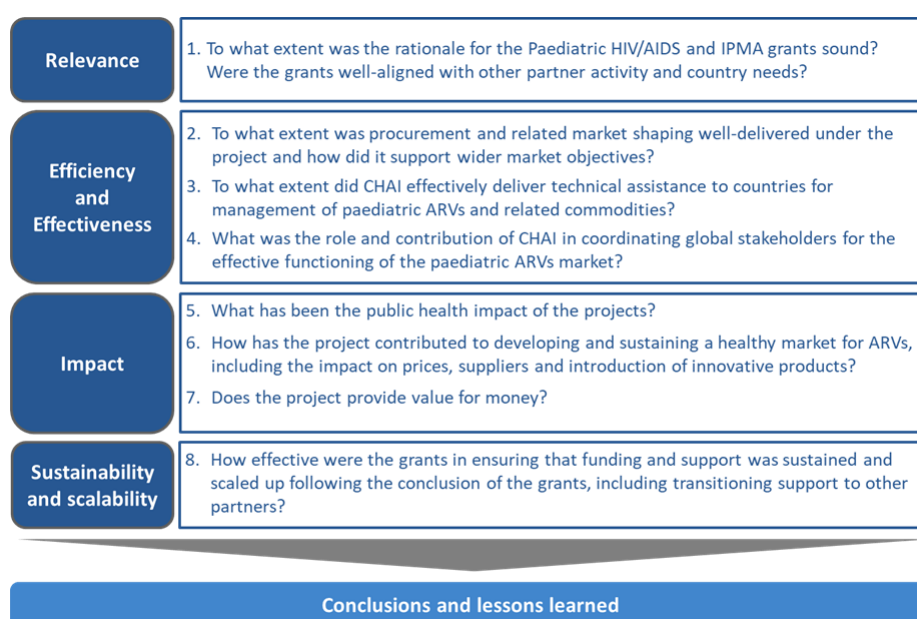
The Paediatric HIV/AIDS, and the subsequent Innovation in Paediatric Market Access (IPMA) projects were both funded by Unitaid and implemented by CHAI. Taken together, the projects aimed to strengthen the paediatric antiretroviral (ARV) market.¹

At the start of the Paediatric HIV/AIDS project, several market failures and supply chain issues had created a number of complexities and limitations. Quality, well-adapted ARVs specifically for children were not reliably available in resource constrained environments. Countries ordered paediatric ARVs sporadically and in small quantities, and suppliers often delayed filling orders until they had a minimum batch size. Until 2006, children living with HIV (CLHIV) were not considered a priority for case detection and treatment in many countries, partly because early diagnosis was not available and treatment regimens were poorly understood. As a result, without ARV treatment, 50% of children born with HIV died before age two. In general, therefore, the detection and treatment of CLHIV lagged severely behind the adult HIV response.

Evaluation objectives and methodology

The main objectives of the evaluation were to assess the public health and market impacts of the two projects, and assess their performance in relation to Unitaid's strategic objectives of promoting innovation, access and scalability. The evaluation framework is shown in Figure A.

Figure A: Evaluation framework



¹ The Paediatric HIV/AIDS project was delivered between 2006 and 2015 for a total spend of US\$359m globally and in 40 low and middle income countries. IPMA was delivered between 2014 and 2016 for a total spend of US\$10m globally and in 26 countries.

The evaluation was based on an extensive document review, quantitative data analysis and consultations with key stakeholders, including Unitaaid, CHAI, global partners such as WHO, the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) and the US President's Emergency Plan for AIDS Relief (PEPFAR), manufacturers and select country Ministries of Health (MoHs).

The following sections summarise the findings by evaluation dimension, followed by overall conclusions and lessons learned.

Evaluation dimension 1: Relevance

The evaluation found that the interventions delivered through both the Paediatric HIV/AIDS and the IPMA projects were highly relevant to the context, challenges and needs at the time.

The Paediatric HIV/AIDS project aimed to address paediatric ARV market failures through increasing children's access to diagnosis and treatment (growing demand), consolidating and coordinating global orders and purchasing patterns (improving market efficiency and visibility), and boosting participation by generic manufacturers (strengthening supply).

By 2010, most countries had successfully incorporated paediatric ARV procurement into their HIV/AIDS programmes, largely funded by the Global Fund and PEPFAR. IPMA was initiated to reinforce market visibility and provide analytical, technical, coordination and capacity building support across the supply chain. The sequencing of the two projects enabled CHAI to adopt a wide-ranging, flexible and multi-faceted role across the end-to end supply chain.

Evaluation dimension 2: Efficiency and Effectiveness

The efficiency and effectiveness assessment encompassed a review of the delivery of key activities under the two grants, namely on paediatric commodity procurement and related market shaping, country technical assistance (TA) provision and global-level market coordination activities.

Project procurement and market shaping

CHAI used a pooled procurement approach which combined country orders to meet minimum batch sizes and consolidate procurement around a limited number of treatment regimens. This approach helped drive down costs and reduce delivery times. The use of "cost-plus" tendering enabled suppliers to decrease costs while maintaining a reasonable commercial return, passed on as lower prices for ARVs, and also promoted understanding and transparency of drug manufacturing costs. For higher volume markets, CHAI selected more than one supplier ("split volumes approach"), which helped attract smaller manufacturers to bid even if there was an established dominant supplier (notably having contributed to the expansion of the Lopinavir/Ritonavir (LPV/r) market). Non-price criteria was introduced to incentivise manufacturers to register in more countries and to decrease production lead times and delivery delays.

Despite a slow start, the project successfully increased consolidation around fewer, more optimal drugs. By 2014 only 11 different formulations were procured by the project, down from 39 in 2010 and 46 in 2007. Regimens were increasingly consistent with the Inter Agency Task Team (IATT) Optimal List of paediatric formulations, including a clear focus on first-line drugs. That said, and while the project was limited by the availability of products that could be procured in the early years and it is recognised that it takes time to change treatment regimens in countries, consultations plus our analysis suggests that more could have been done to ensure greater ARV prioritisation earlier on in the project, which is likely to have reduced the burden of managing a large number of tenders.

CHAI focused on market-shaping for paediatric ARVs relative to the other commodities procured by the project (diagnostics, opportunistic infection medicines and Ready-to-use Therapeutic Foods (RUTFs)), which could be regarded as a missed opportunity, although we note the specific natural barriers that limited the extent to which CHAI could influence these markets. That said, the project had an indirect impact on national capacity building in the use of dried blood spot (DBS) approaches, and also supported countries with the upfront cost of diagnostics infrastructure to allow them to expand the use of early infant diagnosis (EID).

Technical assistance delivery

The main areas of country-level technical assistance (TA) provided by CHAI included procurement and supply chain management, scaling up testing and treatment services, the adoption of WHO treatment guidance and IATT optimal formulations, and securing alternative funding sources. The evaluation found that:

- There was a clear need for TA given the previously limited focus on paediatric HIV programmes and it was appropriate to make this an explicit priority under IPMA. TA support has facilitated effective HIV programme management across countries in terms of updating of country guidelines and reductions in stock-outs.
- Needs were identified in close partnership with local teams and ministries of health (MoHs). While there were standardised tools used across various countries in TA provision, the focus of assistance was country-specific.
- TA was often substitutive rather than capacity strengthening which led to dependency by MoHs on CHAI for skills such as quantification and forecasting. There was no evidence found that CHAI continually evaluated their TA, and there is potentially a missed opportunity to improve TA provision, for example by strengthening institutional, rather than individual capacity.

Global coordination activities

The two projects enabled CHAI to adopt an end-to-end approach to support the demand for and supply of paediatric ARVs from product development right through to approval, market development and uptake. CHAI performed a number of roles including coordination, data and information management, and technical expertise for different paediatric ARV working

groups engaged at global and country levels. CHAI was the only major partner active across all initiatives. This role and contribution was unique and would have been difficult for any other organisation in the global architecture to take on. It enabled CHAI to build coherence between the stages of commodity development and implementation that would not have been possible without the Unitaid IPMA grant. The effect of this engagement was to make the market more transparent and accessible for suppliers, buyers, implementing partners, and decision-makers.

Evaluation dimension 3: Impact

Public health impact

The projects have been instrumental to supporting increased antiretroviral therapy (ART) coverage and scale-up. The public health impact of the Paediatric HIV/AIDS project is directly observable through 431,916 new children initiated on ART in the 40 project countries over the period 2007-14, resulting in an estimated 159,809 deaths averted and 9.3m life years gained. The indirect impact of the treatment scale-up through this project and continued work under the IPMA grant is reflected in 165,850 more children being treated in 2016 compared to 2013, to which both projects can be viewed to have made a substantial contribution. Based on the new treatment figures for IPMA, an estimated 61,364 deaths were averted and 1.1m life years gained.

Targets in high volume countries were generally not met but these may have been unrealistic. The rapid expansion in the numbers of children on treatment was underpinned by a significant improvement in the coverage of EID which enabled eligible children to be identified much earlier than before. Between 2007 and 2014, the Paediatric HIV/AIDS project ran nearly 2.1m EID tests.

ARV market impact

The overall aim of the two projects was to foster and sustain a healthy market for paediatric HIV treatment commodities, which is defined as having low barriers to entry and a sufficient number of suppliers and buyers to ensure high-quality products are provided in a timely way at competitive prices. The evaluation found that:

- The pooled procurement approach generated sufficient demand to incentivise suppliers to enter the market. In 2007, for example, there were on average three suppliers for key ARVs, whereas by 2017 this had doubled to six. New and more optimal commodities also became available and still continue to come onto the market.
- Supply has been relatively concentrated, mainly due to limited uptake of registration. Further support to increase competition around the most popular commodities may have been warranted. There has, however, been an increase in generic suppliers replacing innovators across most ARVs.

- Since 2004, prices of all ARVs reviewed have declined by 35-85%. Significant price reductions were experienced before the start of the Paediatric HIV/AIDS project, but these also continued during project implementation, while new ARVs that were introduced have also experienced declines over time.

The Unitaid-CHAI projects have been instrumental in creating a market for paediatric ARVs that previously did not exist, with all stakeholder consultations for the evaluation emphasising the path-breaking work through these projects. The focus of the projects was in ensuring that a sufficient number of suppliers for optimal products were available to supply ARVs, particularly generic manufacturers, and at reduced prices; and while ongoing market challenges remain with the niche and the long-term shrinking market that characterises paediatric ARVs, as well as constant innovation for new and optimal products, it is clear that the work undertaken by CHAI has had a critical and lasting impact in creating an improved market for paediatric ARVs.

Value for money

The Unitaid-CHAI Paediatric HIV/AIDS and IPMA projects have undoubtedly delivered value for money in relation to the money invested. Using a full income approach, the return on investment of both projects combined was estimated to be US\$11 of net benefit for every dollar of cost.² The financial savings made as a result of price reductions were estimated to be US\$821m. Thus for every US\$1 spent by Unitaid, US\$2.22 of cost savings in national HIV and AIDS treatment programmes were realised through these price reductions.

Evaluation dimension 4: Sustainability and Scalability

After 2010, funding for the Paediatric HIV/AIDS project largely transitioned to other partners, including the Global Fund, PEPFAR and national governments, and despite CHAI's role in supporting countries, transition was a fundamental challenge and not adequately planned for/coordinated, also coinciding with wider funding challenges particularly the cancellation of the Global Fund's Round 11 funding.

CHAI had mixed success transitioning their work under IPMA. Although global coordination activities were successfully transitioned either to the Global Fund or to other CHAI projects such as the Optimal ARVs project also being funded by Unitaid currently, as noted previously, country TA proved more difficult to transition given dependencies within MoHs on the one hand and limited alternative service implementers on the other. Procurement management and forecasting capacity has been built in countries over time, although there are evolving TA needs in relation to implementing the latest WHO guidance and incorporation of updated formulations.

² The full income approach aims to capture the value of life years gained as a multiple of average GDP across low and lower-middle countries - based on the approach used in the Lancet Global Health 2035 report. ROI calculations compare whole-of-life benefits with costs incurred during childhood only, so should be interpreted with caution.

Despite the progress made, many challenges persist in the paediatric ARV market. As a rapidly evolving field, guidelines for optimal treatment protocols change often and many manufacturers still find it difficult to invest in new formulations. Many paediatric formulations recommended by WHO are still not available as FDCs, and several optimal ARVs used to treat adults are not available for children. Despite substantial improvements made in the paediatric ARV market as a result of the Unitaid-CHAI project work, the positives of declining CLHIV and improving optimal treatments means that the market itself continues to remain fragile.

Given the continuing challenges, a number of initiatives have been launched by global HIV partners across the development cycle, and more recently the Global Accelerator for Paediatric Formulations (GAP-f) initiative was launched to help accelerate the introduction of new paediatric ARVs, and Unitaid's ongoing Optimal ARVs grant to CHAI will also contribute to this effort.

Summary findings, conclusions, and lessons learned

The evaluation found that the Unitaid grants enabled CHAI to deliver to its strengths during a critical period for global paediatric HIV care and scale up. CHAI built on its experience working on adult ARV markets, taking a problem-solving, adaptive, and highly responsive approach to identify and address key barriers. Pooling ARV procurement helped generate supplier interest, making ARV formulations more accessible, timely, and affordable. Nudging countries and suppliers towards more optimal formulations for children supported the delivery of better outcomes. While this type of large scale procurement is no longer an approach used by Unitaid, it was critical to overcoming multiple market failures affecting paediatric ARVs. The IPMA grant was well placed to address new and additional barriers encountered as the market matured, in particular market smoothing and end-to-end market shaping (i.e. encompassing a wide range of market shaping issues).

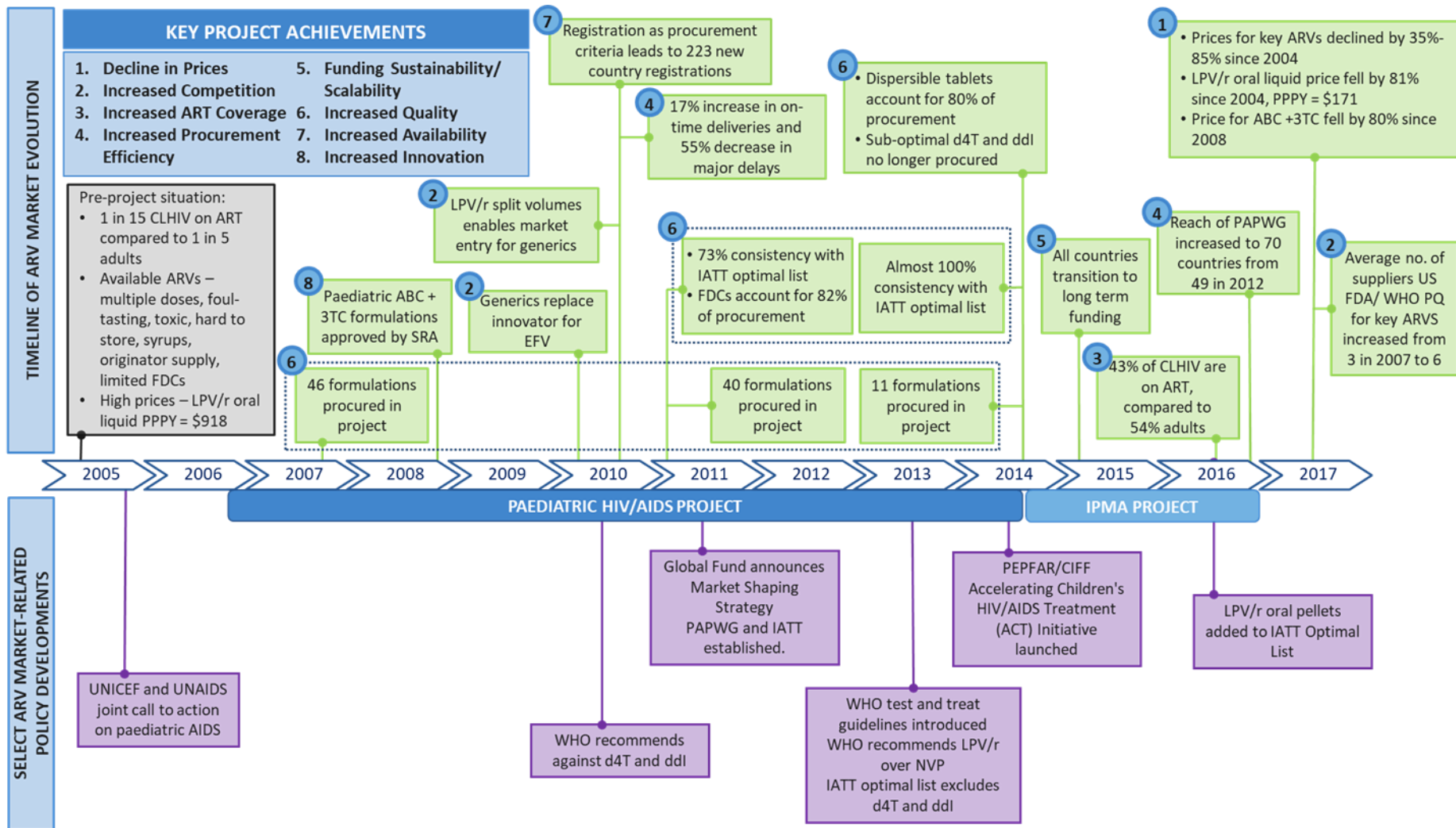
One of CHAI's key strengths was its ability to work across a range of settings with a variety of actors, taking a unique interlocution role connecting private sector manufacturers, country HIV programmes, and international partners/funders. CHAI used its comparative advantage to drive progress and achieve genuine impact, with an estimated 586,046 additional children have been initiated on treatment during the lifespan of the programme. For every dollar of Unitaid funding, US\$11 of net benefits have been realised as a result of additional life years gained, and US\$2.22 of cost savings made due to the reduction in ARV prices.

The technical assistance provided by CHAI delivered mixed results. Although relevant and appropriate, CHAI's approach focused on providing short term substitutional technical support rather than on developing long-term capacity.

The paediatric ARV market remains fragile, particularly in the face of declining CLHIV numbers. However, the evaluation found that the Unitaid-CHAI projects have played a vital role in significantly advancing and shaping the paediatric ARV market, fundamentally

transforming paediatric diagnosis and treatment in high burden countries. A summary of the key achievements of the project is provided in Figure B below.

Figure B: Key successes and market development outcomes



ACRONYMS AND ABBREVIATIONS

Acronym	Full description
APWG	ARV Procurement Working Group
ART	Antiretroviral Therapy
ARV	Antiretroviral
CDC	U.S. Centers for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
CLHIV	Children Living with HIV
EID	Early Infant Diagnosis
FDC	Fixed Dose Combination
GPRM	Global Price Reporting Mechanism
IATT	Inter-Agency Task Team for the prevention and treatment of HIV infection in pregnant women, mothers and children
IPMA	Innovation in Paediatric Market Access
LMIC	Low and Middle-Income Countries
LYG	Life Years Gained
MoH	Ministry of Health
OI	Opportunistic Infection
PAPWG	Paediatric ARV Procurement Working Group
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PfSCM	Partnership for Supply Chain Management
PLHIV	People Living with HIV
PMTCT	Prevention of Mother-to-Child Transmission
PHTI	Paediatric HIV Treatment Initiative
PPPY	Price per patient year
RfP	Request for Proposal
RUTFs	Ready-to-use Therapeutic Foods
SRA	Stringent Regulatory Authority
TA	Technical Assistance
TOR	Terms of Reference
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
VfM	Value for Money
WHO PQ	World Health Organization Prequalification Team: medicine

1. INTRODUCTION

Cambridge Economic Policy Associates (CEPA) was appointed by Unitaid to conduct an end of project evaluation of two grants provided to the Clinton Health Access Initiative (CHAI) on paediatric HIV/AIDS titled the “Paediatric HIV/AIDS Project” and “Innovation in Paediatric Market Access” (IPMA). This report presents our evaluation analysis and findings, alongside overall conclusions and lessons learned.

In the introduction section, we set out the evaluation scope and objectives (Section 1.1), evaluation methodology (Section 1.2) and structure of the rest of the report (Section 1.3).

1.1. Evaluation scope and objectives

Based on the Terms of Reference (TOR), the objectives of this evaluation are:³

- To provide an assessment of the programmatic impact (i.e. pre and post) of the projects, with a focus on public health and market impacts.
- To consider the performance of the projects in relation to Unitaid’s strategic objectives of innovation, access and scalability.

Further, discussions with the Unitaid Secretariat indicated that the evaluation should also consider the value for money (VfM) of the Unitaid investment. As such, the focus of the evaluation is on the results and impact of the projects.

1.2. Evaluation methodology

Evaluation framework

Figure 1.1 presents the evaluation framework, structured as three core and inter-related dimensions of:

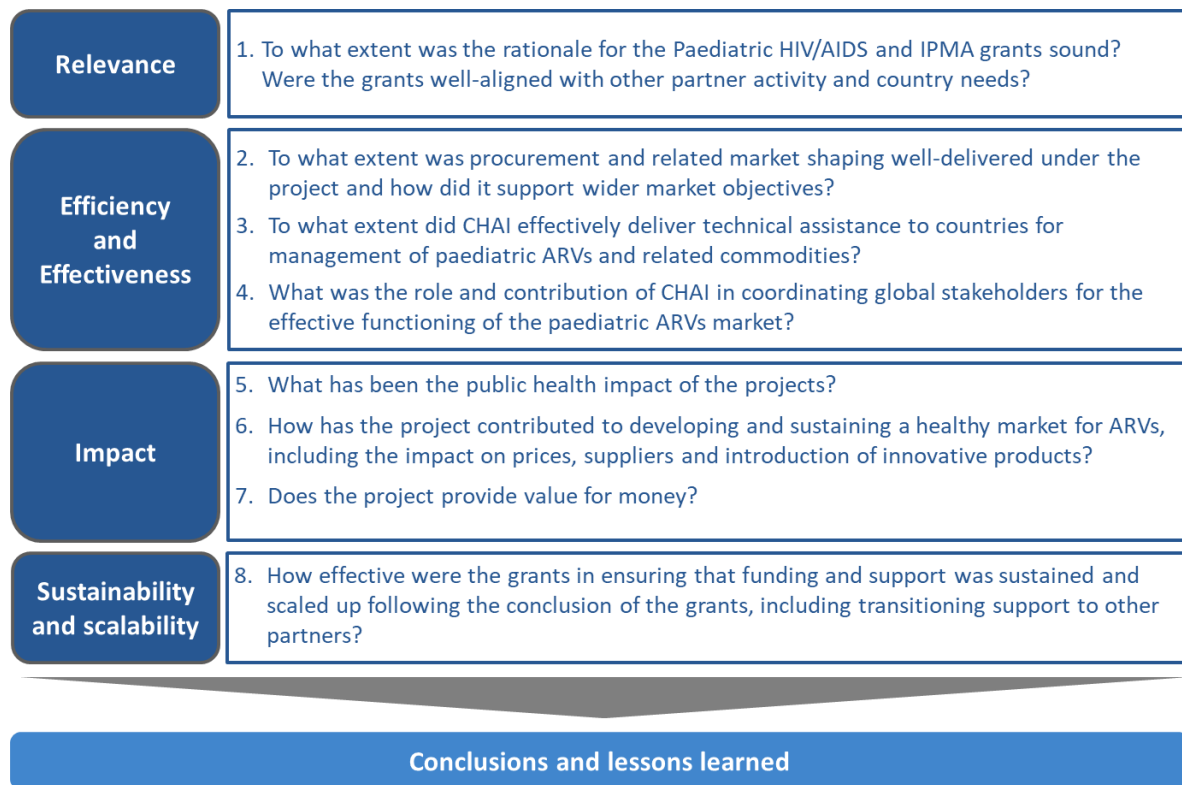
- **Relevance** – encompassing a review of the rationale for the two grants and their alignment with the work of other global actors and country needs.
- **Efficiency and effectiveness** – assessing efficient and effective implementation of the main areas of work across the two grants namely, procurement and related market shaping, in-country technical assistance (TA) and global coordination.
- **Impact** – examining the public health and market impacts of the grants, in addition to assessing VfM.

³ The TOR note the scope of the evaluation to encompass the Organisation for Economic Cooperation and Development – Development Assistance Committee (OECD DAC) evaluation criteria of relevance, efficiency, effectiveness, impact and sustainability, including a consideration of the achievement of the project goals, outputs and activities. Given this is an end of project evaluation as well as the in-depth review undertaken as part of the mid-term evaluation of the Paediatric HIV/AIDS project, we do not conduct a detailed assessment of project management efficiency and effectiveness by CHAI in terms of budget and timeline management; rather, our balance of effort lies on impact assessment.

- **Sustainability and scalability** – assessing the extent to which results have been sustained and scaled-up since the grants were completed, and determining remaining challenges in the market.

The assessment across these dimensions informs evaluation conclusions and lessons learned.

Figure 1.1: Evaluation framework



Evaluation methods

This was a desk-based evaluation of documents and data as well as telephone and face-to-face consultations with stakeholders. Specifically, key methods include the following:

- **Document review:** Key reference documents included project grant agreements and plans, M&E reports, CHAI country reviews and project summaries, alongside wider paediatric HIV documentation, including World Health Organisation (WHO) guidelines, Inter-Agency Task Team (IATT) for the prevention and treatment of HIV infection in pregnant women, mothers and children optimal lists, Global Fund strategies, pricing and procurement documentation, etc. Annex A provides the bibliography.
- **Data analysis:** Data analysis was conducted for project impacts including the public health impact and market impact on prices, supply, etc.
- **Stakeholder consultations:** Consultations were conducted with key stakeholders including Unitaid, CHAI, funders (Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), US President's Emergency Plan for AIDS Relief (PEPFAR)), partners

(Partnership for Supply Chain Management (PfSCM)) and manufacturers. In addition, telephone consultations have also been conducted with select country representatives (CHAI personnel and Ministry of Health (MoH)) in Kenya, Malawi and Uganda. Annex B provides the list of consultees and supporting interview guides.

Key limitations of the evaluation methodology include limited country-level feedback (given lack of country visits and telephone consultations with only a handful of the project countries), some loss of institutional memory of the grants (given their long time period and changing personnel at both Unitaid and CHAI) and therefore limited details on the initial context and grant management, as well as gaps in the databases (e.g. lack of completion of the Global Price Reporting Mechanism (GPRM)⁴, challenges in finding data sources and detailed calculations for some of the numbers presented in the CHAI progress reports, etc.). Despite these limitations, we believe that this evaluation is a strong and robust piece of analysis, following detailed document and data analysis and good corroboration with the range of stakeholder consultations.

1.3. Structure of the report

The rest of the report is structured as follows:

- Section 2 provides the context and description of the two projects;
- Section 3-6 present our analysis and findings on the evaluation dimensions of relevance, efficiency and effectiveness, impact, and sustainability and scalability;
- Section 7 presents the summary of the findings, conclusions and lessons learned.

The main report is supported by the following annexes: Annex A presents the bibliography, Annex B presents the consultee lists and interview guides, Annex C provides trends in Children Living with HIV (CLHIV), treatment coverage and the impact of Prevention of Mother to Child Transmission of HIV (PMTCT) programmes, Annex D presents developments WHO recommendations for paediatric treatment and IATT optimal lists, Annex E reviews country coverage under the projects, Annex F summarises the procurement of other HIV commodities under the project, and Annex G provides an analysis of supply and pricing for key antiretrovirals (ARVs) procured under the Paediatric HIV/AIDS project.

⁴ The GPRM is a database collated by WHO that contains information on transaction prices, sources and quantities of antiretroviral medicines (ARVs) purchased by HIV/AIDS programmes in low and middle income countries (LMICs).

2. BACKGROUND

Project context

In 2006, there were an estimated 2.6m CLHIV globally, with more than 2.2m of these living in Africa.^{5,6} However, only one in 15 children in need of ARV treatment were receiving it, compared to one in five adults.⁷ Without ARV treatment, 50% of children born with HIV will die before they are two, while 80% will die before the age of five.⁸

CLHIV have historically been concentrated in countries with weak health systems, large poverty rates and low access to treatment, care and prevention, including effective PMTCT programmes. Countries that could afford access to ARV treatment for children (and had the health systems capable of finding and treating HIV positive children) had very little demand for it, and as a result there was little incentive for companies to invest heavily in developing effective formulations designed especially for children. Of those that were available, several were expensive, hard to store and involved multiple, foul-tasting daily doses.

In 2005 the United Nations Children’s Fund (UNICEF) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched a call to action to address the impacts that HIV/AIDS were having on children and the lack of support provided to CLHIV.⁹ Prior to its publication, CHAI had initiated discussions with key stakeholders, and in 2005 launched a preliminary programme to treat 10,000 children in one year. This initial programme was the first sizeable commitment for purchasing ARVs for CLHIV.¹⁰

Paediatric HIV/AIDS project description

This initiative laid the foundation for the first Unitaid grant to CHAI for the Paediatric HIV/AIDS project, initially designed to last two years and treat 100,000 CLHIV in 2007 and 200,000 in 2008 across 40 countries.¹¹ The grant was designed such that Unitaid support would primarily fund treatment, diagnostic and other commodity-related costs of programmes, while CHAI would source funding from other partners to fund programme management activities. We understand that this was among the first grants to be approved by the Unitaid Board, and was

⁵ UNAIDS Data (2017).

⁶ CLHIV is defined by UNAIDS as children between the aged 0-14 infected with HIV.

⁷ CHAI (2006), *Proposal to Expand Paediatric AIDS Care to 100,000 HIV-positive children in 2007: Annex 1 Project Legal Agreement*.

⁸ Newell et al. (2004), Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis.

⁹ UNAIDS and UNICEF (2005), *A Call to Action – Children: The missing face of AIDS*.

¹⁰ CHAI (2006), *Proposal to Expand Paediatric AIDS Care to 100,000 HIV-positive children in 2007: Annex 1 Project Legal Agreement*.

¹¹ Countries supported through the Paediatric HIV/AIDS Project included Angola, Benin, Botswana, Burkina Faso, Burundi, Cambodia, Cameroon, China, Cote D’Ivoire, Dominican Republic, the Democratic Republic of the Congo, Ethiopia, Guyana, Haiti, India, Jamaica, Kenya, Liberia, Lesotho, Malawi, Mozambique, Namibia, Nigeria, the Organisation of Eastern Caribbean States (comprising Antigua and Barbuda, Dominica, Grenada, Montserrat, Saint Kitts and Nevis, Saint Lucia and Saint Vincent and the Grenadines), Papua New Guinea (PNG), Rwanda, Senegal, Swaziland, Tanzania, Togo, Uganda, Ukraine, Viet Nam, Zambia and Zimbabwe.

initiated during the previous business model where Unitaid funded large, commodity scale-up grants, as opposed to the smaller-scale, market catalytic grants that are characteristic of more recent grants.

Key activities under the project involved implementing a pooled procurement approach for purchasing paediatric ARVs and catalysing the market for these commodities in low- and middle-income countries (LMICs). While ARVs were a key focus, the project also included support for procuring early infant diagnosis (EIDs) as well as treatment for opportunistic infections (OIs) and ready-to-use therapeutic foods (RUTFs).

Despite initial documentation suggesting that the grant would only be implemented over a few years, the project was implemented until 2015, with additional children treated, and disbursements totalling nearly US\$359m over the course of the project against a budget of around US\$439m.¹² The main reasons for extending the project was to ensure appropriate transition mechanisms were in place, notably that the cost of activities supported by Unitaid would be covered by other partners including the Global Fund, PEPFAR, and national governments.

IPMA project description

While the Paediatric HIV/AIDS project was seen as essential for creating the market for paediatric HIV treatment and mobilising other actors to fund support in this area, key issues remained. For example, at the global level, demand remained fragmented across a range of countries, where despite the number of CLHIV globally still being around 2.2m, this was spread across several countries with different requirements, funders and procurement agents. In addition, some countries did not have sufficient capacity to effectively forecast their commodity requirements and manage country supply and coordination of paediatric commodities. Further, given the paediatric ARV market is constantly evolving, with optimal formulations changing relatively frequently, countries required support to ensure optimal commodities were incorporated into national guidelines and responses.

To address these needs, Unitaid launched the IPMA project, which involved funding CHAI to provide TA in 26 countries across sub-Saharan Africa and South and South East Asia related to forecasting and implementing procurement activities for paediatric HIV treatment and diagnostics.¹³¹⁴ The project also included supporting the global paediatric HIV response, including developing and publishing market intelligence regarding paediatric HIV commodities, establishing global paediatric commodity development and procurement

¹² CHAI annual reports. Note that the US\$439m budget and the US\$359m disbursement figures differ from the US\$417m budget and US\$334m total disbursement figures quoted on the Unitaid web page.

¹³ Unitaid (2017), Innovation in Paediatric Market Access (IPMA): Project description webpage, accessed [here](#).

¹⁴ Countries supported under the IPMA project included the following (with those also supported under the Paediatric HIV/AIDS project in bold italics): **Benin, Botswana, Burkina Faso, Burundi, Cambodia, Cameroon, Cote D'Ivoire, Ethiopia, India, Kenya, Lesotho, Liberia, Malawi, Mozambique**, Myanmar, **Nigeria, PNG, Senegal**, South Africa, **Swaziland, Tanzania, Togo, Uganda, Viet Nam, Zambia and Zimbabwe**.

mechanisms and supporting the consolidation of optimal ARVs.¹⁵ IPMA was implemented from 2014 to 2016, and according to the Unitaid website slightly over US\$10m had been spent on the project, out of a total budget of US\$11.6m.

The work conducted by CHAI under the IPMA grant has been taken forward through further support from Unitaid under a new grant on Optimal ARVs.¹⁶

Goals, outcomes and outputs of the projects

Table 2.1 below summarises the goal, outcome and outputs of the two grants.

Table 2.1: Project goal, outcomes and outputs

Result level	Paediatric HIV/AIDS Project	IPMA
Goal	Support scale-up and create sustained access to HIV treatment for children living with HIV in low and middle-income countries.	To promote sustained access to diagnostics and treatment for HIV-exposed and positive children.
Outcome	Optimal, quality-assured paediatric ARVs continued to be supplied to beneficiary countries at lower prices, alongside other related commodities.	To ensure that the optimal, quality-assured and affordable paediatric ARV and EID commodities are consistently and reliably available at affordable prices for low- to lower-and upper-middle income countries.
Outputs	<ol style="list-style-type: none"> 1. Increase the supply base for optimal, quality-assured paediatric ARVs. 2. Reduce prices for optimal, quality-assured paediatric ARV formulations. 3. Maintain supply of optimal paediatric ARVs and diagnostics to match need of beneficiary countries. 4. Increase uptake of optimal, quality-assured paediatric ARV formulations (as defined by the draft WHO IATT formulation guidance). 5. Identify long-term funding sources for paediatric ARVs and related commodities, and support countries in securing these funds. 6. Development and implement a joint approach with stakeholders for sustaining the paediatric ARV marketplace and project achievements post-transition. 	<ol style="list-style-type: none"> 1. Consolidation of optimised paediatric HIV commodities. 2. Market intelligence on global demand, key trends and new product development landscape. 3. Acceleration of development and uptake of optimised paediatric products.

¹⁵ We note that acceleration of developing and increasing uptake of optimised paediatric drugs was included as part of a reprogramming of the IPMA grant in response to CHAI's changing role in the Paediatric HIV Treatment Initiative (PHTI).

¹⁶ Unitaid (2018), Making the best HIV drugs available in lower-income countries: Project description webpage, accessed [here](#).

3. RELEVANCE

1. To what extent was the rationale for the Paediatric HIV/AIDS and IPMA grants sound? Were the grants well-aligned with other partner activity and country needs?

Our approach to assessing project relevance focuses on: understanding the context/ rationale for the two grants in terms of the pre-grant situation as well as linkages between the two grants; alignment of the grants with other partner activity; and country focus of the grants in relation to CLHIV burden. Project relevance from the perspective of the Unitaid Strategy and mandate is not considered as has been reviewed as part of the Unitaid call for proposals and grant approval process. However, as noted in Section 2, large scale-up grants like the Paediatric HIV/AIDS project grant are no longer the approach followed by Unitaid.

Project rationale and partner alignment

At the start of the Paediatric HIV/AIDS project, a situation analysis of the paediatric ARV market highlighted its fragility and fragmentation.¹⁷ As also noted in Section 2.1, there were:

- **Several market failures and supply issues:** Quality, well-adapted ARVs specifically for children were not reliably available in resource constrained environments, which was exacerbated by poor investment in product development. Country orders to suppliers were sporadic and small, with most having short time horizons. Suppliers tended to delay filling orders until they had a critical number to make batch manufacturing economically worthwhile.¹⁸ Between countries, adoption of different formulations led to a proliferation of products making harmonisation more difficult.
- **Poor treatment rates and public health impacts:** The focus up until 2005/06 was on PMTCT efforts, with considerably less emphasis on paediatric HIV treatment. EID tools were not easily available, with low diagnosis and high mortality of paediatric cases. The impact of this situation was that the detection and treatment of HIV in children under 15 lagged severely behind the adult HIV response. With this low level of treatment, there were around 380,000 AIDS-related child deaths in 2006.¹⁹

In this context, the Unitaid-CHAI Paediatric HIV/AIDS project was launched, to make available optimal, quality-assured paediatric ARVs at low prices, to support sustained and scaled-up access to HIV treatment in countries. The programme theory of change was that by consolidating and coordinating global demand, generic manufacturers would recognise paediatric ARVs as a commercially viable market would improve production on a regular schedule.

¹⁷ CHAI (2015), ARV Market Report: The State of the Antiretroviral Drug Market in Low- and Middle-Income Countries, 2014-2019.

¹⁸ Bowen, A et al (2008), Global challenges in the development and delivery of paediatric antiretrovirals.

¹⁹ UNAIDS (2006), 2006 Report on the global AIDS epidemic.

Agreements were made between donors and with countries that Unitaid would initially be the primary source of funding for paediatric ARVs in a number of countries.^{20,21} Indeed, the significance of the Paediatric HIV/AIDS project was such that, *“Uptake of new paediatric fixed-dose combinations (FDC) outside of UNITAID [was] low. UNITAID accounted for 97-100% of 2008-2009 market volume. In total, 33 and 34 countries reported solid or dispersible FDC purchases in 2008 and 2009, respectively, [and] most purchases were made through UNITAID.”*²² Consultations with both Global Fund and PEPFAR as well as the range of other stakeholders for our evaluation have strongly emphasised the role of the Unitaid-CHAI project on paediatric HIV treatment commodities, at a time when there was a large need and not much funding and activity from other partners.

By 2010 the centralised approach to ordering ARVs was mainly ending, and paediatric ARVs procurement had shifted to individual countries, the Global Fund, and PEPFAR (discussed further in Section 6.1). However, while dissolving central procurement was widely recognised as a necessary step to ‘normalising’ the market, the lack of coordination amongst partners around procurement was considered a risk to continued market stability. The Global Fund’s Market-Shaping Strategy, presented during the 23rd Board Meeting in May 2011, recognised this risk and shortly thereafter the Paediatric ARV Procurement Working Group (PAPWG), with CHAI support, was created with the aim of expanding the work undertaken by the Paediatric HIV/AIDS project and strengthening coordination among the various partners (discussed in more detail under Section 4.3).

The IPMA project was designed to help overcome a number of market and country level challenges and the orientation of the programme ensured it worked alongside on behalf of all main partners working in this area and closely aligned with the PAPWG. CHAI’s support included analytical, technical, coordination, and capacity building and stretched from global to country level. An important aspect was CHAI’s role in managing a cumulative forecasting process that combined relatively small individual country forecasts into a single, grouped forecast by regimen that manufacturers would find more lucrative to respond to. In order to undertake this role and through several annual cycles, CHAI effectively established and consolidated its position as global coordinator, achieved a level of trust among partner countries and their implementing partners, and was seen to be accountable for the outcome of the process.²³

As such the two Unitaid paediatric ARV projects had strong synergies and coherence. Following on the Paediatric HIV/AIDS project with IPMA made sense given outstanding

²⁰ The Global Fund (2008), 17th Board Meeting, Report of the Executive Director, April 2008

²¹ In countries not covered by Unitaid, Global Fund-supported HIV programmes procured paediatric ARVs independently, although such funding had less of a focus on market-shaping aspects relative to the Unitaid grant, particularly for facilitating FDC treatment.

²² Waning, B et al. (2010), The global pediatric antiretroviral market: analyses of product availability and utilization reveal challenges for development of pediatric formulations and HIV/AIDS treatment in children.

²³ For example, the midterm review and the Irish Aid reviews of CHAI performance identified these behaviours and outcomes.

challenges and the absence of any other actor obviously able and ready to take the multi-faceted role of global coordinator. The IPMA project addressed emerging end-to-end market shaping, market smoothing challenges that continued to create barriers to availability of paediatric ARVs in programme delivery. Together, the two programmes can be shown to have supported barriers at different stages of paediatric scale-up across high burden LMIC countries.

Country focus

With regards to the relevance of the grants in terms of the extent to which countries with the highest burden of CLHIV were considered, the Paediatric HIV/AIDS project covered 17 of the top 20 countries in terms of CLHIV prevalence in 2006, suggesting relatively good coverage. Importantly however, South Africa with the highest estimated CLHIV prevalence was not included in this project. Consultations with CHAI indicate that the reasons for South Africa's exclusion were the need to prioritise lower income countries in the grant (in line with Unitaids' strategic priorities). Other relatively higher income countries with high levels of CLHIV prevalence such as Thailand (14,000 CLHIV or 21st highest) and Brazil (13,000 CLHIV or 24th highest), as well as key low / lower-middle income countries such as Ghana (40,000 or 13th highest) and Central African Republic (16,000 or 18th highest) were also excluded from the initial grant. CHAI has cited reasons for the exclusion of some low-income countries as the level of CHAI capacity in these countries at that time as well as country MoH willingness to engage with the project.

For IPMA, key countries excluded were the Democratic Republic of Congo (55,000 or 12th highest), Angola (21,000 or 14th highest) and Rwanda (20,000 or 15th highest), which were initially included in the Paediatric HIV/AIDS grant. CHAI note that reasons for excluding these countries were that many had successfully transitioned from the initial Unitaids funding and were also undertaking their own procurement activities. Annex E provides more details.

In conclusion, while there was not full alignment between country coverage under the projects and extent of CLHIV prevalence, the majority of the high burden countries were covered and exclusions were reasonable/ practical.

Summary findings:

The Paediatric HIV/AIDS and the IPMA projects worked in tandem with one another to fill a recognised vacuum in the global HIV response. The rationale for the two grants was sound under the circumstances at the time of their initiation and there was clear synergy in their sequencing and delivery.

4. EFFICIENCY AND EFFECTIVENESS

The second evaluation dimension on efficiency and effectiveness encompasses a review of the delivery of key activities under the two grants, namely on paediatric commodity procurement and related market shaping, country TA provision and global-level market coordination activities, and the extent to which they have contributed to overall results. Section 4.1 reviews ARV and other paediatric HIV commodity procurement, Section 4.2 reviews country TA delivery by CHAI and Section 4.3 assesses CHAI's role and performance in global paediatric ARV coordination.

4.1. Project procurement and market shaping

2. To what extent was procurement and related market shaping well-delivered under the project and how did it support wider market objectives?

The main thrust of the US\$335m Unitaid-CHAI Paediatric HIV/AIDS project was ARV procurement, and as such, an assessment of the efficiency and effectiveness of this procurement is central to our evaluation. Procurement of other HIV commodities including diagnostics, OI medicines and RUTFs was also conducted under the project, however this was not the emphasis and as such our review is also lighter touch on these other commodities.

We consider the appropriateness of the procurement approaches for different commodities undertaken by CHAI and their implication and/ or contribution to procurement related efficiencies and market outcomes. Overall impact on the market is considered in Section 5.2.

4.1.1. Appropriateness and utility of CHAI ARV procurement approaches

The overall model of the Paediatric HIV/AIDS project was pooled procurement through consolidation of relatively smaller orders across a number of countries, for more clearly defined, WHO recommended, treatment regimens enabling minimum batch sizes to be met and stimulating growth in supplier interest, and thereby leading to reduced prices and delivery times.

Our review of CHAI's procurement approach for ARVs has been positive, and this has been supported through our consultations with both internal and external project stakeholders (including a number of manufacturers consulted for this evaluation). CHAI's procurement experience under this project has also had a broader indirect impact on other countries – for example, we understand from CHAI that learnings from the Unitaid-CHAI tender helped inform CHAI's support to the government of South Africa in its tenders for ARVs, helping to secure lower prices and substantial cost savings.²⁴

Key aspects of the approach and their impacts are discussed below.

²⁴ CHAI (2012), Case study – South Africa tender to achieve millions in cost savings.

Cost-plus approach

In addition to the traditional procurement approach of requesting for the best and final offer from suppliers, CHAI employed cost-plus approach to procurement (i.e. requesting an “open book” tender response from suppliers, providing details on the costs incurred plus a reasonable profit margin, which would be subject to negotiation based on discussions between CHAI and the supplier on options for cost reduction). The project procurement reports suggest that generic suppliers were the main respondents to the cost-plus tenders, whereas originator companies would offer products in line with their access pricing for the given countries.

Consultations with CHAI and other stakeholders highlights the considerable benefits of the approach namely:

- According to project procurement data for the 2010 tender, cost-plus negotiations resulted in price reductions in three of four paediatric ARV categories, while for 2012 and 2013 cost-plus negotiations resulted in improved pricing across all the different categories.²⁵
- Given the early stage of development of the market, this open-book and negotiations approach allowed for greater understanding and transparency of drug manufacturing costs and options for reduction. The CHAI Drug Access Team (DAT) worked with manufacturers of key ARVs to identify ways in which prices could be reduced while also maintaining suitable profit margins for these companies.

Enlisting multiple suppliers and split volumes

Another useful aspect of the procurement approach was that prices were revealed to other manufacturers once a primary supplier for an ARV had been selected, and manufacturers who could match these prices would be selected as secondary suppliers or pooled suppliers, if the ARV required larger volumes of procurement. For example, as part of the 2012 tender secondary suppliers offered lower prices when prices were revealed for primary suppliers for the nevirapine (NVP) oral solution as well as the abacavir + lamivudine (ABC+3TC) and zidovudine + lamivudine (AZT+3TC) tablets.²⁶

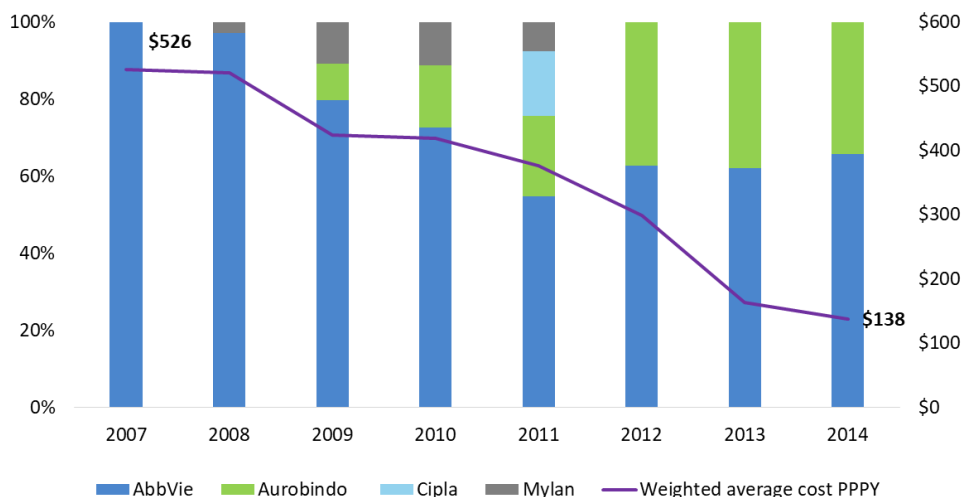
More generally, CHAI selected more than one supplier for high volume markets (“split volumes approach”) to support growth and competition as well as transparency. For example, taking the various formulations of Lopinavir/Ritonavir (LPV/r) that were purchased by the project, enlisting additional suppliers to AbbVie allowed for expansion of the market, and as argued by CHAI, initial payment of a premium to new market entrants ultimately contributed

²⁵ Paediatric categories included: Azidothymidine/Zidovudine (AZT) products, Efavirenz (EFV) products, Didanosine (ddI) products and Protease Inhibitors (PIs).

²⁶ CHAI (2012), CHAI Review and Recommendations by Adjudication Panel and the Contract Review Committee (CRC).

to overall reduction in treatment prices over time, as depicted in Figure 4.1 below. CHAI estimated total cost savings of US\$7.3m as a result of this approach.^{27,28}

Figure 4.1 Supplier share in project procurement (% of total, left hand side axis) and weighted average cost per person per year (PPPY) (right hand side axis)²⁹



Source: CEPA analysis based on project procurement data (supplier share) and the GPRM database (for prices of paediatric Unitaaid-funded procurement).

Additional non-price criteria

During the initial years of the Paediatric HIV/AIDS project, price was used as the sole criteria for selecting suppliers. However, in 2010 non-price factors, particularly the extent to which suppliers were registered nationally in project countries as well as past performance of suppliers in delivering products (including lead times and extent of delays in delivery), were also included. Based on project procurement reports, the maximum score for these factors was 15 points each, while for price the maximum score was 70 points.

While price remained the key factor in selecting suppliers, performance and proactive engagement with project countries could tip the balance. This is an example of how CHAI used market shaping interventions combined with real country experiences to help make ARV markets work better for CLHIV in poor countries.

²⁷ CHAI (2012), Overview of Tendering Best Practices.

²⁸ Based on our discussions during consultations, the upfront investment costs associated with investing in technology needed to produce LPV/r is high and differs from production requirements for other ARVs. As a result, in order to be able to recover initial investment costs prices supplied by generics were considerably high. At the same time it has been argued that innovator supply was not being offered at cost-reflective prices in these countries.

²⁹ The weighted average cost PPPY weights the average treatment cost PPPY by the proportion of a specific formulation and dosage of the ARV by the total value of procurement for that given year. For example, if only one formulation and dosage was used in a given year, the weighted average cost PPPY and the average treatment cost PPPY for that specific formulation and dosage of the ARV.

Market growth and increased procurement efficiencies were achieved through these approaches, as follows:

Increase in product registrations

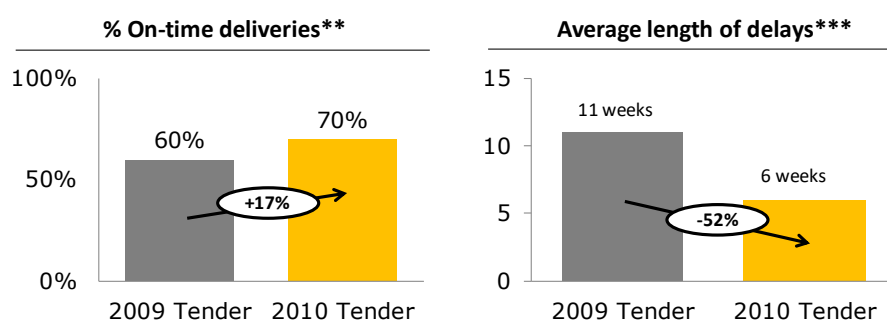
A key barrier to access was that limited product registrations impeded availability of products in countries. With the objective of expanding the paediatric ARVs market, inclusion of tender evaluation criteria on increased country registration helped increase access. Following the 2010 tender when this additional criterion was introduced, 223 new registration dossiers were submitted by suppliers in project countries, even in low-volume countries.³⁰

The positive response of suppliers indicates that although only 15 points of the tender evaluation was given to this criterion, they were valued points. The active response led to a significant shift in registrations on the ground. Making suppliers responsible for applications rather than placing the onus on country authorities to pursue registration of myriad suppliers was a very effective policy.

Increased procurement efficiencies through reduction in delays and lead times

Another major barrier to access were the unpredictable and delayed lead times. The introduction of a criterion in the tender evaluation linked to historical performance was aimed at addressing this barrier, again, placing the onus on suppliers. The inclusion of historical performance in the 2010 tender evaluation criteria appears to have had a positive effect on improving on-time deliveries and decreasing delays. In particular, a comparison of the results from the 2010 tender in relation to that from the 2009 tender conducted by CHAI revealed that under the new tender there was: (i) a 17% increase in number of on-time deliveries (with a 55% decrease in major delays); and (ii) a 52% reduction in the number of weeks of delay for previously delayed orders.³¹ Figure 4.2 provides more details on these efficiencies secured. As noted by CHAI, these improvements helped reduce stock-outs and eased planning for national programmes as well as ensuring timely availability to new, improved products.

Figure 4.2: Reduction in lead times through evolved CHAI procurement approaches



*2010 data based on orders placed in first three quarters to December 2010

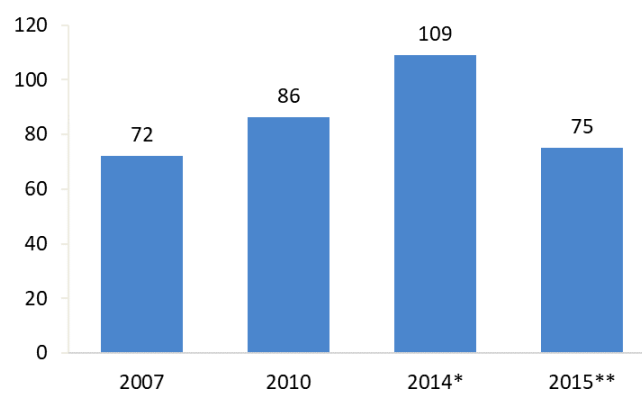
Based on total # of bottles delivered on time.*Based on orders that were previously delayed (delivered after 13 weeks, the average lead time)

³⁰ CHAI (2011), Case Study – Improving supply and availability of ARVs.

³¹ CHAI (2011), Case Study – Improving supply and availability of ARVs.

A key metric measured by CHAI was the number of days between the placement of the purchase order (PO) and the confirmed estimated time of departure (ETD). Figure 4.3 shows how this average changed over time, from the beginning of the Paediatric HIV/AIDS project through to the IPMA project. Important to note in interpreting the trends is that in the final year of the Paediatric HIV/AIDS project (2014) only three countries were still being covered with direct procurement of paediatric ARVs – Malawi, Uganda, and Mozambique. On the one hand, the relatively small sample of countries yet to transition may have distorted the impact the project had on lead times (and hence explaining the increase). On the other hand, though, when orders were placed well in advance of required delivery and therefore well-planned, lead times may have appeared to be increasing reflecting a reduction in the number of emergency orders (and better planning).

Figure 4.3: Average number of days between PO and ETD



*In 2014 only three countries were still covered by the grant: Malawi, Uganda, and Mozambique

**2015 data provided under the IPMA project

Source: CEPA analysis based on Paediatric HIV/AIDS and IPMA Project Reports.

While not specific to CHAI procurement, evidence from the ARV Procurement Working Group (APWG) suggests that the proportion of “well-planned” orders increased significantly from 15% in 2012 to 70% in 2016 for members, suggesting that procurement has become more effective over time.³²³³ However, for non-well-planned orders, lead times have tended to fluctuate.³⁴

Other aspects

As highlighted by CHAI, the open tendering approaches adopted under the project increased transparency, widened the pool of suppliers and thereby best prices, facilitated price

³² While funders and procurement agents have different definitions for “well-planned” orders, this generally refers to a sufficient amount of notice given to suppliers of an intention to procure ARVs.

³³ Following the success of the PAPWG, and recognising that a number of adult ARVs had similar market characteristics to paediatric commodities, in 2016 the mandate of the PAPWG was expanded to cover adult ARVs that required pooled procurement approaches to ensure sufficient orders could be reached, resulting in the name of the working group changing to APWG.

³⁴ The Global Fund (2017), APWG: Progress Review.

predictability, increased supply security, ensured high quality products, facilitated compliance with funder requirements and increased efficiency of country procurement processes.³⁵

Supplier selection was undertaken on an annual basis which was deemed an efficient balance between costs of procurement and maintaining competitiveness. Once suppliers were selected, master supply agreements (MSAs) would be signed between CHAI and the individual suppliers. Some of these MSAs could be in place for multiple years, depending on the product being procured, supporting supply stability.

An issue to note however is that despite introduction of specific procurement criteria, these were not always observed by CHAI during procurement from originator companies. However, given the need for some originators to supply the project due to lack of alternative generics in some cases, as well as capacity concerns of generic manufacturers to supply certain products (as was the case with LPV/r formulations for several years), CHAI still allowed these manufacturers to supply the project. This reflects the constraints of a monopoly/ non-competitive market, and thereby the limited utility/ benefit of procurement criteria suggested by CHAI.

4.1.2. ARV procurement consolidation and consistency rates

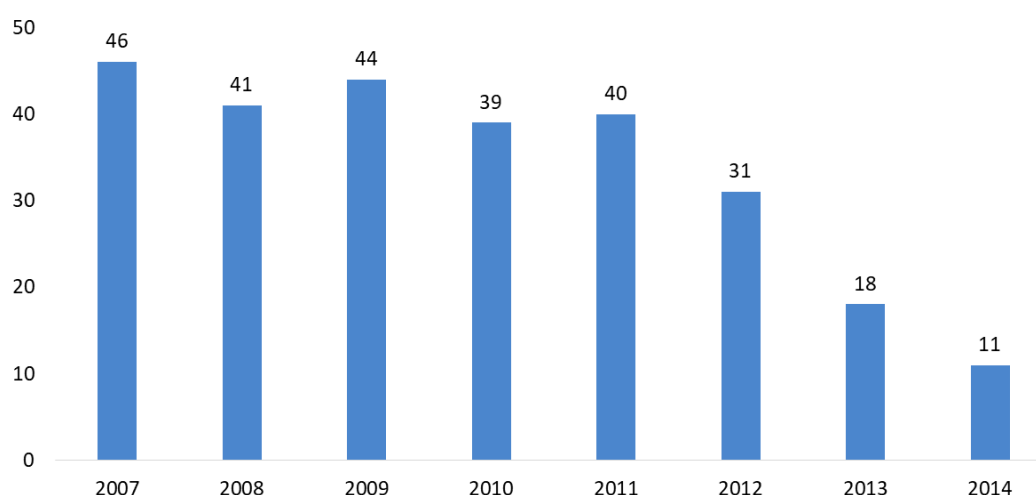
The efficacy of the ARV procurement conducted under the project was reflected in the increased consolidation and improved consistency with the IATT Optimal Lists. However, for several years the number of ARVs procured remained relatively high, while optimal formulations were also relatively low in the early years of the project. While the project was limited by the availability of products that could be procured in the early years and it is recognised that it takes time to change treatment regimens in countries, consultations plus our analysis suggests that it more could have been done to ensure greater ARV prioritisation earlier on in the project, which is likely to have reduced to burden of managing a large number of tenders across the project.

ARV consolidation

As shown in Figure 4.4, the number of ARVs procured under the project decreased from 46 in 2007 to 39-40 over 2010-11 and then 11 in 2014 (although we note there was considerably less procurement this year).

³⁵ CHAI (2012), Overview of Tendering Best Practices.

Figure 4.4: Number of ARV formulations procured by year



Source: CEPA analysis based on project procurement data.

With regards to the period covered by the IPMA grant, between 2013 and 2016 the APWG also reported that the number of unique formulations procured by the consortium reduced from 34 to 26.³⁶

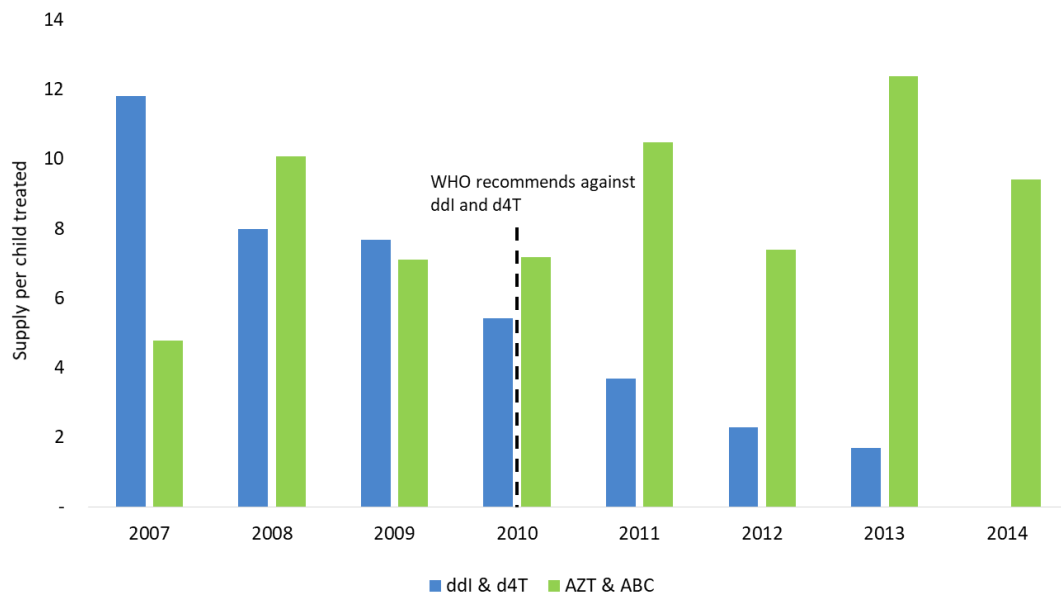
Increased procurement of improved formulations and consistency with IATT Optimal Lists

In 2010, one of the key recommendations made by WHO for treating CLHIV was to reduce paediatric treatment of didanosine (ddl) and stavudine (d4T) due to their toxicity, and replace these with other nucleoside reverse transcriptase inhibitors (NRTIs) such as AZT and ABC.³⁷ In response to this, Figure 4.5 below shows how CHAI was able to de-prioritise procurement of the former two ARVs over time, with significant reductions taking place in later years, including all procurement ceasing in 2014, while the ABC and AZT procurements involved a general increase (albeit varying between years).

³⁶ The Global Fund (2017), APWG: Progress Review.

³⁷ WHO (2010), Antiretroviral Therapy for HIV Infection in Infants and Children: Recommendations for a Public Health Approach.

Figure 4.5: Project supply of ddl, d4T, AZT and ABC-based regimens per child treated over time



Source: CEPA analysis, based on the CHAI Paediatric HIV/AIDS project procurement tracker and annual report figures.

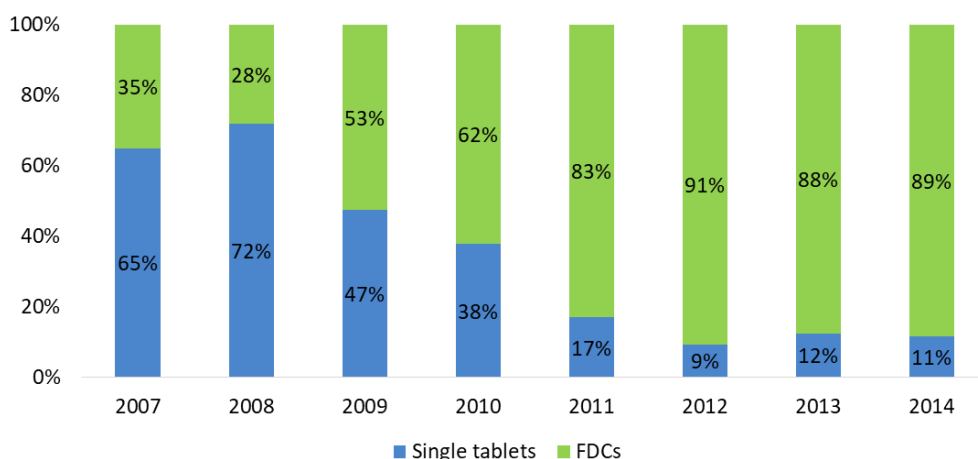
According to the 2017 CHAI market report, AZT and ABC accounted for almost the entire paediatric NRTI market in 2017 and are expected to do so until 2021, although ABC is expected to obtain a greater share of the market relative to AZT, primarily as a result of ABC being part of WHO guidelines for first-line treatment for all children less than ten.³⁸

More generally, during implementation of the Paediatric HIV/AIDS project there was significant improvements in the quality of ARVs procured (noting that these are also a function of product availability). This included:

- FDCs as a proportion of the total value of procurement increased from **38% in 2007 to 82% in 2011**, and remained at similar levels for the duration of the project, which is shown in the figure below.

³⁸ CHAI (2017), ARV Market Report.

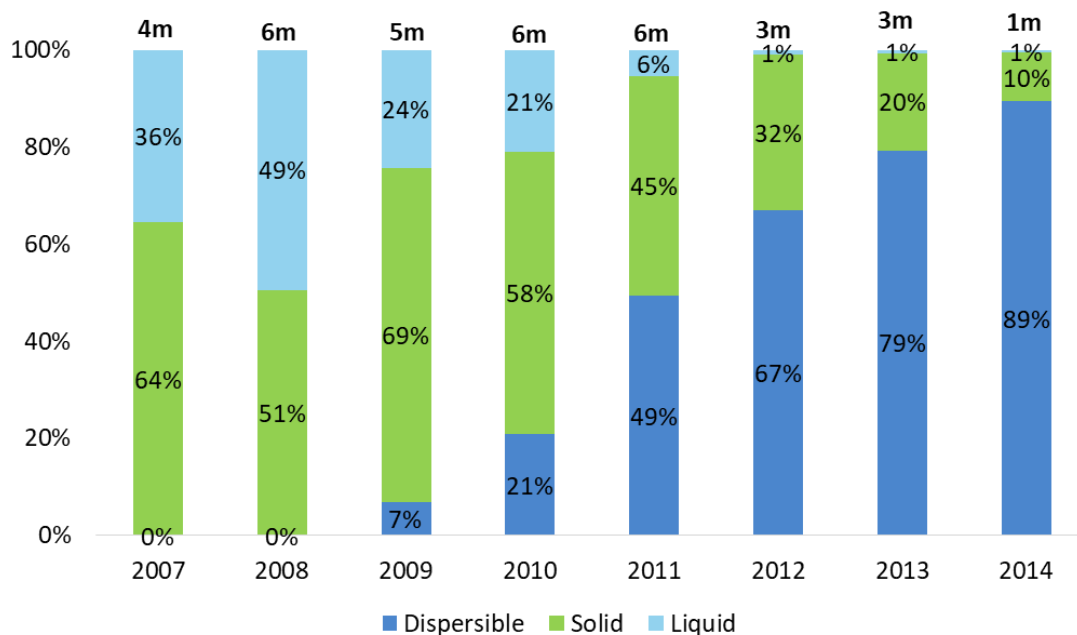
Figure 4.6: Proportion of single and FDC formulations by quantity



Source: CEPA analysis based on project procurement data.

- **Procurement of dispersible tablets also increased substantially** over the course of the project, accounting for more than 80% by the final year of the Paediatric HIV/AIDS project, as is shown in the figure below.

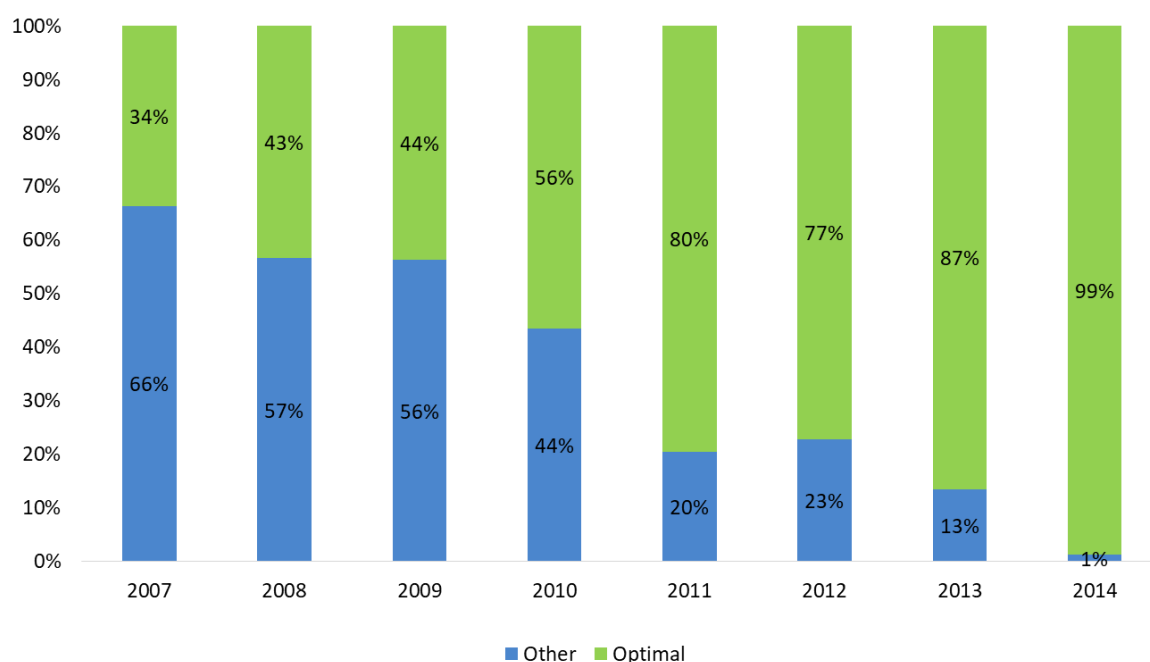
Figure 4.7: Proportion of dispersible, solid and liquid formulations by quantity (total packs shown above graphs)



Source: CEPA analysis based on project procurement data.

- The project was able to prioritise optimal treatments over time, for example, when the IATT list was first introduced in **2011 the Paediatric HIV/AIDS project procured 73% of ARVs on the list, while by 2014 this proportion had increased to almost 100%.**

Figure 4.8: Proportion of IATT Optimal ARVs procured on project



Source: CEPA analysis based on project procurement data.

These trends have also continued under the IPMA project, with the PAPWG procuring 84% of Optimal ARVs in 2014, 95% in 2015 and 94% in 2016 (when considering the paediatric formulation of AZT+3TC+NVP as optimal).³⁹

4.1.3. Procurement of other paediatric HIV commodities

The focus of the Paediatric HIV/AIDS project procurement and market-shaping work was on ARVs, with procurement of other HIV commodities such as diagnostics, OI medicines and RUTFs being undertaken to support the increased treatment efforts. One may view this as somewhat of a missed opportunity, especially given the sizeable investments in other HIV commodities (diagnostics (US\$93m), OI medicines (US\$16m) and RUTFs (US\$35m)), although specific challenges of these markets are recognised. Also, we understand that subsequently Unitaid provided a grant to CHAI together with UNICEF for market shaping of HIV diagnostics.

Specifically in terms of the project (and Annex F provides more information):

- The specific nature of individual diagnostic products implies limited substitution, and coupled with the high investment and laboratory infrastructure requirements, procurement of these commodities was mostly through direct negotiations with respective suppliers. Some price efficiencies were achieved in terms of lower than planned prices for particular diagnostics, but beyond this there was limited market shaping work conducted under the project. We understand that the aim of procuring the diagnostics was to build national capacity on diagnosis and use of dried blood spot (DBS) approaches, as well as support operational development through consideration

³⁹ The Global Fund (2017), APWG: Progress Review.

of bundled systems and linkages with viral load testing given low capacity utilisation through EID testing alone. Also one of the key indirect impacts of the project was that countries could utilize the infrastructure put in place under this project for rolling out other diagnostic products.

- OI medicines were also procured to support the increased treatment efforts, with no real market shaping efforts given the main OI drug (co-trimoxazole) already had a large supply base (and prices did not vary substantially during the project). Other OI drugs were procured under much more strict procedures by CHAI, given that countries had limited experience with the drugs and few alternative drugs had obtained SRA approval.
- RUTFs were procured to support increased nutritional outcomes for CLHIV, increasing efficacy of paediatric ARVs. They were primarily purchased from the patent holder, Nutriset. As products needed to be shipped from France, this increased the price by 15%. By 2012, the supplier base had increased, but CHAI was only procuring 5% of RUTFs globally, limiting their ability to impact the market.⁴⁰ Over the course of the project, however, CHAI went from procuring 83% of RUTFs from Nutriset in 2007 to only 52% in 2012, with 27% being procured from Project Peanut Butter and 21% to Valid Nutrition.

Summary findings:

CHAI's procurement approach for ARVs has been positive, with cost-plus approaches helping drive prices down and improve transparency, split volumes approach supported market entry and use of non-price criteria supporting increased country access and efficiencies through increase in product registration and reductions in supply delays. ARV procurement has become more consolidated over a smaller number of optimal drugs – although some view this progress as being possible to have been achieved earlier. The project has not really impacted market dynamics for other HIV commodities, although some price declines were achieved for diagnostics.

4.2. Technical assistance delivery

The second area of the efficiency and effectiveness analysis examines the technical assistance (TA) provided by CHAI to project countries. This has been examined across the continuum of both the Paediatric HIV/AIDS and IPMA projects, recognising that the IPMA project had explicit Unitaid funding for this.⁴¹

The evaluation question is as follows:

3. To what extent did CHAI effectively deliver technical assistance to countries for management of paediatric ARVs and related commodities?

⁴⁰ Swiss TBH/SCIH (2012), Unitaid Mid-term review of the "Paediatric HIV/AIDS Project" p. 40.

⁴¹ Under the Paediatric HIV/AIDS project, CHAI received funding from the Children's Investment Fund Foundation (CIFF) and the Elton John AIDS Foundation to support their TA work.

Based on our review of the project documentation, the main areas of country-level TA provided by CHAI across the Paediatric HIV/AIDS and IPMA projects were with regards to:

- **Procurement and supply chain management:** activities included forecasting, development and implementation of stock monitoring tools to improve supply chain quantification, amongst others.
- **Managing the scale up of testing and treatment services:** activities included the development of mHealth tools to improve result delivery and reduce lost-to-follow-up (LTFU) of HIV-exposed infants, interventions to strengthen sample transportation networks and results delivery systems, implementation of integrated service delivery models to provide care to HIV positive mothers and their children, TA to support installation and scale-up of nucleic acid testing platforms in central laboratories and other activities with MoH staff to strengthen health services delivery.
- **Adoption of WHO treatment guidance and IATT optimal formulation:** activities included country-specific workshops with the MoH, the creation of job aides, the convening of in-country technical working groups, development of clinical memos supporting uptake of optimal formulations and WHO treatment guidelines, etc.
- **Securing alternative funding sources for paediatric commodities:** activities included TA for funding applications, and handover milestones to ministries of health to support the sustainability of their programmes.

In our assessment of the efficiency and efficacy of the range of TA provided, we consider the following aspects, which are reflective of good TA provision:

- **Whether the TA provided by CHAI to countries was relevant** – What was the approach used by CHAI to identify TA areas? Did it seek to address gaps? Was it country-specific? Did country-partners have a role in identifying TA needs?
- **Whether the TA was implemented appropriately** – Did the implementation of TA activities involve in-country engagement and expertise where possible? Were activities evaluated, and did they capture and incorporate lessons learned?
- **Whether the TA has generated the right impacts** – Was sustainable technical capacity built within countries to be able to function more independently post-CHAI-support? To what extent have country guidelines been updated and the paediatric HIV programme well managed (e.g. through absence of/ reduced stock-outs)?

Our assessment is based on country interviews with CHAI and MoH personnel in three countries – Kenya, Uganda and Malawi, alongside feedback received from the wider stakeholders consulted for this evaluation. This has been supplemented by a desk-based review of project plans and progress reports, although we note that the information in these documents is on activity reporting rather than results achieved such as capacity building.

Key findings are as follows:

Relevance of TA

Given the nascent and limited focus on paediatric HIV programmes in countries before the initiation of the Paediatric HIV/AIDS project, there was a clear need for TA and handholding for countries on a range of levels, and hence provision of these services by CHAI was very relevant.

While TA funding was not provided by Unitaaid under the Paediatric HIV/AIDS project, CHAI provided assistance using other resources. The project progress reporting is not clear on the extent of this TA provision, however the mid-term review of the project highlighted that the approach to identifying and monitoring TA needed improvement.⁴² Building on these findings, the IPMA project implemented a more systematic approach, wherein at the outset of the project, CHAI developed milestone activities reflecting priority areas for transition across IPMA countries. ARV milestone activities included comprehensive ARV forecast planning, ARV product optimization, inventory management system in place, and 2013 WHO guideline adoption.⁴³ EID milestone activities included comprehensive EID forecast planning, use of DBS collection bundles, and transition from manual/semi-automated to fully automated platforms. CHAI collected information on country technical capacity and practices for ARVs and EID commodities for a complete assessment of needs and gaps across countries, ranking them as phase 1 – 3 based on the level of capacity required for the specific milestone activity. These country assessments were used to understand country priorities and formed the basis of IPMA work plans for 2015 and 2016, and the phased tracking allowed for progress to be monitored against these work plans.

Country-based stakeholders reported that the relevant government ministries were heavily involved at the outset in determining the country-specific priorities for TA provision, and that TA areas were determined locally and based upon identified gaps and needs. As a country MoH representative noted: “One of the key things about CHAI’s support is they would approach the Ministry, and together we would identify areas where there were challenges, and that’s where the support would be offered. The MoH had a large role in directing support.”⁴⁴ While there were standardised methods and tools used across project countries (such as validated tools like the CHAI commodity calculator to facilitate procurement of viral load and EID commodities), TA provision was country-specific. For example, as per the project progress reports, in supporting countries with the scale-up of EID, CHAI engaged with MoHs to provide TA where needed. In Ethiopia, Nigeria, and Zimbabwe, CHAI provided TA in the design and piloting of sample transportation systems whereas in Malawi, CHAI assisted the EID laboratory testing network to strengthen data-entry and stock management.

⁴² Swiss TBH/SCIH (2012), Unitaaid Mid-term review of the “Paediatric HIV/AIDS Project” p. 12.

⁴³ WHO (2013), Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.

⁴⁴ Verbal communication by in-country MoH representative to the evaluation team, March 2018.

In summary therefore, the TA provided by CHAI was relevant and appropriate to ensuring that the ARV programme progressed as planned for under the IPMA project, with good country engagement for planning.

Appropriateness of TA implementation

While in-country government partners were closely involved in identifying the needs and gaps for TA, there was a recurring indication from non-CHAI stakeholder consultations that the implementation of TA by CHAI was largely silo-ed. This is because TA delivery came with both technical expertise and human resourcing (i.e. placement of CHAI staff within the Ministry, especially under the Paediatric HIV/AIDS project), and as such a dependency was inadvertently created within some governments. As one stakeholder stated: “Across both projects, there was a dependency by countries on CHAI for aspects like quantification and forecasting; they were seen to be taking on the responsibility and capability of the Ministries. Doing the job for months and years builds an idea that CHAI will deal with it, and there is no need for ownership by the MoH.”

An implication of this was parallel processes and systems for paediatric ART. In Malawi, for example, a separate system for the warehousing and distribution of paediatric ARVs was created even though there was an existing adult ARV programme in place. While both were eventually integrated, allowing for commodities to be managed together within one national warehouse, it was felt that there could have been an opportunity to have done this earlier.

Notwithstanding the above, it is recognised that most countries started with a very low capacity base with regards to paediatric diagnosis and treatment, coupled with high government turnover. Without additional human resources provided by CHAI, it would have been difficult for most country paediatric programmes to take off. One country MoH representative noted: “Most of CHAI’s work was really catalytic work, as we did not have the capacity to do these programmes across the country at the outset. Most of the implementing partners looked at CHAI as the technical arm with the Ministry, co-ordinating relevant partners and providing technical expertise.”⁴⁵

In terms of reviewing the appropriateness of the TA through incorporation of learning and evaluation, the project documentation does not suggest any formal TA evaluation approaches adopted by CHAI (e.g. feedback forms and surveys for the government) which may have presented a missed opportunity to continually fine-tune and improve TA provision (and is also an important limitation for our evaluation to assess quality of TA). During our interviews with country governments however, there were no issues noted on the quality of TA provided by CHAI, although it was noted that high turnover within CHAI impacted the support.

Further, the progress reporting on the TA monitored paediatric HIV programme performance through a number of standardised metrics across countries (discussed further below), rather than the efficacy of the TA itself in terms of increased knowledge and capacity-building within

⁴⁵ Verbal communication by in-country MoH representative to the evaluation team, March 2018.

government (for example, as noted, through some form of surveys from government on improvements in knowledge/ information).

Impact of the TA

We measure the impact of the TA by considering whether sustainable capacity has been built within the government and if the HIV programme has been well run/ managed.

While the phased tracking approach allowed for progress to be monitored against workplans which included capacity-strengthening milestones, as also noted, stakeholder consultations have indicated that with the TA delivery approach entailing human resource provision by CHAI, longer term sustainability was undermined. Based on consultations, there were two main issues relating to sustained capacity that could have been addressed by CHAI during the IPMA programme:

- **Earlier coordination across partners and integration with existing government structures:** In-country informants reported that ministries were working with multiple donors and procurement agents across multiple programmes operating in parallel, and that there should have been a greater commitment at the outset to harmonise the design for procurement and supply chains across commodities.
- **Strengthening institutional and not just individual capacity:** Key informants reported that a major challenge in sustaining capacity was the high level of turnover within government. A review of the TA activities reported in annual progress reports suggest that in all project countries, the TA activities focused on enhancing the capacity of individuals – predominantly through training interventions like the paediatric optimization workshops – with a smaller number of interventions focusing on developing institutional capacity (e.g. cross government department training given frequent movement between government departments). In-country stakeholders reported that they would have benefitted from a greater focus on TA handover, and establishing larger pools of expertise within Ministries to offset the shocks when individuals shifted between departments.

To some extent, the lack of or slow handover was exacerbated by a reluctance by some governments to take on programme management for either the paediatric or the adult ARV programmes given the complexity of the markets, the extent to which donors funded commodities and perceptions about the technical precision needed. However, the fact that donors appeared willing to fund TA to perform these roles meant that the pressure on national authorities – including from CHAI – to take on these responsibilities was in fact not great. An important and very different viewpoint argued by some of those consulted is that sustainability was not a priority goal in the face of the objective to eliminate paediatric HIV.

While data on how CHAI-funded full-time equivalent (FTE) staff changed over the course of the two grants was not reported on, our consultations have indicated that over time CHAI transitioned from funding embedded staff within ministries at the outset, to providing more

arms-length advisory services in recent years. Under the Paediatric HIV/AIDS project, CHAI had country teams based in country, with staff numbers dependent on the scope of work in that country. Under the IPMA project, almost no country teams had direct FTE staffing through CHAI, as agreed with Unitaid. Instead, CHAI worked with countries through a team of Regional Support Associates. A similar approach of advisory, rather than embedded TA, continues in the Unitaid-CHAI Optimal ARVs project (2016-19).

Further, while country capacity to implement various aspects of paediatric programmes have been strengthened under both projects over time (with declining FTE from CHAI), it was noted that TA needs have changed rather than diminished over time. For example, while a number of countries have the internal capacity to effectively manage procurement, undertake forecasting and develop plans for diagnosis and treatment today, support for key technical areas, such as implementing technologies or incorporating new treatment into programmes remains. As such, while capacity may have been built, in the long-term the need for TA is likely to remain. With this in mind, many countries routinely incorporate TA requirements into their funding requests to the Global Fund.

On the second aspect, judging the TA placed in countries by CHAI to support the paediatric procurement and distribution process, there are sound metrics to show clear results. For example, Table 4.1 summarises the key metrics on programme management tracked under the IPMA project, showing highly efficacious support across all project countries. The table shows that in the countries where IPMA was operational, all completed annual forecasts, most updated national guidelines, and none experienced stock-outs or had to make emergency orders to cover shortfalls.

Table 4.1: CHAI IPMA grant: Progress against TA indicators (total number of countries =26)

Indicator	2014*	2015*	2016^
Number of countries completing annual paediatric ARV forecast	24	24	25
Number of emergency paediatric ARV orders by product and country due to insufficient forecasting	0	0	0
Number of paediatric ARV stock-outs by product and country due to insufficient forecasting	0	0	0
Number of countries that updated national guidelines per WHO 2013 guidance	21	23	25

**Data not collected in Burundi and Liberia in 2014 and 2015 due to extenuating circumstances*

^Data not collected in Burundi in 2016 due to extenuating circumstances

Summary findings:

Country TA delivery by CHAI was highly relevant to paediatric ARV programme objectives and appears to have been well-delivered for highly efficacious programme management across all countries. CHAI's approach to TA under the Paediatric HIV/AIDS project entailed the placement of human resources within national health authorities to directly support programme objectives rather than specifically focus on institutional capacity building or integration of paediatric services. As a result, longer term capacity building was not prioritized and was not achieved. The context of high national turnover, a very low starting point for capacity and paediatric HIV services should be acknowledged, alongside evolving TA needs within the development of the market. Evaluation of the impact of CHAI provision of TA across the countries and over three years is significantly impeded by the lack of performance monitoring beyond metrics related to programme outputs and outcomes.

4.3. Global coordination activities

4. What was the role and contribution of CHAI in coordinating global stakeholders for the effective functioning of the paediatric ARVs market?

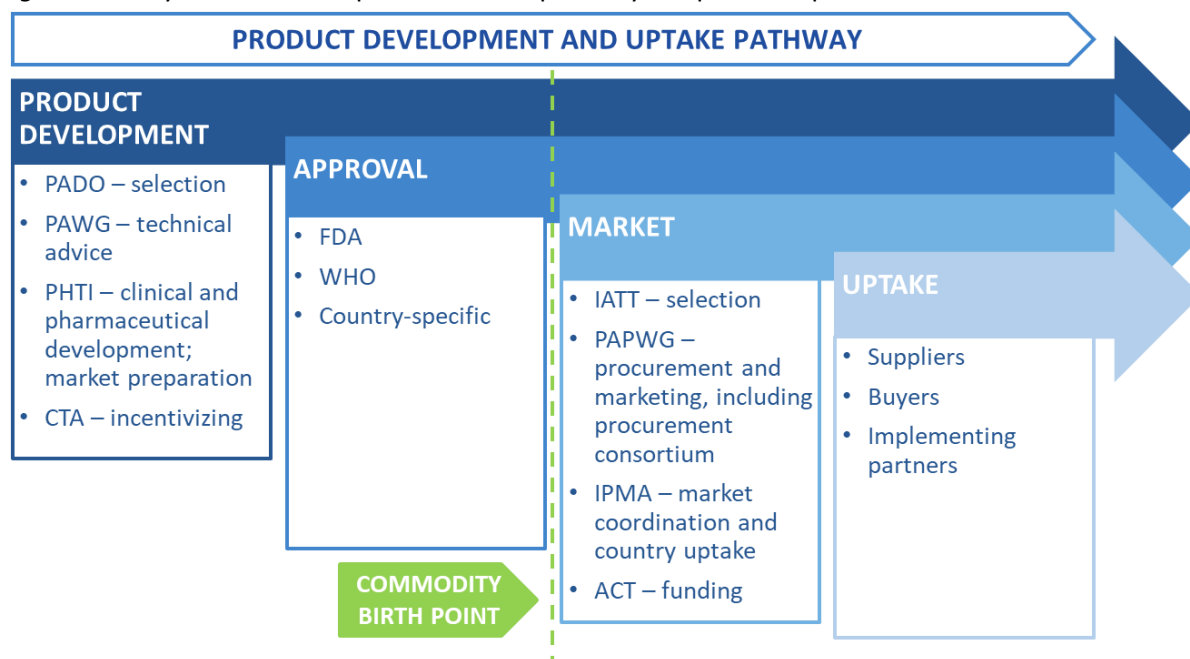
The final area of review under efficiency and effectiveness dimension is with regards to the work of CHAI in supporting global coordination efforts in the paediatric ARVs market, a role that has been largely funded through the IPMA grant provided by Unitaid. In our review, we outline the role of CHAI and provide some overarching comments on the efficacy of this role.

Mapping of key initiatives and partners in the paediatric ARVs market

To understand how CHAI worked across the global system, it is first useful to map out the main initiatives and partners in relation to the ARV development pathway (Figure 4.9). As the figure shows, there are a number of initiatives and different partners engaged at different stages of product development and uptake. CHAI itself suggests that with so many partners linked to the complex chain leading to successful and sustained uptake of paediatric ARVs, it is important that each organisation is clear about its role, its operational processes and is able to work within its mandate.⁴⁶

⁴⁶ The Global Fund (2016), Case Study – Sustaining Paediatric ARV Supply Security with the Paediatric ARV Procurement Working Group

Figure 4.9: Key initiatives and partners in the pathway to uptake for paediatric ARVs



Role of CHAI within this global paediatric ARV landscape

The two Unitaid grants provided scope for CHAI to engage right across this development and uptake pathway. At each stage, CHAI was involved as a partner, often coordinating the group, managing data and information flows, and providing technical expertise.

Table 4.2 outlines the main initiatives engaged at the global level in the paediatric ARV landscape alongside their core function and highlights CHAI’s role in relation to each.

Table 4.2: Role of CHAI in the global paediatric ARV landscape

Initiative	Function	CHAI’s formal and informal role ⁴⁷
Product Development		
Pediatric ARV Drug Optimization (PADO)	The PADO conference engages experts to establish mid- and long-term priorities for pediatric ARV drug development and to identify research gaps in ARV use in infants, children, and adolescents.	CHAI contributes by promoting evidence-based approaches and considerations to product development, sequencing, and introduction (based on its experience working in countries). CHAI provides recommendations to the WHO expression of interest that prompts drug development with the aim of ensuring that manufacturers have the best possible understanding of priority products.
Pediatric ARV Working Group (PAWG)	Set up in 2005 to work with the WHO HIV department in the development of the dosing recommendations contained in WHO ART recommendations.	CHAI is a member of the PAWG and deploys a clinical team to support the development of ARV weight band dosing recommendations, providing technical expertise on discussions around therapeutic drug exposure, drug

⁴⁷ Based on written communication from CHAI to the evaluation team, March 2018.

Initiative	Function	CHAI's formal and informal role ⁴⁷
		clearance, dosing schedules and others related matters.
Pediatric HIV Treatment Initiative (PHTI)	The PHTI was launched in 2014 with the aim to provide a platform for the exchange of information among key partners, including Drugs for Neglected Diseases Initiative (DNDi) and Medicines Patent Pool (MPP), necessary to accelerate the development of paediatric formulations in line with recommendations by the WHO, PADO and PAWG.	CHAI is a member of the PHTI and in 2015, committed to support product development, regulatory, and market introduction activities for DRV/r, DTG, and, depending on the pediatric development timeline, combination products that include TAF. CHAI supports market uptake activities for LPV/r oral pellets, as well as the forthcoming MPP-supported ABC/3TC/EFV product
The Global Paediatric ARV Commitment-to-Action (CTA) ⁴⁸	The CTA brought together leading organizations to accelerate the development and introduction of new, high-priority paediatric ARV co-formulations for first- and second-line treatment.	Founding members of the Paediatric ARV CTA included: PEPFAR, the Global Fund, and the partners forming the PHTI which include Unitaid, CHAI, Drugs for Neglected Diseases initiative (DNDi), the Medicines Patent Pool (MPP), WHO.
Market		
The Paediatric ARV Procurement Working Group (PAPWG) Now: ARV Procurement Working Group (APWG)	Following on from the CHAI Paediatric HIV/AIDS project, the PAPWG aimed to support continued global collaboration and coordination amongst key partners including through procurement, promoting optimal products and regimens to ensure the paediatric ARV market continued to grow, while remaining coordinated and responsive to country needs.	CHAI took responsibility to lead in the area of market coordination and support. It provides secretariat support to the PAPWG/ APWG which included the task of preparing the standard operating procedures of the group. CHAI has played an instrumental role in establishing the quarterly order cycles that have been fundamental to the improvements in the paediatric ARV market.
Interagency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and	Started in May 2011 under WHO to develop an optimal paediatric formulary list to serve as guidance to national programmes, procurement agencies, funders, and manufacturers. The IATT was created to respond to a concern that there would be a	CHAI was the co-chair of the Child Survival Working Group (CSWG) of the IATT (until 2017). As co-chair, CHAI supported the development of the IATT Optimal Formulary and Limited-use List, which includes the minimum number of ARV formulations needed to provide all currently recommended WHO preferred first- and second-line regimens for all paediatric

⁴⁸ Note that the CTA timespan was from 2014 to 2017.

Initiative	Function	CHAI's formal and informal role ⁴⁷
their Children (IATT)	proliferation of formulations once CHAI stopped being the main procurer of paediatric ARVs.	weight bands. The Formulary is updated regularly.

CHAI's role was also to pull together and regularly update market information in ways that made the market more transparent and visible both for suppliers, buyers, implementing partners and decision-makers. Two main vehicles were used to share market intelligence: (i) the CHAI annual ARV market report (the main publication collating ARV orders and provides prospective material, news about upcoming products and a situation analysis regarding people reached, preferred regimens and product development) and the PAPWG progress reviews (the progress review is retrospective and measures the main key performance indicators for the PAPWG/ APWG).

Efficacy of CHAI's role and work

Looking at the partnerships that were formed between 2006 and 2016 in support of the paediatric ARV arena, CHAI was the only partner present in each one (Figure 4.10). This ubiquity was both a strength and a challenge for the sector as it matured (e.g. the need for the creation of the PAPWG as CHAI stepped back as the single/ lead procurer). At the same time, all stakeholders consulted under this evaluation noted CHAI's unique role and comparative advantage being at the nexus of government, public sector procurers and funders such as the Global Fund and PEPFAR along with the private sector manufacturers – a role that no other organisation in the global architecture is able to play. Global Fund and PEPFAR in particular flagged the constraints of their organisational set-up in terms of engaging with the private sector, as compared to the position of CHAI.

Figure 4.10: CHAI's role in all initiatives

	Efforts to Accelerate Access to Pediatric ART			CTA Convening Partners					Collaborating Partners	
	CHAI	DNDI	Global Fund	MPP	PEPFAR	UNITAID	Generic Manufacturers	HMRIF	WHO	
1. Commitment to Action	●	●	●	●	●	●	●	●	●	
2. Inter-Agency Task Team (IATT)	●	●			●				●	
3. Innovation in Paediatric Market Access (IPMA)	●					●				
4. Paediatric ARV Procurement Working Group (PAPWG)	●	●	●		●	●			●	
5. Paediatric ARV Drug Optimization (PADO)	●	●		●	●				●	
6. Paediatric HIV Treatment Initiative (PHTI)	●	●		●		●			●	

Source: International AIDS Society (2016)

These initiatives, and CHAI's role within them, responded well to the complex end-to-end challenges associated with ARV development production and uptake. Some aspects of this engagement have objectively gone very well, including:

- Significant gains in stabilising the paediatric ARV market by aligning demand and supply, compiling orders, increasing visibility of the market for manufacturers, and working with countries to ensure rapid adoption of the best formulations and regimens available. Global reach of the PAPWG has increased from 49 countries in 2012 to 70 countries in 2016, and the proportion of non-essential products procured via the PAPWG decreased from roughly 30% in 2010 to only 5% in 2015.^{49,50}
- Reinforcing the market to reduce fragility, focus suppliers on optimal commodities and support the development and adoption of new products.

At the same time, CHAI identified some crucial lessons for success, especially linked to country engagement, including:

- Clear, timely information to countries to encourage new product evaluation especially for new regimens given the costs to countries not just of the products themselves but also of training health staff and possibly adjusting logistical arrangements.
- Collating cumulative orders across countries and time is a vital role that has enabled CHAI to improve information to suppliers and maintain security, minimising stock outs. Having said this, some manufacturers did note that on a number of occasions they have over-supplied as a result of inaccurate forecasts while still having to bear the cost of this production, suggesting that there were instances where forecasting could have been improved in order to minimise costs to companies alongside the broader challenge of ensuring forecast accuracy.

Underpinning these lessons is experience gained through ten years of working on strengthening access to paediatric ARVs. The engagement role that CHAI was able to take on across 26 focus countries under IPMA (and 40 countries under the Paediatric HIV/AIDS project) in turn ensured that it was constantly bringing fresh, relevant and accurate experience and feedback to its global coordination role. As CHAI notes, *“Regular communication with partners to support accurate paediatric forecasting, promote partner confidence to drive data transparency, foster healthy relationships with suppliers, and build*

⁴⁹ The Global Fund (2017), ARV Procurement Working Group (APWG): Progress Review.

⁵⁰ The Global Fund (2015), Paediatric ARV Procurement Working Group: Progress Review.

consensus on key performance indicators all proved instrumental in achieving consolidation of the fragmented paediatric market.”⁵¹

Summary findings:

CHAI has played a key role across all global initiatives and commodity development stages to coordinate the paediatric ARV market, including playing a central role in establishing some initiatives or partnerships. CHAI was the only major partner active across all initiatives. This role and contribution was unique and would have been difficult for any other organisation in the global architecture to take on. It enabled CHAI to build coherence between the stages of commodity development and implementation and would not have been possible without the Unitaid IPMA grant.

⁵¹ Based on written communication from CHAI to the evaluation team, March 2018.

5. IMPACT

Our review of the impact of the two grants is the key focus of the evaluation, encompassing an assessment of the contribution to improving public health (Section 5.1), developing a healthy market for paediatric commodities (Section 5.2), as well as the overall value for money of Unitaid's investment (Section 5.3).

5.1. Public health impact

5. What has been the public health impact of the projects?

The overarching objective of the CHAI Paediatric HIV/AIDS and IPMA projects was to increase access to HIV treatment for children. In our analysis of the public health impact of the two projects, we consider:

- In Section 5.1.1, the rate of paediatric programme scale-up, based on the number of new children on ART and EID tests conducted, as reported in the annual progress reports of the Paediatric HIV/AIDS grant. Given the scale of Unitaid's investment, the total number of children on ART in project countries has been presented against global figures on CLHIV and on ART, to contextualise the achieved results and estimate the contribution of the project in closing the paediatric HIV/AIDS treatment gap.
- In Section 5.1.2, the measurable health effects of the Paediatric HIV/AIDS and IPMA projects through estimations of the deaths averted and life years gained (LYG) as a result of the cumulative scale-up of the paediatric programme.

5.1.1. Analysis of increased coverage and scale-up

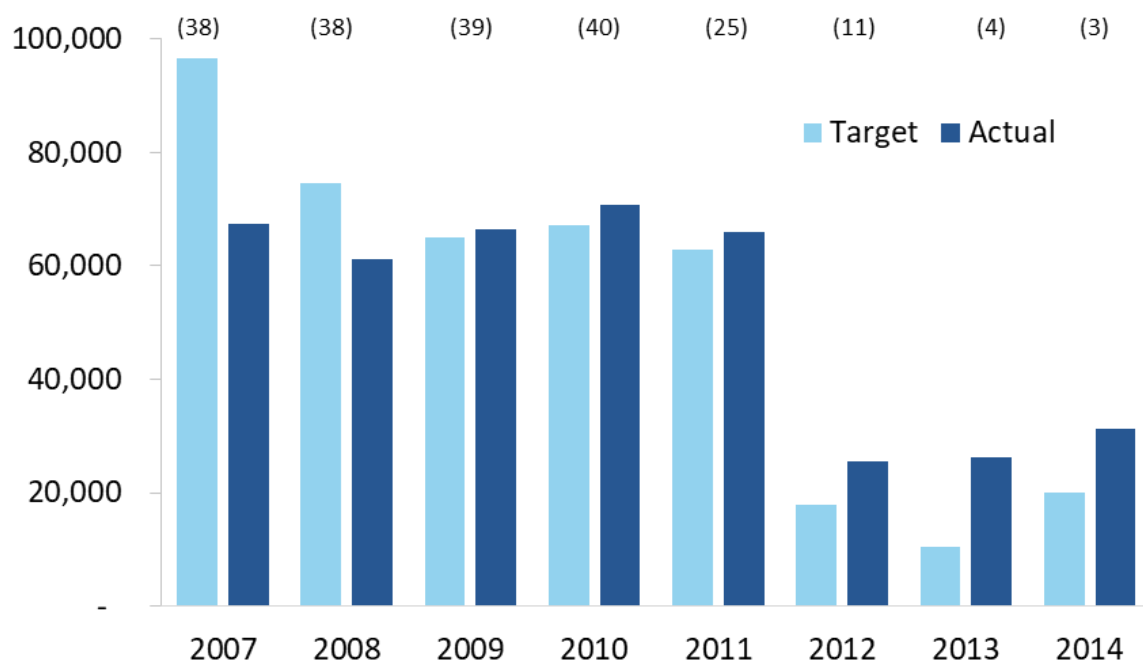
As mentioned, we look at the number of children on ART and EID tests conducted under the Paediatric HIV/AIDS project. Further treatment trends during the IPMA project years are also presented.

Number of children on ART

Between 2007 and 2014, the Paediatric HIV/AIDS project initiated a total of 431,916 children on ART across the 40 project countries. Figure 5.1 presents the target and actual number of new children initiated on ART during the project for each year, noting that the number of countries covered under the CHAI project declined after 2010 with transition of funding to other partners.⁵² As can be seen from the figure, the Paediatric HIV/AIDS project was a substantial undertaking and there was a greater than targeted achievement in most years of the project.

⁵² Actual figures represent reported figures only from countries, and in order to compare against targets we exclude annual contingency figures.

Figure 5.1: CHAI Paediatric HIV/AIDS project: treatment scale-up across project countries (value in brackets represents the number of project countries for that year)⁵³



Source: Paediatric HIV/AIDS Annual Reports 2007 – 2014

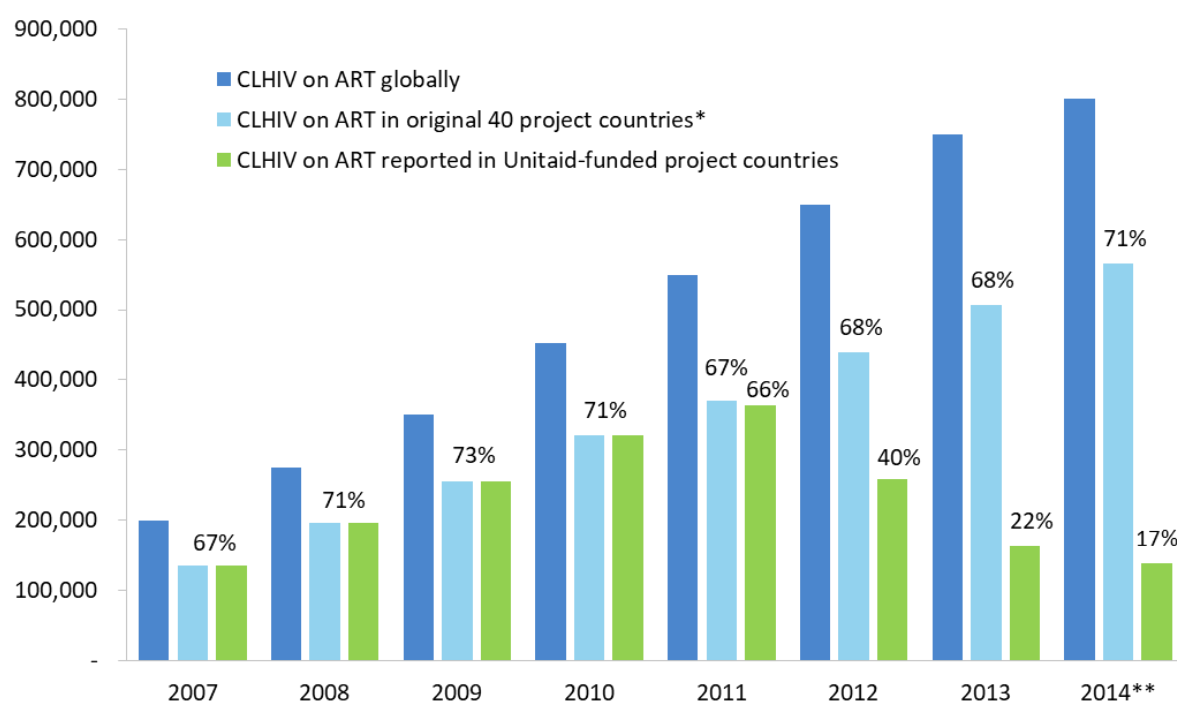
From 2009 onwards, CHAI surpassed targets on the number of new children initiated on ART in project countries, achieving as high as 2.5 times its target in 2013. In examining why targets were not met in the first two years, CHAI undertook a review where compared performance in high and low volume countries, as well as those where CHAI had a well-established presence and track-record of experience in-country. In high-volume countries that did not achieve targets, the review concluded that CHAI and Unitaids' targets could have been better informed and aligned with government targets, which had been met. Lessons were also incorporated into subsequent annual strategies and workplans. In Uganda, for example, CHAI failed to accurately assess its ability to influence implementation and delivery of care in-country. Outside of the high-volume countries, CHAI observed a dramatic difference in countries where they had prior/existing programmes in place in partnership with the government. Performance in these countries was nearly 90% compared to targets, whereas performance in those countries where CHAI had no prior experience was less than 40%. As such, we view that some of these challenges may potentially have been averted through better coordination with government and other partners for combined/ coordinated results in country.

Figure 5.2 contextualises the results achieved, presenting the global number of CLHIV on ART as compared to those in the 40 project countries. CHAI reports on CLHIV on ART in their focus

⁵³ While seven countries received funding in 2013, only four countries were set targets, which explains the numbering above the figure for this year.

countries only (which changed over time with transition of funding to other partners), so we have also sourced data on CLHIV on ART in the full 40 project countries overtime.^{54,55} The figure illustrates that: (i) the global paediatric treatment achievements were significantly attributable to the CHAI Paediatric HIV/AIDS project between 2007-10 (reflecting the high CLHIV burden countries covered by the project) and (ii) the catalytic and indirect impact of the project in supporting continually increasing treatment rates.

Figure 5.2: Global paediatric HIV treatment progress and Unitaid-CHAI project contribution⁵⁶



Source: CHAI Paediatric HIV/AIDS Annual Reports, UNAIDS Aidsinfo 2007 – 2014, UNAIDS Global Report 2010 – 2013, UNAIDS Gap Report 2014, and UNICEF Children and Aids Seventh Stocktaking Report 2016.

*Data from 2007-10 (i.e. before transition started) is the same as the CHAI reported data. We were unable to find data for most OECs countries and China in 2013 and 2014.

**2014 figures were unavailable, and hence have been estimated by taking the midpoint between 2013 and 2015 figures

While the above relates to the Paediatric HIV/AIDS project, we also consider scale-up impact through the IPMA project (which is not directly comparable to the numbers from the Paediatric HIV/AIDS project given different sets of countries covered). For the 26 project countries covered by the IPMA grant, we find that the rate of increase of CLHIV on ART was 12% from 2011 to 2012 and 17% from 2012 to 2013 (i.e. pre IPMA)⁵⁷, with a similar percentage

⁵⁴ UNAIDS Data (2017).

⁵⁵ The figures of new and total children on ART are indicated to be net of attrition in the CHAI Paediatric HIV/AIDS project progress reports.

⁵⁶ Please note that the CLHIV on ART in Unitaid-funded project countries differs from CLHIV on ART in original 40 project countries given that the number of countries that were funded by Unitaid changed over time, particularly after 2010.

⁵⁷ CEPA analysis based on UNAIDS Global Report 2012 and 2013, and UNAIDS Gap Report 2014.

increase of 17% from 2014 to 2015⁵⁸, and then increasing to 19% over 2015 to 2016⁵⁹. In total, we estimate an additional 165,850 children were started on ART over the IPMA project. This progress can be viewed to have been contributed to by the work under the IPMA grant, alongside other country and partner contributions.

Number of EID tests

EID plays a crucial role in closing the paediatric treatment gap, and between 2007 and 2014, close to 2.1m EID tests were administered in the CHAI Paediatric HIV/AIDS project countries (Table 5.1). Over the period 2007-10, as estimated by CHAI, the tests conducted met an increasing need from 9% in 2007 at the outset of the project to 38% in 2010.

Table 5.1: CHAI Paediatric HIV/AIDS project: Number of EID tests administered in project countries

Year	No. of project countries	EID tests run
2007	38	94,367
2008	38	173,837
2009	39	286,622
2010	40	372,810
2011	25	344,168
2012	11	349,364
2013	7	257,883
2014	3	220,010
Total		2,099,061

Source: CHAI Paediatric HIV/AIDS Annual Reports, 2007-2014

While figures on the number of EID sites for all years of the Paediatric HIV/AIDS grant were not reported on, there was a steady increase in the first three years with 1,300 EID sites in 2007 growing to 2,900 in 2008, and 4,600 in 2009.

5.1.2. Analysis of select public health metrics

This section considers the public health impact of the treatment scale-up described above in terms of deaths averted and life years gained. These estimations are simplified to present a rough order of magnitude and not based on detailed modelling which would be outside the scope of this evaluation.

Deaths Averted

We estimate the number of deaths averted by the initiation of new children on ART due to the Paediatric HIV/AIDS and IPMA projects through an examination of the counterfactual (i.e.

⁵⁸ IPMA Annual Report (2015).

⁵⁹ IPMA Annual Report (2016). This figure does not include Cambodia, for which data was not available.

expected deaths had the children not been initiated on treatment). This is estimated through the following calculation:

$$\text{Deaths Averted}_{\text{ART}} = \text{Expected Mortality}_{\text{ART}} \times \text{Treatment Success} \times \text{Number of Children}_{\text{ART}}$$

where:

Expected Mortality_{ART} is the mortality expected in CLHIV who are not treated;

Treatment Success is an informed estimation of treatment success; and

Number of Children_{ART} is the number of children initiated on treatment.

Newell et al. (2004) conducted a pooled analysis of mortality of HIV infected infants in Africa and found that more than one-half of HIV-infected infants will die within the first two years of life without ART. We therefore use an expected mortality rate of 50%.⁶⁰

With paediatric ART failure rates due to LTFU, adherence, and drug success ranging from 19.3% to over 32% in resource limited settings, we estimate an average of ART treatment failure rate of 26%, and therefore a value for treatment success as being $1 - 0.26 = 74\%$.⁶¹

As such, with the CHAI Paediatric HIV/AIDS project initiating a total of 431,916 children on ART across the 40 project countries between 2007 and 2014, an estimate of the deaths averted is 159,809. Further, given the CHAI IPMA project supported the initiation of 165,850 children on ART across 26 project countries between 2014 and 2016, the number of deaths averted through this programme is estimated to be 61,364. Taking both projects together (and accounting for any double counting across projects by excluding children treated under the CHAI Pediatric HIV/AIDS project in 2014), an estimated 566,512 additional children received treatment as a result of the projects, resulting in an estimated 209,609 deaths averted.

Please note these are basic estimates only and do not take into account several other factors such as varying treatment failure rates across countries and settings, other causes and interactions with other diseases impacting mortality, etc. An additional limitation in the IPMA-related calculation is that the CHAI IPMA project did not directly fund the purchase and provision of paediatric ART treatment, and therefore this estimate of deaths averted could be considered less directly attributable to the project.

Life years lived

To estimate life years lived due to ART of HIV positive children (0-14 year olds), we consider the following calculation:

⁶⁰ Newell et al. (2004), Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis.

⁶¹ Bernheimer, J. et al. (2015), Paediatric HIV Treatment Failure: A Silent Epidemic.

$$\text{YLL} = \text{Deaths Averted}_{\text{ART}}^{62} \times \text{average life expectancy}$$

UNAIDS data confirms that if ART is initiated early and taken for life, the life expectancy for patients living with HIV is estimated to be the same as that of a child not taking ART (notwithstanding treatment failure rates already accounted for in our estimates of deaths averted).⁶³ Based on WHO Global Observatory data, we have taken the weighted the average life expectancy in the 40 countries of the Paediatric HIV/AIDS project from 2015 (i.e. the year closest to the time the project ended for where there is data available), which is 62.⁶⁴ As a simplification, we do not make any further adjustment for age at which treatment is commenced—effectively assuming that deaths are averted at age 0.

Therefore, with 431,916 CLHIV initiated on ART under the Paediatric HIV/AIDS project results in 9.8m YLL. For IPMA, data suggests that the additional 165,850 children were initiated on treatment in the 26 project countries over the project period. Given a weighted average life expectancy for the 26 countries of 58 in 2016, we estimate a YLL figure of 1.2m. Taking both project figures (and adjusting figures to avoid double counting for 2014) gives a total figure of 10.3m YLL. These estimation does not distinguish between the age of receiving ART given this data is not provided in the CHAI progress reports, amongst several other simplifying assumptions.

Summary findings:

The public health impact of the Paediatric HIV/AIDS project is directly observable through 431,916 new children initiated on ART in the 40 project countries over the period 2007-14, resulting in an estimated 159,809 deaths averted and 9.8m years of life lived. The indirect impact of the treatment scale-up through this project and continued work under the IPMA grant is reflected in 165,850 more children being treated, 61,364 deaths averted and 1.2m years of life lived during the implementation of this project, to which both projects can be viewed to have made a substantial contribution. Taking both projects together (and accounting for any double counting across projects), an estimated 586,046 additional children received treatment as a result of the projects, resulting in an estimated 209,609 deaths averted and 10.3m life years gained.

5.2. ARV market impact

6. How has the project contributed to developing and sustaining a healthy market for ARVs, including the impact on prices, suppliers and introduction of innovative products?

The overall aim of the two projects was to create and sustain a healthy market for paediatric HIV treatment. A healthy market can be characterised as one where barriers to entry are low

⁶² From previous calculations.

⁶³ UNAIDS (2017), The power of antiretroviral medicines - 90-90-90 treatment for all.

⁶⁴ WHO (2018), Global Health Observatory Data.

and a sufficient number of suppliers and buyers are operating in a market where high quality products are provided at competitive prices.

The Unitaid-CHAI projects have been instrumental in creating a market for paediatric ARVs that previously did not exist, with all stakeholder consultations for the evaluation emphasising the path breaking work through these projects. The focus of the projects was in ensuring that a sufficient number of suppliers for optimal products were available to supply ARVs, particularly generic manufacturers, and at reduced prices; and while ongoing market challenges remain with the niche and the long-term shrinking market that characterises paediatric ARVs as well as constant innovation for new and optimal products, it is clear that the work undertaken by CHAI has had a critical and lasting impact in creating an improved market for paediatric ARVs.

We have undertaken a detailed review of a number of key ARVs procured as part of the Paediatric HIV/AIDS project and assessed how the market for these products has evolved over time in terms of supply base and prices (see Figure 5.3 below).⁶⁵ Our selection of ARVs for review was guided by a number of factors, including the extent to which they were procured under the Paediatric HIV/AIDS project, their inclusion in WHO guidelines or in the IATT Optimal ARV lists. The figure shows the share of the key commodities by volume and value.^{66,67} In particular:

- The AZT+3TC+NVP-based formulations accounted for more than a quarter of all project procurement by volume and value. The paediatric dispersible tablet formulation (60mg+50mg+30mg) accounted for the vast majority of AZT+3TC+NVP procurement, accounting for 24% and 23% of procurement by volume and value respectively.
- Other FDCs included in the project include AZT+3TC and ABC+3TC, accounting for a further 9% and 11% of all procurement by volume and value respectively. For AZT+3TC, 80% and 60% of project procurement by volume and value respectively was

⁶⁵ An important point to note regarding our analysis of prices and supply to the market is that this has largely been based on analysing data submitted to the GPRM. Some transactions may not have been submitted to the GPRM, and as such the analysis may not have captured the full picture regarding market trends, particularly for procurements in 2017.

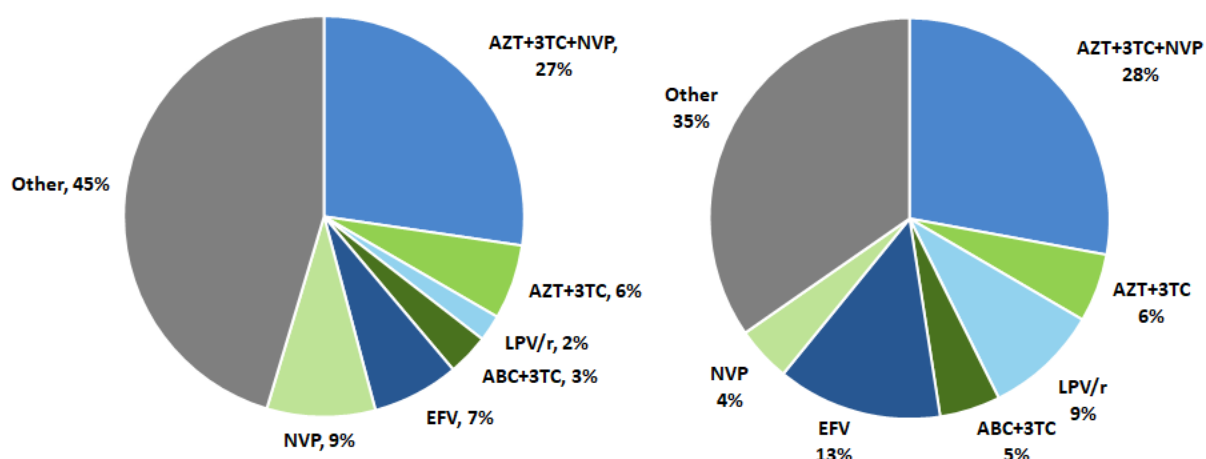
⁶⁶ The following individual ARVs and formulations were included in the analysis: AZT+3TC+NVP (300mg+150mg+200mg oral tablets and 60mg+30mg+50mg oral tablets and dispersible tablets); AZT+3TC (300mg+150mg and 60mg+30mg oral tablets); LPV/r (200mg+50mg and 100mg+25mg oral tablets, 40mg+10mg oral pellets and 80mg/ml+20mg/ml oral solution); ABC+3TC (60mg+30mg oral and dispersible tablets); EFV (200mg, 100mg and 50mg oral tablets); and NVP (200mg;100mg;50mg and 20mg oral and dispersible tablets; 50mg/ml oral suspension and 100mg extended release oral tablet. More detailed analysis was undertaken on specific formulations that accounted for a significant amount of procurement of individual ARVs.

⁶⁷ One point that should be noted is that annual procurement of some key ARVs changed significantly over time. For example, during the early years of the project d4T-based FDCs were one of the key commodities procured, however their procurement declined in later years, while paediatric formulations of AZT+3TC+NVP became far more important in project procurement once they were introduced into the market in 2008.

for paediatric formulations, while paediatric formulations accounted for all ABC+3TC procurement.

- While only accounting for 2% of procurement by quantity, the protease inhibitor (PI) LPV/r represented 9% of procurement by value, demonstrating that the price of this ARV was high relative to its volume. LPV/r was reviewed due its importance in first and second-line treatment as well as the relatively unique market dynamics associated with it (see Annex G for more details).
- The two key non-nucleoside reverse transcriptase inhibitors (NNRTIs) efavirenz (EFV) and NVP accounted for 16% and 17% of project volume and value respectively.
- Overall, the various formulations of these ARVs accounted for 55% of procurement volumes and 65% of procurement by value, demonstrating their importance on the project (and thereby justifying our focus on this selection).

Figure 5.3: Key ARVs procured by volume (left) and value in US\$ (right)



Source: CEPA analysis based on project procurement data.

We consider market impact through a review of the evolution of the following parameters:

- increase in supplier base for key paediatric formulations based on number of new suppliers approved through US Food and Drug Administration (US FDA) and/ or the WHO Prequalification Team: medicine (WHO PQ) (Section 5.2.1);
- the extent to which the supply/ procurement base has been concentrated or diversified as well as extent of generic versus innovator supply (Section 5.2.2); and
- the extent of decline in prices (Section 5.2.3).

5.2.1. Increase in supplier base for key paediatric formulations

One of the main market objectives for the two projects was to improve the supply base for key paediatric ARV formulations, including greater use of FDCs in paediatric treatment programmes as well as ensuring countries effectively transitioned to optimal ARV treatments.

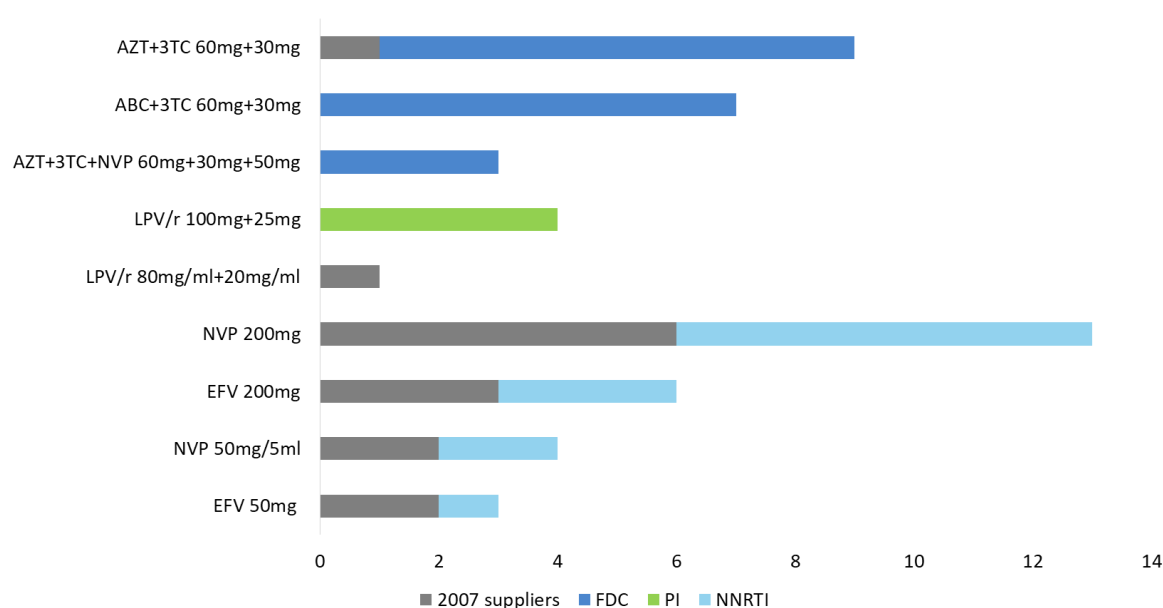
Prior to Unitaid support, the paediatric ARV market consisted mainly of syrup-based treatments that required children to take multiple foul-tasting doses every day. In addition, the supply base for key drugs was relatively limited, for example:

- Paediatric triple FDCs were very limited, with d4T+3TC+NVP formulations only just coming to market while paediatric AZT+3TC+NVP formulations were not yet available. Key paediatric double FDCs were also not widely available on the market.
- LPV/r formulations were only supplied by the innovator company (Abbott, later AbbVie), was only available as a liquid syrup for that could be used to treat children and was considerably more expensive than other ARVs used for second-line treatment or NNRTIs used in first-line treatment (especially NVP).
- Relatively few generic suppliers were approved by SRAs to supply EFV formulations.
- While a number of suppliers were approved to supply the 200mg of NVP (also used to treat adults), only one generic company had obtained approval for the liquid formulation that could be used in children, while paediatric tablet formulations were not available.

The pooled procurement approach, coupled with CHAI's country-based activities that ensured demand was created for paediatric ARVs, were essential for stimulating suppliers to enter these markets. CHAI also played an important role in supporting generic companies with obtaining SRA through the work of the Drug Access Team (DAT). As a result of this, the supplier base for some key paediatric formulations of ARVs increased under the project. As shown in Figure 5.4 below:

- The number of suppliers of key FDC formulations increased substantially, particularly for double FDCs.
- The supply base for paediatric formulations of LPV/r also increased over the course of the project. However, for liquid forms of the ARV, the supply base has not changed, with AbbVie being the only supplier for this formulation given that Cipla ceased production to focus on its 40mg+10mg oral pellets.
- The supply base for key NNRTIs also increased over the course of the project, although growth in the number of eligible suppliers for paediatric-specific formulations did not increase at the same scale as those that can be used in both adults and children (e.g. NVP 200mg suppliers increased faster than NVP 50mg/5ml suppliers).

Figure 5.4: Change in suppliers with US FDA or WHO PQ approval for key formulations (2007-17)



Source: Paediatric HIV/AIDS and IPMA Annual Reports; CEPA analysis of US FDA and WHO PQ databases.

For the above commodities, the average number of suppliers with US FDA or WHO PQ approval was six in 2017, a significant increase from just three in 2007 for the ARVs that were available at the time – signifying greater market competition.⁶⁸ In addition, some commodities were not even available on the market, particularly the paediatric versions of AZT+3TC+NVP, LPV/r and ABC+3TC, which have been key regimens for treating children in low-income countries over the years. While not shown in the above figure, a range of suppliers also obtained regulatory approval for single formulations of ARVs as well as key FDCs that have been largely phased out of treatment programmes since the Paediatric HIV/AIDS project, such as d4T-based FDCs.

Improved paediatric formulations have continued to enter the market during the implementation of the IPMA project and beyond, including the 40mg+10mg oral pellet for LPV/r, (which has seen considerable uptake in lower income markets, also resulting in a number of supply constraints) and the ABC+3TC 120mg+60mg (which is expected to form an important part of treatment programmes given its lower pill burden than the 60mg+30mg version). Further innovation for improved paediatric formulations is also continuing including the ABC+3TC+LPV/r “4-in-1” FDC for treating children younger than three, the ABC+3TC+EFV FDC for treating children aged three to ten and dolutegravir (DTG) and darunavir/ritonavir (DRV/r) formulations for children. These can be viewed as indirect longer-term impacts of the market catalysing initiated through these projects, and continuing to be supported through further CHAI and other partner contributions.

⁶⁸ Data based on analysis of WHO PQ and US FDA databases, plus data included in project Annual Reports.

5.2.2. Diversification of suppliers and generic supply

We have assessed the extent to which the increase in supply has translated into wider diversification in suppliers as well as supply by generic manufacturers. This analysis has covered the key paediatric commodities mentioned above in Table 5.1 (and also includes different formulations and doses for these ARVs), and details of this analysis for each commodity are provided in Annex G.

Table 5.2 below summarises our findings with regards to supply of different commodities and how this changed over time. Specific findings worth noting include:

- Largely concentrated supply/ procurement:** Both under the Paediatric HIV/AIDS project procurement and wider procurement in low and lower-middle income countries as reported in the GPRM database, supply has been fairly concentrated for several ARVs including AZT+3TC+NVP and ABC+3TC. The limited number of suppliers was mainly as a result of limited uptake of registration of suppliers by a stringent regulatory authority (SRA) or WHO PQ. However, products such as the paediatric version of AZT+3TC+NVP accounted for nearly a quarter of the cost ARVs procured under the project, and in the latter years exceeded 50%. While the challenge of bringing in new suppliers is well noted, given the importance of such commodities, further support to increase competition for these commodities during their initial years on the market may have been warranted (noting the more diversified supply that was eventually realised). Further, some of the NNRTIs have had a wider supply base, yet procurement has still been concentrated amongst a few suppliers. Only AZT+3TC procurements have been from multiple suppliers. Concentrated supply for select ARVs and their formulations is a continued issue tracked by the PAPWG/ APWG.
- Increasing generic supply replacing innovators:** While innovators for several ARVs were key suppliers in the market, they have largely been absent for several years, specifically for ABC+3TC, AZT+3TC, EFV and NVP. For AZT+3TC+NVP, while no innovator companies supply this drug, the market has been dominated by a handful of suppliers, particularly Mylan (previously Matrix Laboratories before it was acquired by Mylan). The key exception is LPV/r, where supply has been dominated by AbbVie (previously Abbott Laboratories), which is a result of lower access prices being offered in lower income markets.

Table 5.2: Summary of findings regarding ARV supply

ARV	Paediatric HIV/AIDS project supply and wider supply in low/ lower middle income countries
AZT+3TC+NVP	<ul style="list-style-type: none"> FDC supplied only by generic manufacturers, given patent restrictions on individual drugs limiting extent to which innovators can supply the market. Primary supply on project dominated by Matrix Laboratories, representing 88% of total procurement. Cipla was also secondary supplier.

ARV	Paediatric HIV/AIDS project supply and wider supply in low/ lower middle income countries
	<ul style="list-style-type: none"> • Matrix/Mylan has also dominated wider supply for the paediatric version of the product, with Cipla and Strides also being key suppliers in low/lower-middle income markets in more recent years.
AZT+3TC	<ul style="list-style-type: none"> • FDC supplied by a wide number of manufacturers, both on the project and more widely. • Key project suppliers included Cipla, Matrix Laboratories/Mylan, Hetero and Aurobindo. • Despite GSK (the innovator supplier) being the main supplier to the initial market, generic companies have been the sole suppliers in the market since 2008.
LPV/r	<ul style="list-style-type: none"> • Unlike other paediatric ARVs, the supply of LPV/r has been dominated by Abbott Laboratories/AbbVie, particularly the liquid version of the product, both on the project and more widely. This is due to the low access prices offered by AbbVie for the drugs in the lower income markets. • Aurobindo has been a key supplier in low and lower-middle income markets for LPV/r, in particular for tablet versions of the product.
ABC+3TC	<ul style="list-style-type: none"> • Supply both on the Paediatric HIV/AIDS project and wider procurement in low and lower-middle income markets for paediatric versions of ABC+3TC has been dominated by Cipla and Mylan/Matrix Laboratories, with limited procurement from other suppliers. • No supply from GSK, the innovator of the FDC, has been provided in low and lower-middle income markets for the paediatric version of the ARV.
EFV	<ul style="list-style-type: none"> • Merck & Co (the innovator company) was the major supplier of EFV formulations during the early years of the project, while in later years this was replaced by Strides, particularly after 2010. • While Merck & Co was an important supplier between 2004 and 2010, there were a relatively large number of suppliers on the market. However, in more recent years Strides has dominated the market.
NVP	<ul style="list-style-type: none"> • Supply of NVP has been relatively diversified, especially for the 200mg version of the ARV. • Prior to the Paediatric HIV/AIDS project, Boehringer Ingelheim were a key supplier. However, this reduced considerably after 2006. • The main generic suppliers were Aurobindo, Cipla and Hetero.

Source: CEPA market analysis based on project procurement data and GPRM

5.2.3. Decline in prices

As regards to prices, the table below highlights how these have varied over time for key ARVs procured on the project in terms of PPPY. As Table 5.3 shows:

- Since 2004 (or when certain ARVs came onto the market), prices have declined across all ARVs reviewed, with percentage changes ranging from 35%-85%. Particularly noteworthy price declines include significant declines in paediatric formulations of

ABC+3TC, as well as drops in oral versions of LPV/r and NVP, despite the former having limited levels of competition in the market.

- For ARVs procured before the start of the Paediatric HIV/AIDS project, most had already experienced significant price declines. The exception to this was the EFV 50mg tablet, which experienced an increase of 38% over this period.
- Between 2006 and 2010, the main years of the Paediatric HIV/AIDS project before transitioning took place, the majority of ARVs reviewed also experienced significant reductions in treatment costs. The exception to this is the liquid formulation of LPV/r, however this price increase reflects a one year increase in average prices linked to extremely high prices in a handful of countries (possibly linked to emergency supply requirements).
- Prices have also continued to fall since 2010 when Unitaid transitioned from being the major purchaser of ARVs. The only exception to this was the oral version of NVP, which has experienced a treatment cost increase of 27%.

Table 5.3: Changes in average treatment costs PPPY for key ARVs in low and lower-middle income countries (green and red denote reduction and increase respectively)

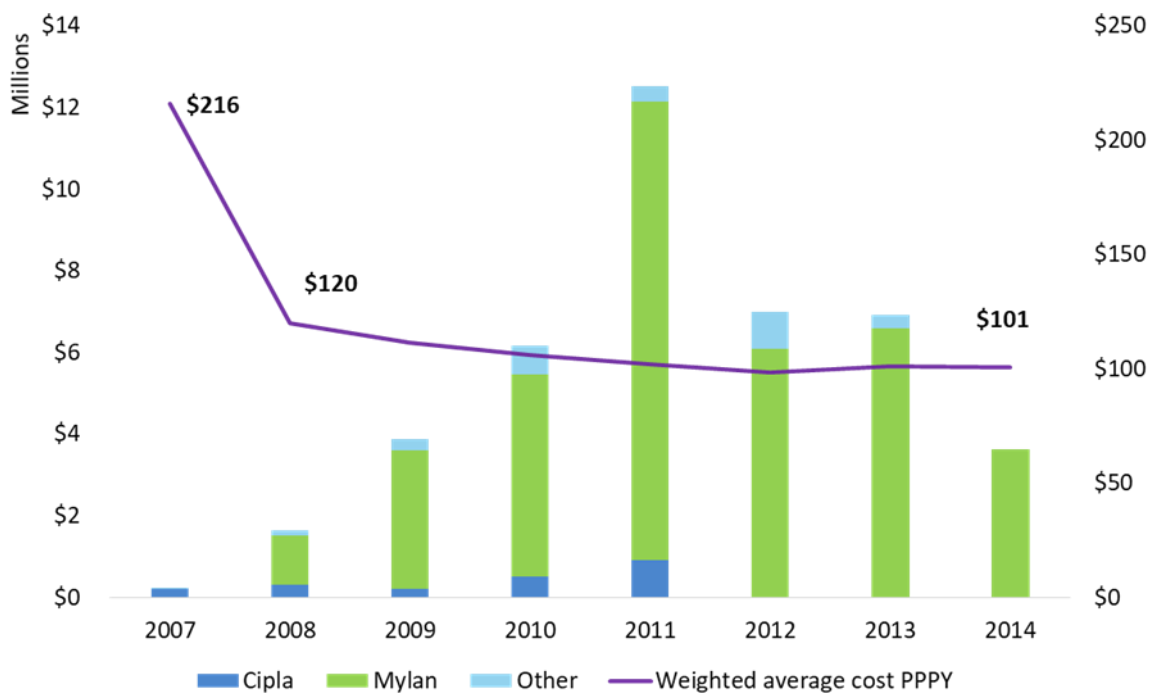
Key ARVs	PPPY				Percentage changes			
	2004	2006	2010	2017	04-06	06-10	10-17	First year – 17
Procured prior to 2006 ⁶⁹								
LPV/r 80mg/ml+20mg/ml	US\$918	US\$395	US\$671	US\$171	57%	180%	75%	81%
EFV 200mg	US\$134	US\$90	US\$42	US\$33	33%	49%	22%	75%
EFV 50mg	US\$120	US\$166	US\$113	US\$53	38%	22%	53%	56%
NVP 200mg	US\$153	US\$63	US\$46	US\$23	59%	35%	23%	85%
NVP 50mg/5ml	US\$405	US\$146	US\$67	US\$85	64%	57%	27%	79%
Procured since 2007	2007		2010	2017	07-10		10-17	First year – 17
LPV/r 100mg+25mg	US\$216		US\$179	US\$140	17%		21%	35%
Procured since 2008	2008		2010	2017	08-10		10-17	First year – 17
AZT+3TC+NVP 60mg+30mg+50mg	US\$114		US\$101	US\$73	22%		53%	36%
AZT+3TC 60mg+30mg	US\$102		US\$73	US\$47	35%		23%	54%
ABC+3TC 60mg+30mg	US\$471		US\$154	US\$96	57%		27%	80%

⁶⁹ Please note that GPRM data dates between 2004 and 2017, and therefore prices for ARVs that were procured prior to 2004 have not been included.

Source: CEPA analysis based on GPRM database

While the project was important for securing price declines, it is noted that prices remained relatively stable for a number of key FDCs. For example, Figure 5.5 below shows how Mylan remained the key supplier of AZT+3TC+NVP during the implementation of the project, and during this time prices (shown here on a weighted average basis) remained relatively stable following a significant fall in the first year of procurement.

Figure 5.5: Left axis: AZT+3TC+NVP project purchases by supplier (US\$m); Right axis: Weighted average treatment cost PPPY (US\$)



Source: CEPA analysis, based on project procurement tracker and GPRM database

A similar trend was also observed for ABC+3TC (details can be found in Annex G), which further suggests that it was difficult to reduce prices further for some key FDCs. This is not a criticism of the project but more a reflection that in some cases it may have been difficult for CHAI to balance short-term price reductions with long-term sustainability of the market for particular FDCs. It should also be noted that single formulations did not display a similar pattern where demand was often met by more than direct project procurement.

A final key point to note is that following the Paediatric HIV/AIDS project, data suggests that supply and prices tended to follow a similar trend to those experienced on the project. For example, despite some short-term variation in price and supply for some products (in particular LPV/r), the prices for other ARVs have continued on a downward trend or remained stable. This suggests successful transition from Unitaaid funding, and many consultees have noted that the PAPWG/APWG has been important for ensuring that these trends have continued.

Summary findings:

The Paediatric HIV/AIDS project was essential for catalysing and strengthening the market for ARV treatment for children. This is evident from CHAI's success at supporting the introduction of key paediatric formulations, including FDCs and paediatric PIs that did not exist before the project, highlighting the project's support for catalyzing innovation. While some ARVs have remained concentrated in a handful of suppliers, the supply base in general has become significantly more diversified over time, with price reductions of between 35% and 81%.

5.3. Value for money

7. Does the project provide value for money?

Proposed metrics to demonstrate VfM of the projects include:

- **Return on investment (ROI)** – which compares the monetary value of the public health benefit (in this case deaths averted) with the project costs.
- **Financial savings from price reductions/market consolidation** – based on the assessments of the project impact on commodity price and in turn treatment cost reduction.

We discuss our methodology and the results for each aspect in turn below.

5.3.1. Return on investment

The ROI analysis aims to capture the benefit achieved per dollar of investment made.

With regards to cost, we have made the following assumptions:

- For the Paediatric HIV/AIDS project, we have used actual project cost data, which includes costs for treatment, diagnostics, OI drug costs and laboratory equipment purchased with Unitaid funds.
- For IPMA, we have included costs associated with delivering the project. However, to provide a more accurate reflection of total costs, we have also estimated treatment costs for children initiated on ART in the 26 IPMA countries during the implementation of the project. To estimate these figures, we have taken the estimated total paediatric ART market size in US dollars as estimated in the CHAI market reports and multiplied this by children on ART for the project countries as a percentage of the number of children on ART globally. We then divided the total number of children on treatment in the project countries by this estimated market size/ treatment cost in project countries, to get cost per treatment, and multiplied this amount by the number of children initiated on ARTs to obtain the final estimated cost of treatment for children initiated during the project. We have also included non-treatment costs (diagnostic, OI drug costs, RUTF etc.) in our estimations, which we have calculated using actual

data from the Paediatric HIV/AIDS project to derive non-ARV costs as a proportion of ARV costs, and then multiplied these by the ARV costs estimated for IPMA.

- In addition to the above costs, we have also included additional health systems costs. This approach was taken in the Lancet Global Health 2035 report published in 2013, where the authors included costs for specific health programmes (reproductive maternal, newborn and child health (RMNCH), malaria, TB and HIV/AIDS) as well as health systems costs (which includes programme management HR costs, infrastructure, health information systems, governance and health financing costs) for a number of low- and middle- income countries.⁷⁰ To derive estimated health systems costs, we have taken the ratio of HIV/AIDS programme costs to health systems costs estimated in the Lancet Global Health 2035 report for all countries in 2015, and divided this by the programme costs for the Paediatric HIV/AIDS and IPMA projects (which includes Unitaid costs as well as other estimated costs).
- Finally, total costs were converted into real terms using the World Banks GDP deflator figures for the United States.

To estimate benefits, we have drawn on calculations by the Lancet Commission which suggest that, in LICs and MICs, the value of a life-year is about 2.3 times GDP per capita.⁷¹ The Commission's calculations were based on asking people how much they would be willing to pay to reduce their risk of dying, and observing how much people actually get paid for risky occupations. The assumptions underlying this figure have been debated in the literature⁷², but we consider it to be a reasonable first approximation. We use a weighted average of GDP per capita across all low and lower-middle income countries, which is multiplied by previously noted estimates of life-years lived (see section 5.1.2).

The ROI figures for the two projects are reported in Table 5.4 below, which reports average annual figures for the two projects.⁷³ For this analysis, we have calculated ROI as the difference between costs and benefits divided by costs.

As these figures show, the projected benefits derived from initiating children on treatment significantly outweighed costs, with ROI figures suggesting that for each dollar spent an estimated US\$9 of benefits were realised for the Paediatric HIV/AIDS project and US\$29 for IPMA. Taking the two project costs and benefits together, **we estimate a ROI of US\$11**. While this figure may appear high (particularly for IPMA), the Lancet Global Health 2035 report estimated a ROI of US\$9 for low income countries and US\$20 for lower-middle income

⁷⁰ D Jamison et al. (2013) Global Health 2035: A World Converging Within a Generation. For the methodology used to estimate costs, please see Annexes 4 and 5, which can be found in a separate document and spreadsheet [here](#) and [here](#).

⁷¹ D Jamison et al. (2013) Global Health 2035: A World Converging Within a Generation. For the methodology used to estimate benefits, please see Annex 3, which can be found in a separate document [here](#).

⁷² A Chang et al. (2017) Economics in "Global Health 2035": a sensitivity analysis of the value of a life year estimates.

⁷³ The Lancet Global Health 2035 report also reports average annual figures, as opposed to total cost and benefit figures.

countries, suggesting that the overall figure for the two projects is broadly aligned with these calculations. It should also be remembered that these figures compare costs incurred during childhood with whole-of-life benefits. ROI would be lower if the cost of continued ARV treatment during adulthood was included.

Table 5.4: ROI for Paediatric HIV/AIDS and IPMA projects

#	Category	Paediatric HIV/AIDS	IPMA
Costs (annual)			
1	Unitaid average project costs (actual)	US\$45m	US\$3m
2	Treatment & non-treatment cost for new patients (IPMA only)	included in above figure	US\$15m
3	Assumed health systems cost (nominal)	US\$373m	US\$129m
4	Total expenditure (nominal)	US\$418m	US\$148m
5	Total expenditure (2010 US\$)	US\$420m	US\$159m
Benefits (annual)			
6	Deaths averted (average annual)	19,976	20,455
7	Life expectancy (weighted average)	62	58
8	Life years lived (row 6 * row 7)	1,228,692	1,183,039
9	GDP per capita (2010 US\$)	US\$1,505	US\$1,769
10	Value of a life year gained, as multiple of LMIC/LIC GDP per capita	2.3	2.3
11	Value of mortality reduction (row 8 * row 9 * row 10)	US\$4,167m	US\$4,802m
12	ROI ((row 11 – row 5) ÷ row 5)	US\$9	US\$29

Source: CEPA analysis; World Bank World Development Indicators; D Jamison et al. (2013).

Note that figures have been rounded.

As noted above, these figures rely on making a number of assumptions. In particular, costs associated with delivering health systems for both projects have been taken as indicative figures and may be higher or lower than reported, as well as treatment and non-treatment costs for IPMA. As such, these estimations should be interpreted as indicative. However, based on comparing ROI figures with similar estimations that have been undertaken, and given the nature of the interventions, we believe these figures are an appropriate estimation of the magnitude of the benefits accrued from these projects.

5.3.2. Financial savings

Another way to present VfM is to compare the financial savings from price/ treatment costs reduction with the investment provided to the projects.

Our calculation of financial savings as a result of the project interventions draws on approaches taken by CHAI to estimate savings brought about through introducing new suppliers for the 200mg+50mg formulation of LPV/r, wherein they estimated that as a result of splitting tenders, generic suppliers were able to bring cost down to levels offered by the originator company, and such competitive pressures resulted in originator price reductions that afforded US\$7.3m in cost savings.⁷⁴

Following a similar approach, we have estimated the financial savings as a result of price reductions on key paediatric ARVs discussion in Section 5.2 between 2006 and 2016, comparing what costs would have been for treating the given number of patients with treatment costs that were realised (using 2006 as the reference year or the first year products were available if ARVs came onto the market later). Key sources of information for this analysis include:

- **Figures for children on ART in generic-accessible LMICs:** Based on figures provided by UNAIDS.
- **Market share estimations of key paediatric NRTIs and NNRTIs/PIs:** Drawing on data from the Paediatric HIV/AIDS project, CHAI ARV market reports and data from the PAPWG procurements.
- **Treatment costs in PPPY:** Based on data from the GPRM for key paediatric formulations.

From this analysis, we conclude that price reductions have resulted in **total cost savings of an estimated US\$821m**, showing that substantial cost savings have been brought about by the significant price reductions realised since the commencement of the Paediatric HIV/AIDS project. Taking the total project cost of both projects, this analysis suggests that **for every US\$1 spent by Unitaid, US\$2.22 of cost savings have been realised**. Given price reductions were realised for other ARVs procured, this is likely to under-estimate the full cost savings from all paediatric ARVs.

Summary findings:

The Unitaid-CHAI Paediatric HIV/AIDS and IPMA projects have undoubtedly delivered value for money in relation to the money invested. In terms of return on investment as a result of deaths averted, we estimated that for every dollar invested (both by Unitaid and other partners) US\$11 of benefits were realised. In addition, for every US\$1 invested by Unitaid through the two grants, financial savings of US\$2.22 were realised as a result of price reductions for key paediatric ARVs.

⁷⁴ CHAI (2012), Overview of Tendering Best Practices.

6. SUSTAINABILITY AND SCALABILITY

8. How effective were the grants in ensuring that funding and support was sustained and scaled up following the conclusion of the grants, including transitioning support to other partners?

We consider the extent to which sustainability considerations were addressed under both grants for longer-term scalability, as well as briefly present wider paediatric ARV market challenges going forward.

6.1. Sustainability of grant funding

6.1.1. Paediatric HIV/AIDS grant

As discussed previously, the Paediatric HIV/AIDS project was initially conceived as a two year investment only, aimed at treating 100,000 CLHIV in 2007 and 200,000 in 2008 across 40 countries. However, the Unitaid Board decided to continue funding paediatric treatment given the strategic importance of the grant to the organisation. After 2010, Unitaid began to transition funding for commodities procured under the Paediatric HIV/AIDS project to other key partners. This included:

- **The Global Fund:** As part of its 23rd Board Meeting in 2011, the Global Fund set out a “market shaping” strategy in which procurement of paediatric ARVs was stated as a key priority in order to avoid gaps in funding treatment following the conclusion of the Unitaid project. As mentioned, one action that Global Fund took was to establish the PAPWG, in which CHAI played an important technical role. Additional interventions that Global Fund set out in this strategy was to seek joint product introduction programmes with Unitaid, given the role of the latter in market shaping for new products and the role of the former in bringing products to large scale, as well as streamlining product selection, which resulted in the establishment of the IATT optimal products list.⁷⁵ The Global Fund was the primary entity responsible for taking on the transitioning of funding, and by 2013 accounted for 45% of funds for paediatric commodities.⁷⁶
- **PEPFAR:** While PEPFAR was not a major purchaser of paediatric commodities during the initial years of the implementation of the Paediatric HIV/AIDS project, it was a key contributor to service delivery for paediatric care and treatment in its priority countries. However, as part of the transition away from Unitaid funds it became a key contributor to procuring commodities in Rwanda, Guyana, Namibia, Vietnam, Botswana, Nigeria, Haiti, Tanzania and Uganda once full transition had taken place. By 2013, PEPFAR accounted for 12% of funding for paediatric commodities.⁷⁷ In addition,

⁷⁵ The Global Fund (2011), Report of the Market Dynamics and Commodities Ad-hoc Committee.

⁷⁶ CHAI (2014), IPMA Project Plan.

⁷⁷ Ibid.

following full transition of funding, PEPFAR in collaboration with CIFF, launched the Accelerating Children's HIV/AIDS Treatment (ACT) Initiative between 2014 and 2016, which enabled 562,000 children to receive ART in nine high-priority countries in Sub-Saharan Africa.⁷⁸

- **National governments:** In a number of countries governments became either primary or co-funders of paediatric programmes, which included China, OECS (through a pooled procurement mechanism for the states), PNG, Namibia, Botswana, Senegal, India, Swaziland and Zimbabwe. Overall national governments accounted for 28% of the paediatric commodities market in 2013, with South Africa accounting for 21% alone.⁷⁹

As part of transition arrangements, CHAI played an important role in supporting countries, such as incorporating paediatric commodities into their Global Fund applications, and also worked with funders and procurement agents at the global level to ensure supply was not interrupted.

Despite full transitioning of the ARVs eventually taking place, many have noted that this was the most fundamental challenge faced as part of the project. For example:

- At the outset and during the early years of implementation, transitioning of funding from Unitaid was not considered, given the initial priority (“emergency”) of putting children on treatment.
- When it did come to transitioning, many consultees have noted that other partners felt that Unitaid strategic priorities were being shifted onto them, with little consultation or consideration of other ongoing priorities and issues.
- In some cases, without Unitaid funding continuing some countries simply would not have been able to fund paediatric commodities, and as a result CLHIV would no longer have been treated.
- Coupled with these issues, the timing of transitioning away from Unitaid funding coincided with wider funding issues being faced by other partners, particularly the Global Fund who had to cancel majority of its funding under Round 11 on account of many donors pulling funding to the organisation.

As a result of the above issues, transitioning of Unitaid funding over the Paediatric HIV/AIDS project lasted over four years, with the final three countries (Uganda, Malawi and Mozambique) transitioning from project funding after 2014. While transitioning of funding is challenging for all Unitaid projects, many consultees noted that the experience under the Paediatric HIV/AIDS project stood out from many others, with some consultees drawing

⁷⁸ PEPFAR/CIFF (2017), Accelerating Children's HIV/AIDS Treatment: Promising Practices and Lessons Learned from Implementation of the ACT Initiative.

⁷⁹ CHAI (2014), IPMA Project Plan.

comparisons to the relative ease of transition under the second-line adult ARV treatment project which was being implemented by CHAI and funded by Unitaid.⁸⁰

Consultations noted that Unitaid and CHAI drew important lessons from the challenging transition experience under the Paediatric HIV/AIDS Project and this has helped shape how Unitaid accords priority and works through sustainability and scalability of its grants since.

6.1.2. IPMA

Given the focus of IPMA, the main areas with regards to sustainability were i) ensuring that global coordination activities undertaken by CHAI were maintained; and ii) transitioning country-based TA away from CHAI and to government.

With regards to the former, CHAI's secretariat role has since been transitioned to the Global Fund, although some of the technical and analytical activities are still being undertaken by CHAI as part of the Optimal ARVs project as well as the wider PHTI. In terms of country TA, as discussed in Section 4.2, CHAI's approach of providing human resources alongside technical capacity may have undermined sustainability objectives, although many view this approach as suitable in the face of the priority of eliminating paediatric HIV. Procurement management and forecasting capacity has been built in countries over time, although there are evolving TA needs in relation to implementing the latest WHO guidance and incorporation of updated formulations.

6.2. Sustainability of the paediatric HIV market

Despite the progress made under the two grants, many noted that the wider market continues to face a number of challenges. For example:

- Given changing guidelines and optimal treatments, manufacturers indicated that they often find it difficult to invest in new formulations, given the length of time it takes for products to reach the market, by which point guidelines and optimal treatments have changed again.
- Related to this, manufacturers continue to find it difficult to justify investments in new paediatric ARVs on a commercial basis, given the small size of the overall market and demand for individual formulations. This is specifically in relation to the fact that while the market is expected to remain in the short to medium term, the overall trends in paediatric HIV are likely to decline given PMTCT efforts as well as children moving on to adult formulations, which creates a long-term challenge for investing in such treatments.

⁸⁰ The Second-Line Adult ARV Project started in 2007 with the objective of reducing the price of second-line ARVs for LMICs, enabling greater access to second-line treatment for patients in need. By project completion in 2012, Unitaid had committed US\$290 million to the project and provided treatment for more than 200,000 patients across 25 countries.

- Despite these issues outlined above, many paediatric formulations recommended by WHO are still not available in FDCs, including ABC+3TC+EFV or ABC+3TC+LPV/r. In addition, several optimal ARVs used in adults (including DTG) are still not available for younger children.

Given the above challenges, a number of initiatives have been launched by global HIV partners across the development cycle. In addition to the initiatives discussed in Section 4.3, the Global Accelerator for Paediatric Formulations (GAP-f) initiative was launched in 2017 to help accelerate the introduction of new paediatric ARVs. Unitaid's ongoing Optimal ARVs grant to CHAI will also contribute to this effort, given its focus on reducing the lead time of optimal paediatric ARVs coming to market. While a number of manufacturers welcomed such initiatives, both manufacturers and country partners remained concerned with the implications of the challenges outlined above.

Summary findings:

ARV commodity procurement under the Paediatric HIV/AIDS project was transitioned to other partners, although this transition process could have been better planned for and managed by Unitaid and CHAI. Learnings from this experience have however driven greater sustainability planning for Unitaid grants. IPMA project work has been transitioned to other partners, although CHAI continues to play a much-needed key role, with subsequent ongoing funding from Unitaid as well. This is also in relation to evolving and continuing TA needs at the country level. Despite substantial improvements made in the paediatric ARV market as a result of the Unitaid-CHAI project work, the positives of declining CLHIV and improving optimal treatments means that the market itself continues to remain fragile.

7. SUMMARY FINDINGS, CONCLUSIONS AND LESSONS LEARNED

This evaluation of the two Unitaid investments in the paediatric HIV treatment space implemented through CHAI suggests that CHAI was the right organisation to deliver a complex, multifaceted programme that evolved considerably over several years. The Unitaid grants enabled CHAI to deliver to its strengths during a critical period for global paediatric HIV care.

In 2006, paediatric HIV treatment lagged considerably behind adult treatment on a number of levels and ARV formulations for children were limited in range and presentation, with sporadic orders from countries filled against unpredictable timeframes by a narrow range of suppliers. Across LMICs, paediatric diagnosis and treatment options had simply not kept pace with the focus on PMTCT and adult diagnosis and treatment. As a market, paediatric ARVs were never likely to be large, and successful HIV programmes would result in fewer and fewer HIV positive children (as PMTCT achieved elimination goals and HIV positive children on treatment passed to adult programmes).

In the context of this challenging situation, Unitaid and CHAI embarked on working to improve the ARV market and access to treatments. Building on its experience and knowledge gained from working on adult ARV markets and operating at a time when, as an organisation, CHAI was still in a formative period itself, it took a problem-solving, adaptive, and highly responsive approach to identifying and addressing key barriers.

During the implementation of the Paediatric HIV/AIDS project, efforts to pool ARV procurement across multiple high-burden countries helped catalyse supplier interest in an otherwise commercially unviable market and made ARV supply more accessible, timely and affordable. Nudging countries and suppliers towards improved WHO-recommended treatment regimens and optimal ARVs improved quality of products for children and supported the delivery of better outcomes. While large scale procurement is no longer Unitaid's strategic approach, the evidence suggests that given the specific challenges of the paediatrics treatment market, early interventions were critical to addressing and fixing multiple market failures and Unitaid's willingness to make (relatively) large scale investments in paediatric ARVs was crucial to stimulating supply.

As the market matured, new and additional barriers to the reliable availability of paediatric ARVs were created. Building on experience, the IPMA grant aimed to address these, particularly market smoothing and end-to-end market shaping. The market-coordinating role played by CHAI over several years of the IPMA grant (and ongoing) was well received and widely valued by stakeholders across the market chain.

For example, one clear strength was CHAI's ability to work across a highly varied range of settings including with private sector actors – innovator and generic, right through to large, formal, global entities that can be bound by protocols and procedures that slow their ability to act (and react). CHAI's flexibility and responsiveness was certainly one of its strengths and it optimised its role using its unique position and comparative advantage at the nexus of

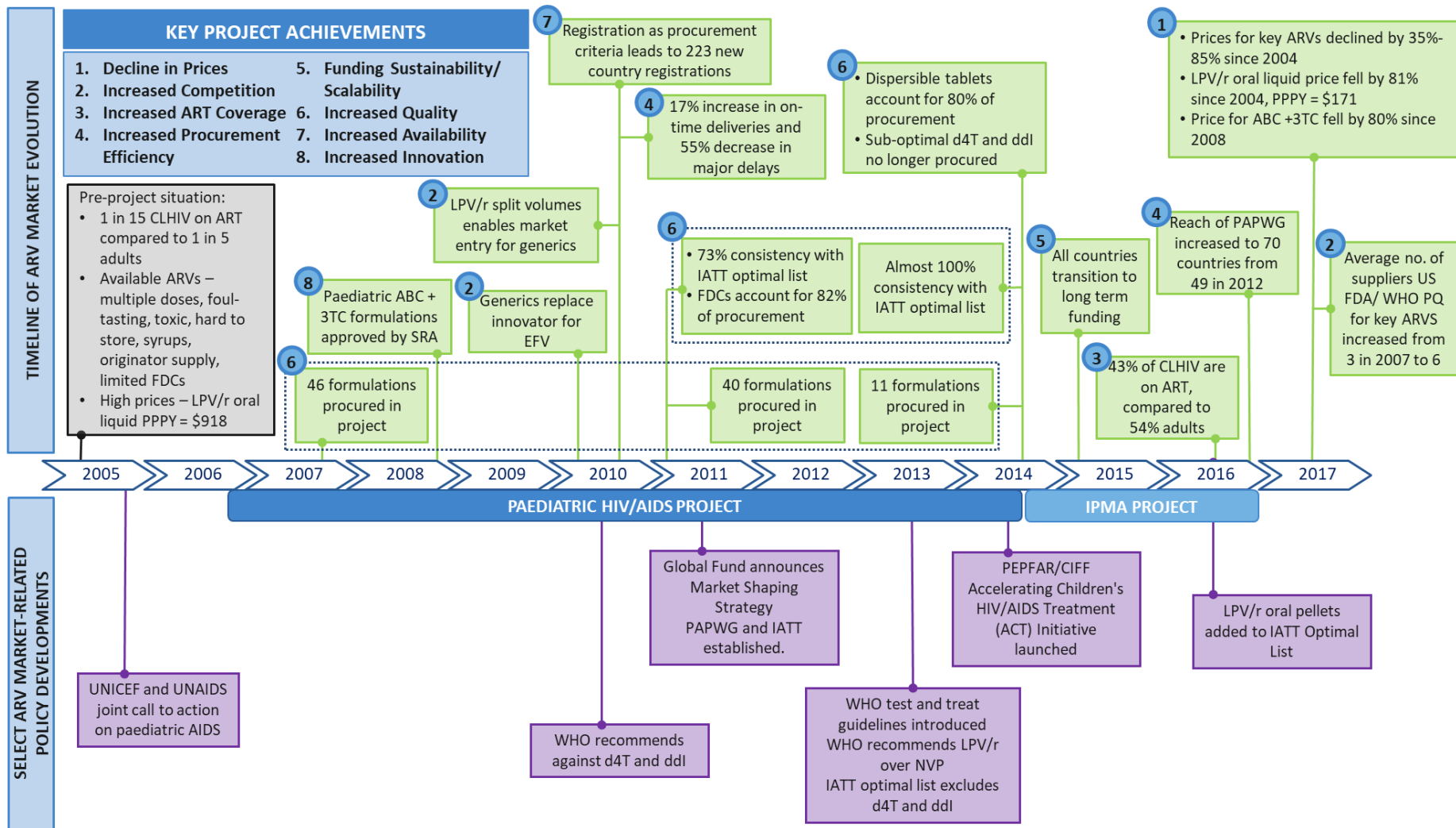
private sector manufacturers, country HIV programmes and international partners/ funders to drive progress.

The long-term (and continuing) investment by Unitaid in the paediatric HIV treatment space has widely been seen as one its most successful interventions, and one that has exceeded expectations as many did not consider possible when the project was first initiated. Since the start of the project:

- Market improvements and thereby increased access to treatments has resulted in an estimated **586,046 additional children being initiated on treatment** under both projects.
- Based on these treatment figures, we estimate that **for every dollar of Unitaid funding US\$20 of benefits have been realised as a result of additional life years gained.**
- The reduction in ARV prices have resulted in cost savings such that for **every dollar of Unitaid funding under the two projects, US\$2.22 of cost savings were realised** for key paediatric formulations.

These achievements are based on the contribution of the projects in completely revolutionising the paediatric ARVs market, as shown in Figure 7.1.

Figure 7.1: Key successes and market development outcomes



CHAI's role in providing technical assistance to individual countries has delivered mixed results. On the one hand, TA was much-needed and was largely considered appropriate to ensuring that the ARV programme progressed at a good pace. TA was well planned for under the IPMA project, with good country government engagement around planning and TA needs adapted to country needs. Using metrics linked to the paediatric ARV programme delivery, TA placement supported some key objectively verifiable results. For example, most countries regularly updated country specific guidance, no countries experienced stock outs and emergency orders were eliminated. However CHAI's approach to TA was focused on providing technical support (gap-filling) and less on developing long-term capacity. There were advantages to this approach but some important limitations as well. CHAI's value added and strength was to "get the job done" rather than develop country-specific capacity-strengthening health systems investments given the priorities of the programme were focused on making the end-to-end market chain function. Going forward, a more carefully thought out approach to country facing investment in capacity building may be more helpful for long term systems strengthening.

Other challenges and related lessons:

- There was poor planning for sustainability and transition of ARV funding to other donors, although ultimately this transition was achieved. However, the experience of the project has provided an important lesson for Unitaid on the importance of upfront sustainability planning and coordination with other funders.
- While there were improvements in the consolidation of procurement and increases in optimal treatments overtime, this push may have been created somewhat earlier within the project, notwithstanding the challenges posed on account of supply availability. This does not take away from the substantial success of the project, but is more of a reflection with the benefit of hindsight.
- The project included the procurement of other HIV commodities (diagnostics, OI medicines and RUTFs) but did not focus specifically on market shaping for these commodities and unsurprisingly, did not impact supply and prices for these markets. Given the substantial project investments in these other commodities, this may have presented an element of a missed opportunity.
- Finally, while the projects have had a large market impact, key barriers continue to exist including: supply concentration for certain key ARVs, and the potential risks imposed by this; lack of availability of a number of key paediatric formulations recommended by WHO including the ABC+3TC+EFV or the ABC+3TC+LPV/r formulations as well as several optimal ARVs used in adults (including DTG); and poor and inaccurate forecasting as well as long time to product registrations detracting supplier interest.

As such, the paediatric ARV market remains fragile, also with declining CLHIV and continually revised optimal treatment regimens. The contribution of the Unitaid-CHAI projects in however breaking this market and creating scale cannot however be overemphasised.

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ANNEX B CONSULTEE LIST AND INTERVIEW GUIDES

B.1. Consultee List

Table B.1: Inception phase consultations

Stakeholder	Organisation	Name	Position
Funder	Unitaid	Philippe Duneton	Deputy Executive Director
		Robert Matiru	Operations Director
		Vincent Bretin	Results Lead
		Gauri Khanna	Monitoring & Evaluation Manager, Results
		Carmen Perez Casas	Technical Manager, Strategy
		Jane Galvao	(ex) Manager, CHAI grants
		Ekaterina Rykovanova	Programme Manager, Operations
		Dessislava Tarlton	Programme Officer, Operations
Project grantee	CHAI	David Ripin	EVP of Access Programs; Chief Scientific Officer
		Carolyn Amole	Senior Director, HIV Access Program
		Rebecca Lopez	Senior Director, Operations, Access Programme

Table B.2: Core phase consultations – Global stakeholder consultee list

Stakeholder	Organisation	Name	Position
Project grantee	CHAI	Nandita Sugandhi	Clinical Advisor
		Shaffiq Essajee	Senior Advisor, HIV, Medicine & Science
		Sylvia Rowe	Advisor, Unitaid Team
		Joanna Sickler	Deputy Director, Drug Access Team
		Bethany Stewart	Paediatric Manager
		Vineet Prabhu	Associate Director, HIV Market Intelligence
Global Partners	Global Fund	Martin Auton	Manager, Global Sourcing: Pharmaceuticals

Stakeholder	Organisation	Name	Position
	PEPFAR - OGAC	Amb Deborah Birx	Ambassador at Large and US Global AIDS Coordinator
Procurement organisation	PfSCM	David Jamieson	Deputy Director, Supply Chain Management System
Pharmaceutical companies	Macleods	Vijay Agarwal	Senior Vice President, HIV and Infectious Diseases, SSA
	Cipla	Sharadd Jain	Director of Operations
	Aurobindo	Umesh Krishnamoorthy	HIV Programmes

Table B.3: Core phase consultations – Country stakeholder consultee list

Stakeholder	Organisation	Name	Position
Project grantee	CHAI Uganda	Jeff Grosz	Former Country Director
		Andrew Musoke	Current Country Director
	CHAI Malawi	Andrews Gunda	Country Director
	CHAI Kenya	Jackson Hungu	Deputy Country Director
Government/MoH	Uganda MoH	Charles Kiyaga	National Coordinator for EID
		Peter Elyanu	Paeds/PMTCT Lead
	Malawi MoH	Tadala Hamisi	Pharma Supply Chain and Logistics
		Caroline Ntale	HIV Supply Chain and Logistics Officer

B.2. Interview guides

This annex includes interview guides to support our consultations with: (i) CHAI; (ii) global funders/ partners working on paediatric HIV; and (iii) country-based stakeholders with knowledge of the country-specific paediatric HIV programme.

B.2.1. CHAI

Relevance – project context and rationale

1. Please describe the main public health and market challenges that set the context and rationale for the Paediatric HIV/AIDS project? *Specific examples, particularly in terms of characterising the market for paediatric treatments when the grant was approved, would be appreciated.*
2. What was the nature and extent of global funder/ partner engagement at the start of the Paediatric HIV/AIDS project? *Discussions around the evolution of other funder priorities, and the work of other partners like CHAI would be helpful.*

3. Was the country scope and focus for both the Paediatric HIV/AIDS and IPMA grants appropriate and were there any missed opportunities (e.g. exclusion of South Africa from the Paediatric HIV/AIDS grant, only a sub-set of countries being taken forward for the IPMA grant)?

Efficiency and effectiveness

Procurement

4. Please provide details regarding the procurement strategies adopted for different commodities (ARVs, diagnostics, OI drugs, RUTFs) under the Paediatric HIV/AIDS project – whether a consistent or changing approach during the project.
5. What was the rationale for the different approaches?
6. Have the respective procurement strategies had the intended impact on the market, in terms of prices, suppliers, new products, etc.? If so, could you provide specific examples? If not, could you describe observed challenges and/ or missed opportunities?
7. How have the procurement strategies evolved with the conclusion of the project and how does this correspond to the evolution of the market?
8. To what extent could further price reductions (and other aspects of a healthy market) have been achieved for commodities procured under the project apart from ARVs i.e. diagnostics, OI drugs and RUTFs?
9. To what extent was the procurement under the projects efficient? What key metrics have been analysed on procurement efficiency (e.g. lead times) and what have been overall observable trends (positive and negative)?
10. Did the outsourcing of some operational activities to the IDA Foundation have an impact on grant implementation? If so, please describe these.

Country technical assistance

11. Please describe the main areas and approaches for provision of technical assistance (TA) by CHAI to country governments.
12. Please provide examples of successful TA provided to countries? *It would be helpful to discuss the context to the TA, prioritisation of activities and observable results.*
13. Please provide examples of where TA provision was particularly challenging to yield results? What were the main challenges during TA delivery?
14. How was CHAI's approach to TA for countries developed and are there examples of cross-country sharing of experiences and TA tools and products?
15. To what extent was in-country capacity built in the areas that were supported so that countries could transition away from CHAI support?

Global coordination

16. Please describe CHAI's role in coordination at the global-level, specifically outlining its role in different initiatives (PADO, PAWG, PHTI, IATT and the PAPWG (now APWG)). How has this role changed over time? What role did CHAI have in establishing these initiatives (particularly the PAPWG) and how has this changed/transitioned over time?
17. What have been the key success and challenges that have arisen with regards to global coordination of key stakeholders in paediatric HIV?
18. What feedback has been received on CHAI's role in gathering and sharing market intelligence at the global level? What have been key aspects of this work, and within this, what has worked particularly well and less well?

Project impact

Public health impact

19. How would you define the public health impact of the CHAI grants? What are the key metrics of significance and how would you best contextualise the importance of any observable trends (e.g. in relation to global trends, 90-90-90 targets, adult treatment rates, etc.)?
20. How would you measure the "indirect" public health impact of the project i.e. in terms of projected impact going forward? *It would be helpful to discuss key data and assumptions on projections.*
21. Could you provide country-specific examples of the extent of public health impact – particularly positive or less positive examples?

Market impact

22. How would you define the market impact of the CHAI grants? What are the key metrics of significance and how would you best contextualise the importance of any observable trends (e.g. in relation to the market conditions prior to the grants)?
23. What do you view as the main achievement with regards to the impact of the CHAI grants on price reductions, supplier entry, new product/ formulation entry, market competition and other aspects that may contribute to a healthy market (e.g. supply stability) for paediatric ARVs? *Specific aspects/ examples would be useful to discuss.*
24. Please provide details on CHAI's activities prior to Unitaids' funding, particularly the previous programme to provide access to treatment for 10,000 children in 16 countries. What activities were undertaken as part of this project, particularly with regard to negotiating with key suppliers on price reductions? How did the activities under this project link to the support provided by Unitaids?
25. How has CHAI supported suppliers to ensure key products were available on the market at affordable prices? What was the importance of this support relative to other

project activities that were looking to stimulate supply (including actual procurement of commodities)?

26. To what extent have healthy and sustainable markets been realised for other paediatric HIV commodities, particularly diagnostics, OI treatments and RUTFs?
27. To what extent did activities as part of these grants impact other countries, particularly with regards to pricing and access to key commodities?

Sustainability and scalability

28. What worked well and less well in terms of the experience of transitioning away from Unitaid/ CHAI commodity support under the Paediatric HIV/AIDS project? Were there any aspects that could have been managed better?
29. What worked well and less well in terms of the experience of transitioning away from Unitaid/ CHAI TA support under the IPMA project? Has country capacity to manage paediatric HIV programmes and procurements improved?
30. What are the main challenges for paediatric HIV treatment going forward and how might these be best addressed?

B.2.2. Global partners

This guide has been tailored further for specific partners.

1. What do you view as the main 3-5 contributions of the Unitaid-CHAI grants on paediatric HIV?
2. In the absence of the Unitaid support, what do you believe would be the current state of the market for paediatric HIV treatment?
3. What has been the main benefit/ value of CHAI's work under the Unitaid funding in relation to what other global partners are doing?
4. How has CHAI worked with other partners in the paediatric HIV space, has this been effective and what might be areas for improvement?
5. What role has CHAI played in coordinating other actors in the paediatric HIV market? Do you believe CHAI has been effective in ensuring that coordination between different actors has been maintained?
6. What is your view on the efficacy of CHAI's procurement approach for the different paediatric HIV commodities? To what extent have others adopted similar approaches following the conclusion of the Paediatric HIV/AIDS grant?
7. Has CHAI been able to effectively engage with country governments and other in-country actors to support paediatric HIV programmes? How effective has CHAI been in ensuring that optimal ARVs are incorporated into country plans? Has CHAI been

able to build sufficient capacity in countries to ensure there is less need to rely on external partners to procure HIV commodities?

8. How effective has CHAI's coordination and support to suppliers been to ensure that new suppliers and products are entering the market and that sufficient quantities of commodities are procured at affordable prices?
9. What are the main challenges for paediatric HIV treatment going forward and how might these be best addressed?

B.2.3. Country consultations

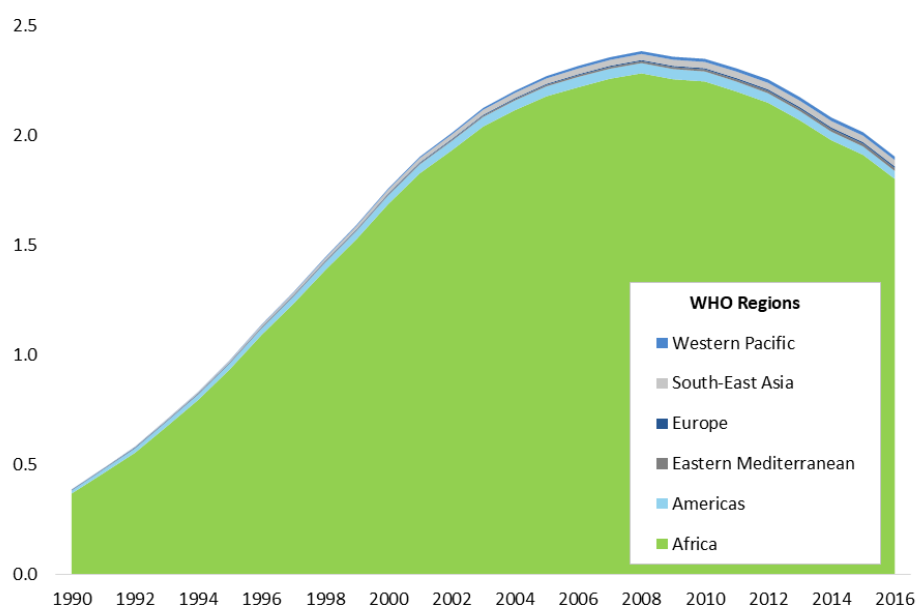
1. Please provide the context for paediatric HIV in your country in terms of CLHIV over time, ART coverage rates, policy updates, optimal product procurements, etc.
2. What has been the role and main areas of work by CHAI in your country under the Unitaid funded projects?
3. What has worked well and less well with regards to ARV commodity procurements and delivery?
4. What has worked well and less well with regards to procurement and delivery of other paediatric HIV commodities such as diagnostics, OI drugs and RUTFs?
5. Has your country experienced any short-term stock-outs in key commodities? If so, what were the reasons for these and how could they have been avoided?
6. How are paediatric HIV commodities currently funded in your country?
7. What have been the main areas of TA provision by CHAI with regards to the paediatric HIV programme? What has worked well and less well with regards to TA provided by CHAI in country? To what extent has sustained capacity been built in country and what remain as key challenges?
8. How are CHAI's forecasting tools, IATT policy toolkit and other related guides used to support HIV programmes in the country? Do you believe these have addressed key country needs?
9. How has CHAI support contributed to improved public health outcomes in the country?
10. What do you view as the main contributions of the CHAI work in country?
11. What key gaps remain and how might these be best addressed?

ANNEX C CLHIV PREVALENCE AND TREATMENT RATES OVER TIME

This annex provides a summary of key UNAIDS prevalence statistics related to CLHIV.⁸¹

Figure C.1 shows that CLHIV increased rapidly from 1990, reaching a peak of nearly 2.4m in 2008, and starting to decline thereafter. The figure also shows that while paediatric HIV can be found in most regions, Africa has accounted for almost the entire burden.

Figure C.1: HIV prevalence among children by WHO region



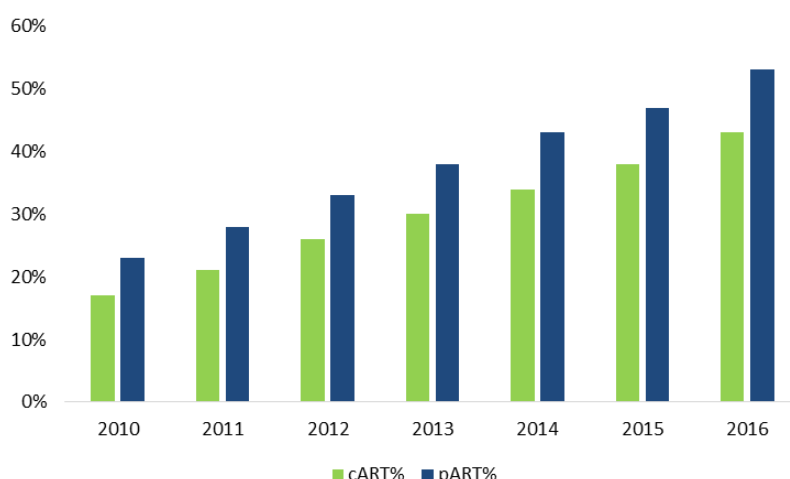
Source: UNAIDS (2017)

As regards treatment, Figure C.2 shows that while the proportion of CLHIV on ARTs (cARTs %) has grown since 2010, this remains below figures for all people living with HIV (PLHIV), with the differential in proportions being around ten percentage points in 2016.⁸² The overall proportion of CLHIV and PLHIV on ARTs remains very low at 43% and 53% in 2016.

⁸¹ Figures are based on modelled UNAIDS estimates as opposed to actual data.

⁸² Please note that 2010 is the earliest year in which UNAIDS provides treatment data.

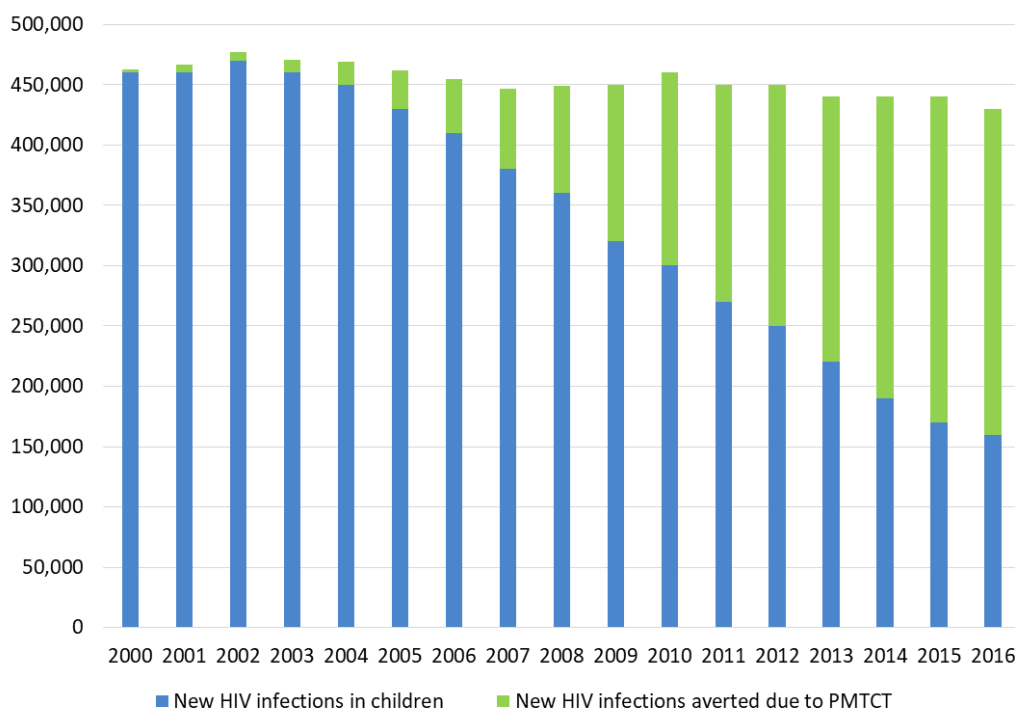
Figure C.2: Proportion of CLHIV and PLHIV on ARTs



Source: UNAIDS (2017)

While overall treatment remains relatively low for CLHIV, significant progress has been made in reducing HIV incidence among children, with one of the key reasons for this being the success of PMTCT interventions. As Figure C.3 below shows, estimates suggest that since 2000, a substantial number of new infections have been averted due to PMTCT interventions.

Figure C.3: Paediatric HIV infections averted due to PMTCT interventions



Source: UNAIDS (2017)

The key for reducing HIV infections in newborns has been through initiating pregnant mothers living with HIV onto treatment, with ART coverage nearing 80% by 2016, a significantly higher proportion than PLHIV overall.

ANNEX D WHO PAEDIATRIC ARV RECOMMENDATIONS AND IATT OPTIMAL FORMULATIONS

D.1. WHO Treatment Guideline Revisions for Paediatric ART (2006 – 2016)

Table D.1: Summary of WHO Treatment Guidelines for Paediatric ART (2006 – 2016)

2006			2010			2013			2016		
	1L	2L		1L	2L		1L	2L		1L	2L
All infants and children	d4T (or ABC or AZT) + 3TC + NVP/EFV	ddl + ABC (or AZT or EFV or NVP) + LPV (or SQV or NFV)	Infants	NVP (or LPV/r) + 3TC + AZT (or ABC or d4T)	LVP/r + ABC (or AZT) + 3TC (or ddl)	Infants <3 yrs	ABC (or AZT) + 3TC + LPV/r (or NVP)	No change	Infants <3 yrs	ABC (or AZT) + 3TC + LPV/r	2 NRTIs + RAL
			Children (2 – 3 yrs)	NVP + 3TC + AZT (or ABC or d4T)		3 - 10 yrs	ABC + 3TC + EFV (or NVP)	AZT (or ABC or TDF) + 3TC + EFV	3 - 10 yrs	ABC + 3TC + EFV	2 NRTIs + (ATV/r + LVP/r)
			Children (3 yrs +)	NVP (or EFV) + 3TC + AZT (or ABC or d4T)		10+ yrs	TDF + 3TC (or FTC) + EFV (or NVP)	AZT (or ABC or TDF) + 3TC (or FTC) + LPV/r	10+ yrs	TDF + 3TC (or FTC) + EFV	2 NRTIs + (ATV/r + LVP/r)

D.1.1. Key Revisions:

2006

- WHO introduces the concept of a public health approach in their ART Guidelines, with simplified and harmonized ART regimens, and tailored guidelines for ART for infants and children.

2010

- d4T and didanosine (ddl) fall out of favour as drugs for use in first-line therapy due their adverse side-effects. In 2010, the World Health Organization recommended against the use of ddl and d4T⁸³.

2013

- Accumulated evidence demonstrated the superior clinical efficacy of Lopinavir/Ritonavir (LPV/r) over NVP, regardless of the child's prior exposure to ART for PMTCT⁸⁴. For this reason, the revised 2013 WHO guidelines recommend the use of LPV/r as 1L ART for all children with HIV younger than 3 years of age.

2016:

- WHO recommends lifelong ART to all children, regardless of CD4 count.

⁸³ WHO (2013), Phasing out Stavudine: Progress and Challenges.

⁸⁴ WHO (2013), Transition to new HIV Treatment Regimens.

- The guidelines make no changes to the first-line paediatric ART regimen recommended in 2013.
- RAL (Raltegravir) is newly recommended in second-line paediatric ART for children younger or older than 3 years after failure of a first-line regimen containing LPV/r.
- Supported by study results, ‘super-boosting’ ritonavir was recommended by WHO in the 2016 guidelines. Rifampicin (for TB treatment in children) has negative interactions with LPV/r⁸⁵. To counteract this effect, the amount of ritonavir (RTV) in the LPV/r combination must be quadrupled in a procedure known as super-boosting. Follow-on studies are examining the safety and efficacy of super-boosting with ritonavir powder and LPV/r pellets and other solid ARVs.

D.2. IATT Optimal ARV Formulary and Limited Use Lists (2011 – 2016)

In mid-2011, the IATT began a selection process for optimal paediatric formulations given the proliferation of product choices and market fragmentation leading to instability in the paediatric marketplace and the need for guidance on the selection and procurement of paediatric ARV’s around a subset of optimal products.

The principles that were followed in developing the IATT simplified tables include:

- Preference for age-appropriate Fixed Dose Combination for any regimen if available
- Oral liquid or syrup formulations should be avoided where possible
- Dispersible tablets are the preferred solid oral dosage forms
- Young children should be switched to available solid oral dosage forms as soon as possible
- Adult tablets that are scored are more easily split.

The Optimal List outlines the minimum number of ARV formulations needed to provide all currently recommended WHO preferred first- and second-line regimens for all paediatric weight bands. Provision for WHO-recommended alternative regimens are considered for inclusion on the Limited-use List. Additionally, the Limited-use List makes provision for ARVs that may be needed during transition, such as product phase-in or out, and/or for special circumstances, such as third-line treatment.

The IATT list is updated and revised when the WHO updates regimen guidance or when new products and formulations become available in low-income settings. CHAI participates and leads a number of IATT committees, most notably the Child Survival Working Group and Formulary Sub-Committee as co-chairs for both.

⁸⁵ DNDi (2018), Superbooster Therapy Paediatric HIV/TB.

Table D.2: IATT Optimal ARV Formulary Use Lists 2011 - 2016

2011	2013				2015				2016			
	Drug Class	Drug	Formulation	Dose	Drug Class	Drug	Formulation	Dose	Drug Class	Drug	Formulation	Dose
ABC + 3TC 30/60 disp scored FDC tab					NNRTI	EFV	Tablet (scored)	200 mg	NNRTI	EFV	Tablet (scored)	200 mg
AZT + 3TC +NVP 60/30/50 disp scored FDC tab	NNRTI	AZT	Oral Liquid	50mg/5mL	NNRTI	NVP	Tablet (disp, scored)	50 mg	NNRTI	NVP	Tablet (disp, scored)	50 mg
AZT + 3TC 60/30 disp scored FDC	NNRTI	NVP	Tablet (disp, scored)	50 mg	NNRTI	NVP	Oral liquid	50 mg/5mL, 100ml	NNRTI	NVP	Oral liquid	50 mg/5mL, 100ml
d4T + 3TC + NVP 6/30/50 disp scored FDC	NNRTI	NVP	Oral liquid	50 mg/5mL	PI	LPV/r	Tablet (heat stable)	100 mg/25 mg	PI	LPV/r	Tablet (heat stable)	100 mg/25 mg
d4T + 3TC 6/30 disp scored FDC	PI	LVP/r	Tablet (heat stable)	100mg/25mg /mL	PI	LPV/r	Oral liquid	80 mg/20mg/mL	PI	LPV/r	Oral liquid	80 mg/20mg/mL
ABC 60mg disp scored tab	PI	LPV/r	Oral liquid	80 mg/20mg/mL	FDC	AZT/3TC	Tablet (disp, scored)	60 mg/30mg	PI	LPV/r	Oral pellets	40mg/10mg
ddl 125mg EC cap					FDC	AZT/3TC /NVP	Tablet (disp, scored)	60 mg/30mg/50 mg	INSTI	RAL	Chewable Tab	100mg
ddl 200mg EC cap					FDC	AZT/3TC /NVP	Tablet (disp, scored)	60 mg/30mg/50 mg	FDC	AZT/3TC /NVP	Tablet (disp, scored)	60 mg/30mg/50mg
ddl 25mg buffered chew tab					FDC	ABC/3T C	Tablet (disp, scored)	60 mg/30 mg, 120 mg/60mg	FDC	ABC/3T C	Tablet (disp, scored)	60 mg/30 mg, 120 mg/60mg
EFV 200mg scored tab												
LPV/r 80/20 mg/mL oral liquid												
NVP 50mg disp scored tab												
AZT 50MG/5ML oral liquid (for PMTCT only)	FDC	ABC/3T C	Tablet (disp, scored)	60mg/30mg								
NVP 50mg/5mL oral liquid (for PMTCT only)	FDC	ABC/AZ T/3TC	Tablet (non disp, scored)	60mg/60mg/30mg								

D.2.1. Key Revisions:

2013

- 10 products. This list represented the final phase-out of D4T and ddl as drugs for use in first-line therapy due their adverse side-effects. WHO guidelines recommend the use of LPV/r as 1L ART.

2015

- 8 products. IATT Formulary List demoted the NVP bottle size to non-essential, choosing to keep the 100ml bottle (produced by Cipla and Aurobindo) as optimal. The AZT/ABC/ 3TC Tablet (60mg/60mg/30mg) and oral liquid formulation of AZT are removed.

2016

- 9 products. The IATT Optimal Formulary was updated to include LPV/r 40/10 mg oral pellets and RAL 100 mg chewable tablets. The oral pellets for LPV/r offer clear advantages to the previously used syrup version in terms of logistics and acceptability. AZT/3TC/NVP FDC scored dispersible tablets were transitioned to the Limited-use List.

Table D.3: IATT ARV Formulary Limited Use Lists 2011 - 2016

2011			2013				
Drug	Formulation	Dose	Drug Class	Drug	Formulation	Dose	Rationale
ABC	Oral Liquid	100mg/5ml	NRTI	3TC	Tablet (disp)	30 mg	For use with TDF single
ATV	Solid oral dosage form	100mg, 150mg	NRTI	TDF	Oral powder	40 mg/scoop	Until FDC available
DRV	Oral liquid	500mg/5ml	NRTI	TDF	Tablet (unscored)	150 mg	Until FDC available
DRV	Tablet	75mg, 150mg	NRTI	TDF	Tablet (unscored)	200 mg	Until FDC available
ddl	Powder for oral liquid*	2g, 4g bottle	NNRTI	ETV	Tablet	25 mg	Special circumstances
3TC	Oral liquid	50mg/5ml	NNRTI	ETV	Tablet	100 mg	Special circumstances
RTV	Oral liquid	400mg/5ml	PI	DRV	Tablet	75 mg	Special circumstances
RTV	Tablet (heat stable)	100mg	PI	RTV	Oral liquid	400 mg/5mL	For boosting non-co-formulated PI's
d4T	Powder for oral liquid	5mg/5ml	PI	ATV	Solid oral dosage form	100 mg	Alternative 2nd line
			PI	ATV	Solid oral dosage form	150 mg	Alternative 2nd line
			<u>Int Inh</u>	RAL	Chew tab (scored)	100 mg	Special circumstances
			FDC	d4T/3TC/ NVP	Tablet (disp, scored)	6 mg/30 mg/ 50 mg	To be phased out
			FDC	d4T/3TC	Tablet (disp, scored)	6 mg/30 mg	To be phased out

2015					2016				
Drug Class	Drug	Formulation	Dose	Rationale	Drug Class	Drug	Formulation	Dose	Rationale
NRTI	AZT	Oral liquid	50 mg/5mL - 100ml	Infant prophylaxis during PMTCT for replacement fed infants	NRTI	AZT	Oral liquid	50 mg/5mL - 100ml	For infant prophylaxis or as part of a neonatal treatment regime
NRTI	ABC	Tablet (dispersible, scored)	60mg	For children <3 years undergoing TB treatment requiring triple nucleoside regimen	NRTI	3TC	Oral Liquid	50mg/5 mL- 240mL	As part of a neonatal treatment regimen
NRTI	AZT	Tablet (dispersible, scored)	60mg	For children <3 years undergoing TB treatment requiring triple nucleoside regimen	NRTI	ABC AZT	Tablet (dispersible, scored)	60mg 60mg	For children <3 years undergoing TB treatment requiring triple nucleoside regimen
NRTI	TDF	Tablet (unscored)	200 mg	Older children <35 kg until FDC available	PI	DRV	Tablet	75 mg	Third Line
NNRTI	ETV	Tablet	25 mg	Special circumstances	PI	RTV	Tablet	25mg	For boosting of noncoformulated PI's (DRV and ATV)
NNRTI	ETV	Tablet	100 mg	Special circumstances	PI	RTV	Oral liquid	400 mg/5mL, 240mL	For super boosting of LPV/r during TB treatment
PI	DRV	Tablet	75 mg	Special circumstances	PI	ATV	Solid oral dosage form	100 mg	Alternative 2nd line
PI	RTV	Oral liquid	400 mg/5mL	For boosting non-co-formulated PI's	<u>Int Inh</u>	RAL	Chew tab	25 mg	Second Line after LPV/r containing first line failure
PI	ATV	Solid oral dosage form	100 mg	Alternative 2nd line	FDC	AZT/3TC/NVP	Tablet (dispersible, scored)	60mg/30mg/50 mg	Alternative first line
PI	ATV	Solid oral dosage form	150 mg	Alternative 2nd line					
<u>Int Inh</u>	RAL	Chew tab (scored)	100 mg	Special circumstance					

D.2.2. Key Revisions:

2013

- 13 products. All ddl formulations were demoted to be non-essential from the Limited Use List. Tenofovir Disoproxil Fumarate (TDF) was deemed safe and efficacious for use in children over two years, but had not met all other criteria defined for product selection. As such it was decided that the available formulations would be included on the limited-use list.

2015

- 11 products. Five products were removed and three added. The 3TC tablet, TDF powder, TDF unscored tablet, d4T/3TC/ NVP tablet, and d4T/3TC tablet were removed from the 2013 list and AZT as an oral liquid, 60mg ABC tablet, 60mg scored AZT tablet were added.

2016

- 9 products. Four products were added to the limited-use list and five products were removed. The list was updated to include RAL 25 mg chewable tablets for younger children after LPV/r failure, RTV 25 mg heat stable tablets for the boosting of non-co-formulated Protease Inhibitors (PIs), as well as the removal of TDF 200 mg tablets, ATV 150 mg capsules and all etravirine-containing formulations.

ANNEX E COUNTRY COVERAGE UNDER THE PROJECTS

Table E.1 shows the top 40 countries in terms of number of CLHIV in 2006, followed by other countries included in the Paediatric ARV grant. Countries highlighted in blue are those that were not included in the Paediatric ARV Grant, despite having a high CLHIV Prevalence. Notably, despite having the highest prevalence of CLHIV, South Africa was not covered by the grant. Other high prevalence countries not included are Ghana and Central African Republic, and Thailand, all in the top 25. Consultees from CHAI mentioned that Unitaid's focus on the majority of its funding for low-income countries was a key reason for the exclusion of South Africa. They also mentioned that they selected countries through a combination of those where CHAI was already working, those who were already members of a procurement consortium, and those who had willing Ministers of Health who were requesting support.

Table E.1: Countries covered by the Paediatric HIV/AIDS Project

2006 Rank	Country Name	CLHIV 2006	Prevalence 2006	Included in Paediatric ARV Grant
1	South Africa	360,000	0.75%	No
2	Nigeria	270,000	0.19%	Yes
3	Kenya	210,000	0.57%	Yes
4	Uganda	200,000	0.68%	Yes
5	Tanzania	180,000	0.44%	Yes
6	Mozambique	160,000	0.74%	Yes
7	Zimbabwe	160,000	1.22%	Yes
8	Malawi	150,000	1.12%	Yes
9	Ethiopia	130,000	0.16%	Yes
10	Zambia	120,000	0.97%	Yes
11	India	120,000	0.01%	Yes
12	Congo, Dem. Rep.	52,000	0.09%	Yes
13	Cameroon	47,000	0.26%	Yes
14	Cote d'Ivoire	46,000	0.25%	Yes
15	Ghana	40,000	0.18%	No
16	Rwanda	25,000	0.27%	Yes
17	Botswana	24,000	1.27%	Yes
18	Burkina Faso	23,000	0.17%	Yes
19	Swaziland	18,000	1.61%	Yes
20	Lesotho	18,000	0.92%	Yes
21	Central African Republic	16,000	0.38%	No
22	Namibia	16,000	0.78%	Yes
23	Burundi	14,000	0.18%	Yes
24	Thailand	14,000	0.02%	No
25	Togo	14,000	0.24%	Yes
26	Angola	13,000	0.06%	Yes
27	Brazil	13,000	0.01%	No
28	Chad	12,000	0.12%	No
29	Mali	12,000	0.09%	No
30	Haiti	11,000	0.12%	Yes
31	South Sudan	11,000	0.13%	No
32	Guinea	10,000	0.10%	No
33	Myanmar	7,200	0.01%	No
34	Niger	7,000	0.05%	No
35	Liberia	6,800	0.20%	Yes
36	Benin	6,500	0.08%	Yes
37	Congo, Rep.	5,900	0.15%	No
38	Cambodia	4,700	0.03%	Yes
39	Senegal	4,200	0.04%	Yes
40	Gabon	4,000	0.28%	No
41	Dominican Republic	3,700	0.04%	Yes
42	Indonesia	3,600	0.00%	No
43	Guinea-Bissau	3,200	0.23%	No
44	Vietnam	3,200	0.00%	Yes
48	Ukraine	2,500	0.01%	Yes
49	Papua New Guinea	2,400	0.04%	Yes
67	Jamaica	1,000	0.04%	Yes
71	Guyana	500	0.07%	Yes
-	OECS	N/A	N/A	Yes
-	China	N/A	N/A	Yes

Table E.2 shows the countries covered by the Paediatric HIV/AIDS and IPMA grants, as well their number of CLHIV in 2013, when the IPMA grant was being planned and transition from one grant to the other took place. Highlighted countries are those that were covered by one but not the other. South Africa and Myanmar were both added, and several countries with high CLHIV prevalence were dropped, such as the Democratic Republic of the Congo, Angola, Rwanda, and Namibia. Consultees from CHAI mentioned that countries that had successfully transitioned to procuring their own drugs were not included. Those that were included were either still undergoing transition due to either lower capacity in-country or higher volumes.

Table E.2: Countries covered by the Paediatric HIV/AIDS and IPMA Grants

Country Name	2013 CHLIV	2013 Prevalence	Paeds	IPMA
South Africa	370,000	0.69%	No	Yes
Nigeria	280,000	0.16%	Yes	Yes
Mozambique	220,000	0.83%	Yes	Yes
Zimbabwe	172,000	1.14%	Yes	Yes
Uganda	170,000	0.45%	Yes	Yes
Kenya	150,000	0.33%	Yes	Yes
India	137,000	0.01%	Yes	Yes
Tanzania	130,000	0.26%	Yes	Yes
Malawi	130,000	0.78%	Yes	Yes
Zambia	100,000	0.66%	Yes	Yes
Ethiopia	84,000	0.09%	Yes	Yes
Congo, Dem. Rep.	55,000	0.08%	Yes	No
Cameroon	52,000	0.24%	Yes	Yes
Cote d'Ivoire	41,000	0.19%	Yes	Yes
Lesotho	35,000	1.65%	Yes	Yes
Angola	21,000	0.08%	Yes	No
Rwanda	20,000	0.18%	Yes	No
Swaziland	18,000	1.42%	Yes	Yes
Namibia	17,000	0.73%	Yes	No

Country Name	2013 CHLIV	2013 Prevalence	Paeds	IPMA
Botswana	16,000	0.75%	Yes	Yes
Burkina Faso	14,000	0.08%	Yes	Yes
Burundi	14,000	0.15%	Yes	Yes
Togo	14,000	0.20%	Yes	Yes
Myanmar	9,400	0.02%	No	Yes
Haiti	8,300	0.08%	Yes	No
Benin	7,100	0.07%	Yes	Yes
Vietnam	5,600	0.01%	Yes	Yes
Liberia	5,100	0.12%	Yes	Yes
Senegal	5,100	0.04%	Yes	Yes
Cambodia	5,000	0.03%	Yes	Yes
Ukraine	3,600	0.01%	Yes	No
Papua New Guinea	3,400	0.04%	Yes	Yes
Dominican Republic	2,300	0.02%	Yes	No
Jamaica	500	0.02%	Yes	No
Guyana	500	0.07%	Yes	No
OECS	N/A	N/A	Yes	No
China	N/A	N/A	Yes	No

ANNEX F PROCUREMENT OF HIV DIAGNOSTICS, OI MEDICINES AND RUTFS

This annex provides a summary review of the procurement of HIV diagnostics, OI medicines and RUTFs under the project.

F.1.1. HIV diagnostics

The nature of the diagnostics market is considerably different from that of ARVs. In particular, there is limited product substitution given the very specific nature of diagnostic products, and there is high investment costs and laboratory infrastructure requirements implying that regular tenders are not appropriate for these products. As a result, pricing and supply of diagnostic products under the project were generally based on direct negotiations with suppliers. Discussions with CHAI indicate that market shaping for diagnostics products was not a core objective, rather to procure these products to diagnose children and help put them on treatment. There was also a lot of work done around building national capacity for running diagnostic tests using DBS and also to work around low capacity utilisation of EID testing by complementing with viral load testing. Other innovations in relation to bundling systems were also the focus.

Despite the market shortcomings in the diagnostics space plus the lower level of focus on improving market dynamics for these commodities under this project, CHAI was able to achieve some significant price reductions on key EIDs. For example:

- For **DNA PCR**, CHAI entered into an agreement with Roche which resulted in it offering its Amplicor HIV-1 DNA Test for Unitaid beneficiaries in SSA at US\$8.75 per test for the first 60,000 tests, then US\$7 for each test bought above this amount. Roche also offered instrument bundles, a dried blood spot (DBS) collection bundle and a laboratory consumable bundle to provide all products necessary to run the DNA PCR test. This resulted in the all-inclusive price for the DNA PCR test (excluding instrument purchase but including DBS and laboratory consumables), to be provided at **US\$14.04 per test for the first 60,000 tests, and US\$12.29 per test thereafter, which compared favourably with initial budget provisions of US\$18 per test made by CHAI.**
- For **CD4 tests**, pricing was initially based on 2004 agreements made with Becton Dickenson (BD) under the FACSCalibur and FACSCount instruments. While pricing was initially volume-based, CHAI was able to get an agreement for pricing to be more flat-lined for Unitaid beneficiaries in Africa.
 - Regarding reagents for **FACSCalibur** (high throughput instrument), prices changed from **US\$5 per test for volumes of 75k+ and US\$2.80 for higher to US\$3.52 to US\$3.85 per test**, regardless of volumes, depending on test used and including distributor margins.
 - Regarding reagents for **FACSCount** (low volume), prices changed from US\$3.50 to US\$13.50 depending on volumes, test and whether instruments were leased

or purchased to US\$4.15 to US\$5.90, including all required consumables and distributor margins. BD also agreed in 2007 to a ceiling price for the new CD4 percentage test to be run with FACSCount of US\$4.50. These prices are only for African countries in the CHAI consortium, while other countries would be subject to prices under the previous agreement.

- **For HIV RDTs**, CHAI reached a pricing agreement with Trinity Biotech (TB), the manufacturer of Uni-Gold and Capillus HIV RDTs. Pricing for Uni-gold and Capillus are US\$1.60 and US\$1.39 per test respectively (ex works Ireland). Prices were identical to that offered by SCMS with PEPFAR funding, but key distinctions were i) CHAI prices included distributor margins (which can be up to 50%); and ii) free quarterly training will be provided by TB for recipient countries. Prices were the same for all members of the consortium.

During the later years of the Paediatric HIV/AIDS project, CHAI entered into agreements with suppliers of new products, including those providing diagnostic products based on dried blood spot (DBS) testing. For example, in 2012, the CHAI Laboratory Services Team (LST) supported the introduction of DBS testing and as a result, MiMENDA, a German-based manufacturer, was introduced as the second DBS collection bundle supplier on the market.

In terms of project procurement, we have summarised findings regarding the pricing and procurement of the diagnostic products mentioned above in Table F.1 below, which shows that while commodities have experienced average unit cost reductions, these have been relatively small when compared to price reductions experienced in the ARV market (see Section 5.3 and Annex G for further details of this analysis).

Table F.1: Select diagnostic commodities and price changes based on actual procurements

Diagnostic class	Product	Initial average unit cost (year)	Final average unit cost (year)	% price change
DNA PCR	Amplicor HIV-1 DNA Test	US\$9.42 (2007)	US\$7.70 (2014)	-18%
CD4 tests	FACSCount CD4 Reagent Kit	US\$4.88 (2008)	US\$4.80 (2013)	-2%
HIV RDTs	Uni-Gold HIV ABS test	US\$1.65 (2007)	US\$1.63 (2014)	-1%

CEPA analysis based on project procurement data.

F.1.2. OI medicines

Similar to ARVs, OI drugs were procured using a standard Request for Proposal (RfP) approach, with suppliers invited to provide an indication of proposed pricing (as well as proof of compliance with quality assurance, regulatory approvals, etc.).

Co-trimoxazole was the main OI drug that was procured by the project, with project procurement data suggesting that it accounted for over 90% of OI drug procurement during

the HIV/AIDS Project. Co-trimoxazole is a multi-sourced product with a relatively high supply base, and as a result the project was not expected or targeted to significantly impact the market for this product as was the case for ARVs. This is largely reflected in project data, which suggests that prices did not vary significantly over time. In addition, while there were 12 different suppliers of co-trimoxazole on the market, Cipla accounted for more than 77% of total procurement, suggesting a relatively high degree of concentration on supply.

Other OI drugs were procured under much more strict procedures by CHAI, given that countries had limited experience with the drugs and few alternative drugs had obtained SRA approval.

F.1.3. RUTFs

As with other non-ARV commodities, RUTF was generally supplied under the project to support the uptake in paediatric treatment, in particular, malnourished children are much less likely to have a well-functioning immune system, which in turn limits the effectiveness that ARVs will have for treating patients. In resource-limited settings, RUTF has been used relatively extensively to improve child nutrition, with partners such as UNICEF being key procurers of these commodities. That said, RUTF accounted for nearly US\$35m of procurement under the Paediatric HIV/AIDS project, suggesting that the project was a relatively important procurer of this commodity.

RUTFs were initially sourced from a single supplier, Nutriset, a French manufacturer who has held the patent for RUTFs. However, over the course of the project new suppliers were introduced to the market, which included franchisees of Nutriset based in developing countries (such as Project Peanut Butter in Malawi and Hilina in Ethiopia), as well as independent suppliers. Although new suppliers were used for RUTFs, Nutriset and its franchisees accounted for 85% RUTFs supplied through the project, initially due to the lack of alternatives but once other suppliers were in the market CHAI experienced some issues with obtaining quality products.⁸⁶ Given that the price of RUTFs depended on international market prices for peanuts and milk, which are highly volatile in the short-term, negotiations with suppliers were carried out on a quarterly basis throughout the project. In terms of prices offered, while Nutriset could offer similar prices to local franchisees, the cost of shipping the product from France could add a 15% mark-up, meaning that where possible it was favourable to source products locally. While Nutriset remained a key supplier out the project, project procurement data suggests that in 2011 and 2012 (the last year the Paediatric HIV/AIDS project supplied RUTF), Nutriset France accounted for 40% and 50% of supply respectively.

⁸⁶ An example of this includes sourcing RUTF from JAM, a Mozambique-based supplier. Because the milk powder provided by JAM had gone past its expiry date, the products could not be used by the project, resulting in CHAI having to source the product from Nutriset.

ANNEX G KEY ARV SUPPLY AND PRICING ANALYSIS⁸⁷

This annex provides an analysis of the supply and pricing for key ARVs procured under the Unitaid-CHAI Paediatric HIV/AIDS project. We examine supply and pricing for project procurements (2007-14) and wider procurements for low and low-middle income countries (2008-17).

G.1. Zidovudine + Lamivudine + Nevirapine (AZT+3TC+NVP)

G.1.1. Overview

AZT+3TC+NVP is an FDC of two nucleoside reversed transcriptase inhibitors (NRTIs, AZT+3TC) and a non-nucleoside reverse transcriptase inhibitor (NNRTI, NVP).⁸⁸ The individual formulations of the three ARVs originally received US FDA approval more than twenty years ago, and have been key ARVs used individually for treating HIV. The FDC is not produced by any innovator companies, and is not available in high income countries due to patent restrictions on the individual ARVs.

The main dosage forms of AZT+3TC+NVP are 300mg/150mg/200mg (with NVP sometimes not included in the same tablet as the NRTIs) and 60mg/30mg/50mg, with the latter a paediatric formulation to be provided to children less than 25kg, while the former can be used for adults and children weighing more than 25kg. The tablet should be taken twice daily (although the number of paediatric tablets consumed varies by the weight of the child).

Table G.1 below provides the list of generic manufacturers providing the FDC, alongside US FDA and WHO PQ approval timelines as well as treatment cost PPPY when first approved.⁸⁹ As the table shows:

- Nine suppliers have obtained US FDA and/or WHO PQ approval for the adult and paediatric formulations (which includes co-packaged products), while only three companies obtained approvals for the paediatric-specific formulations.

⁸⁷ The analysis has covered low and lower-middle income countries as defined by the World Bank's Country Income Classification. This reflects the fact that the project of procurement under the Paediatric HIV/AIDS project was undertaken in these countries, plus products and patent restrictions in upper-middle income countries mean that market dynamics in these countries are different from most countries covered by the project.

⁸⁸ NRTIs and NNRTIs both act at the same point in the HIV virus life cycle, but the way in which they inhibit the reverse transcriptase enzyme differs slightly. NRTIs compete with the reverse transcriptase for the interaction with the HIV genetic material, while NNRTIs block the interaction between the reverse transcriptase and the HIV genetic material. Both NRTIs and NNRTIs act to block the process of HIV RNA becoming HIV DNA, which in turn will allow the HIV virus to integrate with the host's CD4 cell DNA and eventually replicate.

⁸⁹ It should be noted that products that have received approval from a stringent regulatory authority (SRA, such as the US FDA or the European Medicines Agency) can obtain WHO PQ through an expedited manner, with the process of obtaining WHO PQ being significantly less burdensome compared to applications without prior SRA approval.

- Approvals for the adult and paediatric formulations were made prior to the Paediatric HIV/AIDS project, while the paediatric-specific formulation was first approved in 2009.
- Initial treatment costs PPPY for the adult formulations have varied from US\$99 to US\$263, while price range for the paediatric versions were US\$97-US\$158, suggesting a slightly lower range.

Table G.1: List of generic manufacturers for AZT+3TC+NVP

Manufacturer	Formulation/dosage	US FDA Approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Adult and paediatric formulations				
Aspen	Oral tablet 300mg/150mg/200mg	2005	Included due to US FDA approval	US\$228
Aurobindo	Oral tablet 300mg/150mg/200mg	2006	Included due to US FDA approval	US\$144
Hetero	Oral tablet 300mg/150mg/200mg	2011	2006	US\$263
Cipla	Oral tablet 300mg/150mg/200mg	2007	2009	US\$231
Strides	Oral tablet (co-packaged) 300mg/150mg+200mg	2007	2014	US\$225
Mylan	Oral tablet 300mg/150mg/200mg	2008	2009	US\$183
Sun Pharmaceuticals	Oral tablet 300mg/150mg/200mg	No approval	2008	US\$263
Strides	Oral tablet 300mg/150mg/200mg	2009	2014	US\$115
Macloeds	Oral tablet 300mg/150mg/200mg	2012	2012	US\$99 ⁹⁰
Paediatric only formulations				
Mylan	Tablet for oral suspension 60mg/30mg/50mg	2010	2009	US\$158

⁹⁰ Note this price is from 2014, when Macloeds first started supplying the market, according to the GPRM database.

Manufacturer	Formulation/dosage	US FDA Approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Cipla	Tablet for oral suspension 60mg/30mg/50mg	2012	Included due to US FDA approval	US\$144
Strides	Tablet for oral suspension 60mg/30mg/50mg	2012	2014	US\$97

Source: US FDA and WHO PQ databases; MSF *Untangling the Web in ARV Prices reports*; GPRM.

Until 2015, the paediatric version of AZT+3TC+NVP was included in the IATT list of optimal ARVs. However, it was removed in the 2016 update as a result of changes in WHO guidance regarding the use of NVP in treating children, with LPV/r being preferred to NVP in children younger than three and efavirenz (EFV) being recommended over NVP for children older than three. Prior to this change, the FDC was part of WHO paediatric treatment guidelines for children under ten. Nevertheless, this FDC remains one of the key drugs for treating HIV among children in developing countries, and is likely to remain so for a number of years before it is phased out.

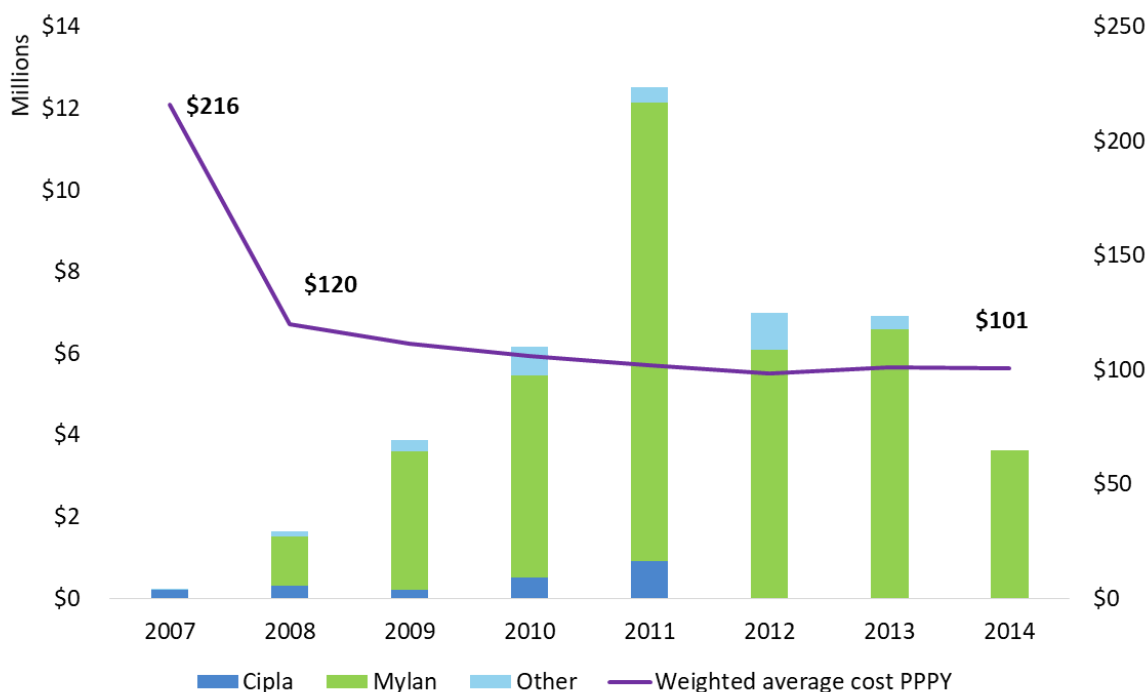
G.1.2. Project supply and pricing

The paediatric formulation of the AZT+3TC+NVP drug was procured in the highest volumes as part of the Paediatric HIV/AIDS project, accounting for nearly 25% of all ARVs procured (and accounted for a similar proportion of the amount spent on ARVs). As such, the project was an important opportunity to catalyse the market for this FDC. It should also be noted that this project primarily procured the paediatric formulation of AZT+3TC+NVP, accounting for 88% of all AZT+3TC+NVP procurement.

As shown in the figure below, with the exception of the first year of the project, the supply of AZT+3TC+NVP was dominated by Mylan (and prior to Mylan's acquisition in 2007, Matrix Laboratories). The switch from Cipla to Mylan in 2008 was attributable to the paediatric formulation of the FDC being available on the market. Overall, Mylan and Matrix Laboratories accounted for 95% of the quantity of AZT+3TC+NVP procured under the project.

As regards prices paid, Figure G.1 below also shows that the large reductions in treatment costs came between 2007 and 2008. After this, treatment costs on the project remained relatively stable at slightly above US\$100 PPPY. While these price are relatively low, this does suggest that for most of the project there was less focus from CHAI to try and reduce prices offered by Mylan further.

Figure G.1: Left axis: AZT+3TC+NVP project purchases by supplier (US\$m); Right axis: Weighted average treatment cost PPPY (US\$)⁹¹



Source: CEPA analysis, based on project procurement tracker and GPRM database

G.1.3. Supply and pricing in low and lower-middle income countries

As regards wider supply of the paediatric formulation of AZT+3TC+NVP (60mg+30mg+50mg), Figure G.2 shows that the market was initially solely supplied by Mylan, although in recent years Cipla and Strides have been supplying the market.⁹² From 2008-13, the Unitaid project was almost the only procurer of this FDC, suggesting that the project was important in maintaining this market in these countries.⁹³

As regards prices, the figure below also shows that the treatment cost PPPY for low and lower-middle income countries has continued to decline over time. While Figure G.1 above shows a weighted average treatment cost PPPY of around US\$100, in 2017, the weighted average treatment cost PPPY for the paediatric regimen of AZT+3TC+NVP was US\$73, suggesting that prices have been able to reduce further than what was achieved on the Paediatric HIV/AIDS project. It is also worth noting that the market size for the paediatric version of the product has been falling since 2013, which is likely related to it being phased out of country programmes as a

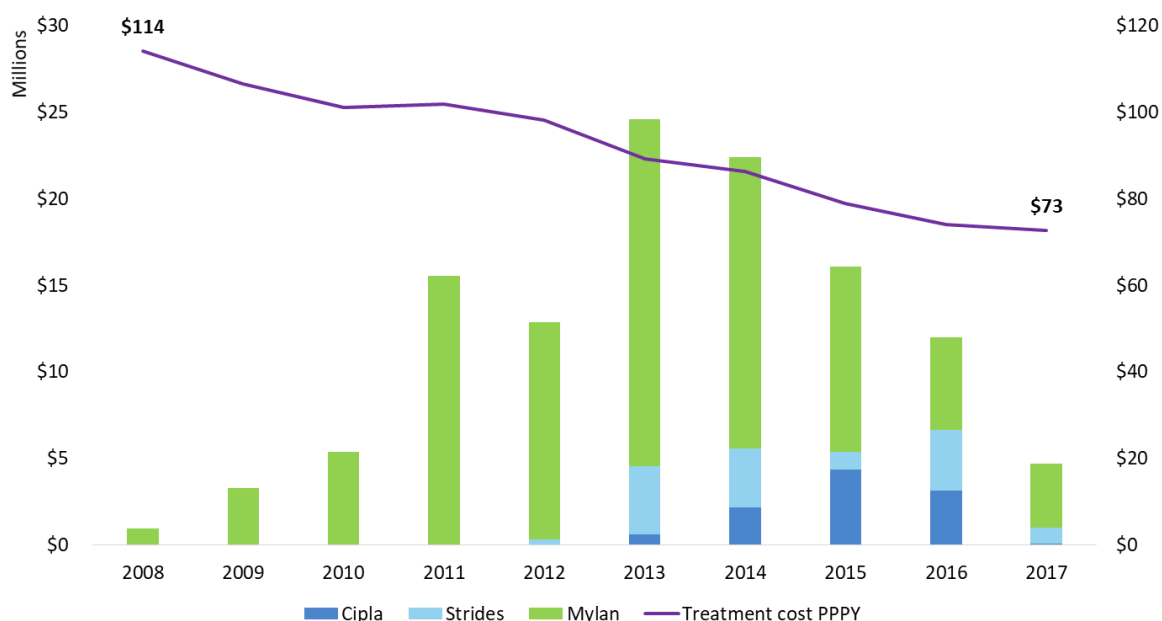
⁹¹ The weighted average cost PPPY weights the average treatment cost PPPY by the proportion of a specific formulation and dosage of the ARV by the total value of procurement for that given year. For example, if only one formulation and dosage was used in a given year, the weighted average cost PPPY and the average treatment cost PPPY for that specific formulation and dosage of the ARV.

⁹² We have focused on only the paediatric formulation of AZT+3TC+NVP in this sub-section as this was the main formulation procured under the project. While the adult formulation was also procured under the project, this was only done on a limited basis.

⁹³ Note that Cipla supply on the Paediatric HIV/AIDS project was primarily for the adult formulation of AZT+3TC+NVP. As a result, they are not included in the data for 2008-10 below.

result of findings that protease inhibitors (PIs) such as lopinavir/ritonavir (LPV/r) are more effective than NVP for treating paediatric HIV (see below for the market analysis for this commodity).

Figure G.2: Paediatric AZT+3TC+NVP supply by manufacturer for low and lower-middle income countries⁹⁴



Source: CEPA analysis, based on GPRM database

G.2. Zidovudine (AZT) +Lamivudine (3TC)

G.2.1. Overview

The AZT+3TC is one of the most well-known FDCs for treating HIV. AZT+3TC was first introduced following the US FDA approval in 1997 to GSK, for its branded version of the product, Combivir. Since 2009, the patent for AZT+3TC has been held by ViiV Healthcare, a joint venture between GSK, Pfizer and (since 2012) Shionogi. The company specialises in the development of HIV treatments, and holds the patents for a number of key paediatric ARVs. The arrival of the drug was a revolution in HIV treatment given that it was the first FDC and has less undesirable side-effects compared to solely AZT and d4T treatment (the two main forms of treatment at the time). AZT+3TC is generally taken with a PI or a NNRTI as part of treating patients. AZT+3TC is available in tablet and dispersible tablet form for paediatric use (both in 60mg/30mg in dosages), as well as 300mg/150mg adult formulations which have been used for treating children. More recently, a 120mg/60mg version has become available, and it is likely to be a key form of paediatric treatment going forward due to the lower pill burden compared to current paediatric versions of the drug.

⁹⁴ Given that this only includes supply of the paediatric version of the FDC, the figure does not fully correspond to the figure that includes project supply, as the latter also includes

There has been a relatively large amount of generic competition for AZT+3TC, mainly as a result of the combination and molecules not being patented in key markets, particularly in India. In 2005, generic versions of the medicine came under threat, as GSK filed a patent application for the combination in India, as a result of the country starting to grant patents on pharmaceutical products. However, following pressure from CSOs (mainly in India), GSK announced in 2006 that it would not file patents specific to FDCs in all countries. Despite this, the cost of the FDC remained high in some middle income countries, particularly China, given that GSK has held the patent for 3TC alone. Table G.2 below provides a list of generic manufacturers and products for the FDC. As the table shows:

- A wide range of generic companies have received SRA or WHO PQ approval for AZT+3TC, both for the adult and paediatric (14) as well as the paediatric-specific (six) formulations.
- These regulatory approvals have dated back to 2004 for the adult and paediatric formulation and 2009 for the paediatric-specific product, indicating that generic supply of this FDC pre-dates Unitaid’s support under this project.
- Approvals have generally been for the tablet formulation, although more recently tablets for oral suspension has been provided for paediatric formulations.

Table G.2: List of generic manufacturers for AZT+3TC

Company	Formulation/Dosage	US FDA Approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Adult and paediatric formulations				
Cipla	Oral tablet 300mg/150mg	2006	2004	US\$197
Sun Pharmaceuticals ⁹⁵	Oral tablet 300mg/150mg	No approval	2005	US\$197
Strides	Oral 300mg/150mg	2015	2006	US\$182
Mylan	Oral tablet 300mg/150mg	2007	2008	US\$128
Emcure Pharma	Oral tablet 300mg/150mg	2007	Included due to US FDA approval	US\$116
Macleods	Oral tablet 300mg/150mg	2009	2011	US\$65

⁹⁵ Sun Pharmaceuticals acquired a 63% stake in Ranbaxy, and the initial WHO PQ was given to Ranbaxy for this product.

Company	Formulation/Dosage	US FDA Approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Micro Labs	Oral tablet 300mg/150mg	No approval	2010	US\$112
Teva Pharms	Oral tablet 300mg/150mg	2011	No approval	Not available
Universal Corporation	Oral tablet 300mg/150mg	No approval	2011	US\$96
Aurobindo	Oral tablet 300mg/150mg	2012	Included due to US FDA approval	US\$103
Lupin	Oral tablet 300mg/150mg	2012	2016	Not available
Hetero	Oral tablet 300mg/150mg	2014	2013	US\$93
Pharmacare	Oral tablet 300mg/150mg	2017	No approval	Not available
Shanghai Desano Bio-Pharmaceutical	Oral tablet 300mg/150mg	No approval	2017	Not available
Paediatric only formulations				
Aurobindo	Oral tablet 60mg/30mg	2009	No approval	US\$146
Mylan	Oral tablet 60mg/30mg	2011	2009	US\$121
Cipla	Oral tablet 60mg/30mg	2011	No approval	US\$78
Cipla	Tablet for oral suspension 60mg/30mg	2012	Included due to US FDA approval	Not available
Mylan	Tablet for oral suspension 60mg/30mg	2014	2014	Not available
Micro Labs	Oral tablet 60mg/30mg	No approval	2015	US\$46

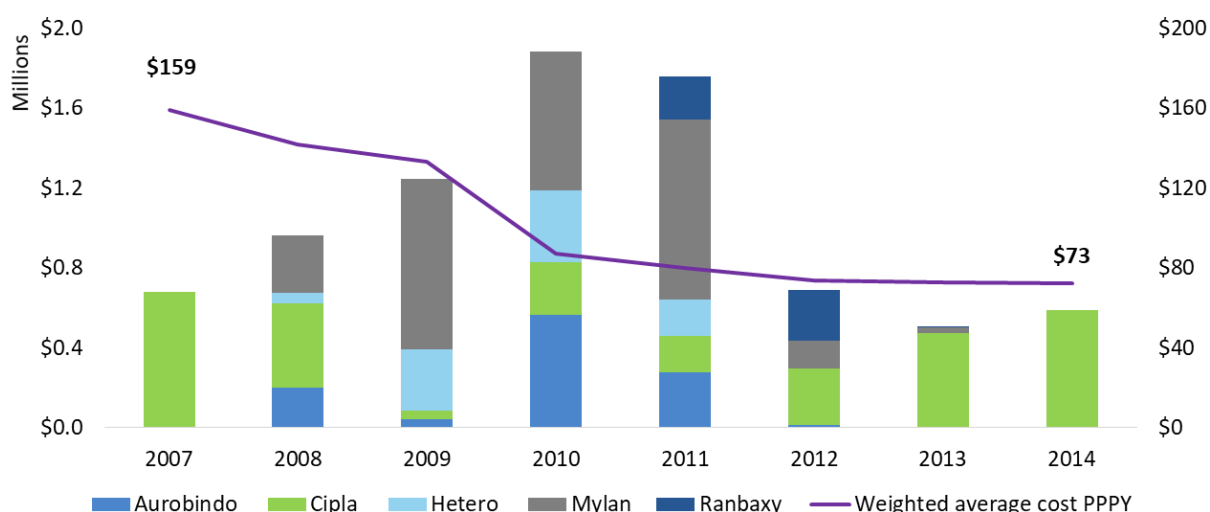
Source: US FDA and WHO PQ databases; MSF Untangling the Web in ARV Prices reports; GPRM.

G.2.2. Project supply and pricing

More than 2m packs of AZT+3TC drugs were procured under the Paediatric HIV/AIDS project (or 6% of all commodities procured), with more than US\$8m of project funding being used to buy the drugs.

As regards key suppliers, Figure G.3 shows that these drugs have been supplied by a number of generic manufacturers, although Cipla and Mylan/Matrix have tended to be the main suppliers in most years. As regards prices, Figure G.3 shows that significant reductions in treatment costs were experienced during the initial years of the project, before levelling off slightly in future years. In 2014, the weighted average treatment cost PPPY was around US\$73 for this FDC, suggesting that prices reduced by more than 50% over the course of the project.

Figure G.3: AZT+3TC procurement by supplier (by value) and weighted average treatment cost PPPY

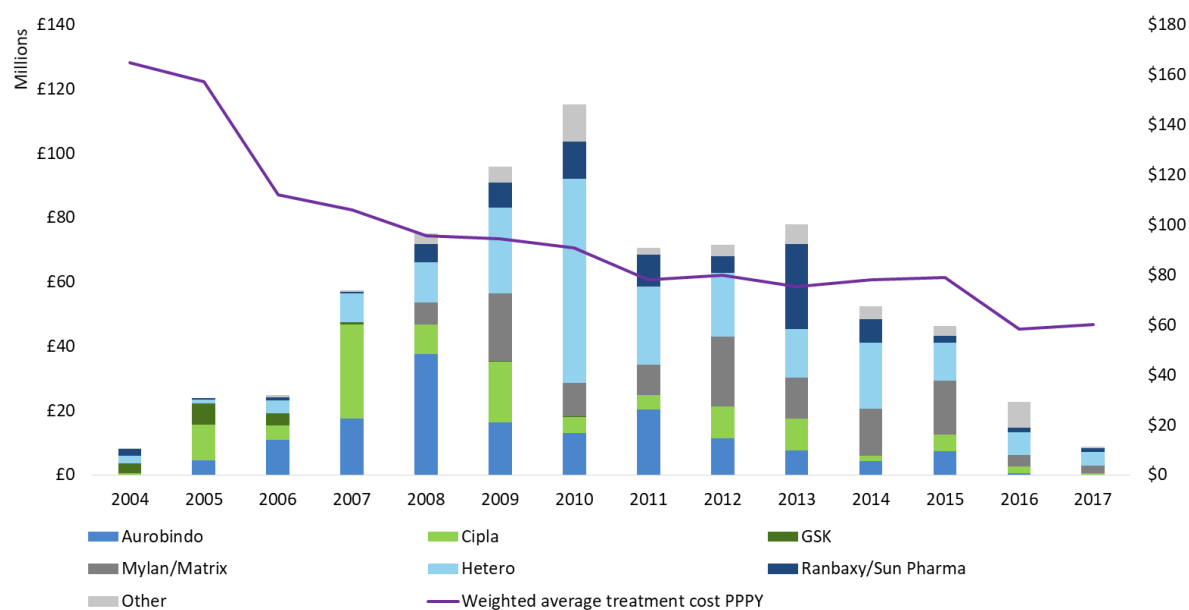


Source: CEPA analysis, based on project procurement tracker and GPRM database

G.2.3. Supply and pricing in low and lower-middle income countries

As regards wider supply in low and lower-middle income countries, Figure G.4 below shows that there have been several suppliers in this market. Key suppliers have included Hetero, Aurobindo, Cipla and Mylan, who accounted for more than 80% of the market over the period. While GSK was initially a key supplier back in 2004 and 2005 when the overall size of the market was relatively small, supply in future years was dominated by generic manufacturers. It should be noted that Unitaaid procurement accounted for almost all of the supply from 2008 until 2010, before falling to 63% in 2011 and declining significantly in the final years of the project. As was the case on the project, treatment costs have been declining steadily over the years, with prices reaching as low as US\$60 in 2017, 43% lower compared to prices in 2007 when the Unitaaid project started and 64% lower than prices in 2004 (i.e. some good price declines were achieved before commencement of the Unitaaid project).

Figure G.4: Left axis: AZT+3TC supply by manufacturer for low and lower-middle income countries (US\$m); Right axis: weighted average treatment cost PPPY (US\$)



Source: CEPA analysis, based on GPRM database.

G.3. Lopinavir (LPV) + ritonavir (r)

G.3.1. Overview

LPV/r has been one of the key protease inhibitors (PIs) used for treating HIV.⁹⁶ LPV is always co-formulated with small doses of ritonavir, as LPV alone has limited bioavailability.⁹⁷ However, by including small doses of RTV, LPV levels are dramatically increased given that RTV slows down the rate at which LPV is metabolised by the liver. LPV/r is generally used alongside other ARVs for the treatment of HIV. LPV/r was the first ARV to contain a drug (LPV) that was not formulated separately.

LPV/r was first approved by the US FDA in September 2000 and in April 2001 in Europe by the European Medicines Agency (EMA). AbbVie (previously Abbott Laboratories) were the innovator company for the drug, and have sold the product under the brand name Kaletra. The original formulation of the drug was a soft gelatine capsule containing 133mg/33mg of LPV/r respectively, with recommended adult dosage being three capsules taken twice daily. Heat-stable versions that required lower pill burdens were released in 2005 (200mg/50mg), while an oral solution (80mg/ml, 20mg/ml) is also available and must be taken with food, and has often been the formulation used to treat children. In 2007, a paediatric-specific version

⁹⁶ PIs refer to a class of ARVs that limit the extent to which HIV releases protease into the body. Protease enables longer HIV protein chains to be broken up that form the immature virus. These smaller HIV proteins then combine to form mature (infectious) HIV. Hence, by limiting the extent to which HIV proteins are broken up, PIs reduce the extent to which mature HIV is made within the body.

⁹⁷ i.e. the proportion of a drug or other substance which enters the circulation when introduced into the body and so is able to have an active effect.

of the drug (100mg/25mg) was made available in the US (and was approved in the EU in 2008).⁹⁸ More recently, a 40mg/10mg oral pellet has been released by Cipla to treat children under three. This is a new heat-stable product that will help overcome cold storage issues. LPV/r has been recommended by WHO for first and second-line treatment since 2010, and is currently recommended by WHO for first-line treatment for all HIV positive children under three, and as part of second-line treatment for children between three and ten. It is also included on the 2016 IATT optimal paediatric ARV list in three different formulations and doses.⁹⁹

Introduction of LPV/r in developing countries has been accompanied by controversy.¹⁰⁰ In these markets, LPV/r has been distributed under the brand name Aluvia. AbbVie has been subject to a significant amount of criticism for not distributing the drug widely enough nor making it affordable enough in developing countries.¹⁰¹ In April 2007, AbbVie offered LPV/r through its preferential pricing programme to all African countries and some additional low income countries at US\$500 PPPY for its 200mg/50mg and 133mg/33mg dosage forms, and to 45 lower and lower-middle income countries at US\$1,000 PPPY, while the 80mg/ml, 20mg/ml oral solution was offered at US\$200 and US\$400 respectively. These prices were considerably higher than other key ARVs (especially nevirapine (NVP) which Hetero was selling at US\$48 PPPY for the 200mg dosage around the same time, but was 90% lower than the cost in the developed world).¹⁰²

Despite AbbVie's lower pricing for LPV/r in low and lower-middle income countries, a number of generic companies have obtained SRA or WHO PQ approval for different formulations and dosages and provided their product at comparable prices. As shown in Table G.3 below, five generic companies have received SRA or WHO PQ approval for the 200mg/50mg tablet version of LPV/r, while there have been six approvals for companies that will enable supply of either the oral solution, the paediatric tablets (100mg/25mg) or, as mentioned above, oral pellets.

Table G.3: Approval of generic manufacturers for LPV/r

Company	Formulation/Dosage	US FDA Approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Adult and paediatric formulations				
Mylan	Oral tablet 200mg/50mg	2009	2009	US\$486

⁹⁸ It should be noted that the 200mg/50mg version of LPV/r has also been used to treat paediatric patients, including as part of the CHAI project.

⁹⁹ The 100mg/25mg heat-stable tablet, the 80mg/ml 20mg/mg oral liquid and the 40mg/10mg oral pellets.

¹⁰⁰ See MSF (2007) *Untangling the Web of Antiretroviral Price Reductions*, plus later versions, for further details.

¹⁰¹ In 2007, Thailand issued a compulsory licence for LPV/r, which resulted in AbbVie withdrawing registration of LPV/r and seven other of its products from the country, citing the government's lack of respect for patents. This was met with wide condemnation by various NGOs.

¹⁰² MSF (2007) *Untangling the Web of Antiretroviral Price Reductions*.

Company	Formulation/Dosage	US FDA Approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Cipla	Oral tablet 200mg/50mg	2009	Included due to US FDA approval	US\$486
Aurobindo	Oral tablet 200mg/50mg	2009	Included due to US FDA approval	US\$511
Hetero Labs	Oral tablet 200mg/50mg	2012	2013	US\$389
Macleods	Oral tablet 200mg/50mg	2016	2015	US\$293
Paediatric only formulations				
Mylan	Oral tablet 100mg/25mg	2011	2009	US\$228
Aurobindo	Oral tablet 100mg/25mg	2009	Included due to US FDA approval	US\$329
Cipla	Oral solution 80mg/ml 20mg/ml	2012	No approval	US\$292
Cipla	Oral pellet 40mg/10mg	2015	No approval	US\$467
Silarx Pharmaceuticals	Oral Solution 80mg/ml 20mg/ml	2016	No approval	Data not available
Macleods	Oral tablet 100mg/25mg	2016	2015	US\$143

Source: US FDA and WHO PQ databases; MSF *Untangling the Web in ARV Prices reports*; GPRM.

It should also be noted that in December 2014, AbbVie and the Medicines Patent Pool (MPP) announced a licensing agreement for paediatric LPV/r that would allow other companies to re-formulate and manufacture LPV/r and r paediatric treatments in 102 countries, including South Africa that previously was unable to access these medicines from other suppliers or at the reduced prices received by CHAI project countries. AbbVie and MPP also announced a licensing agreement for adult formulations of LPV/r in 2015.

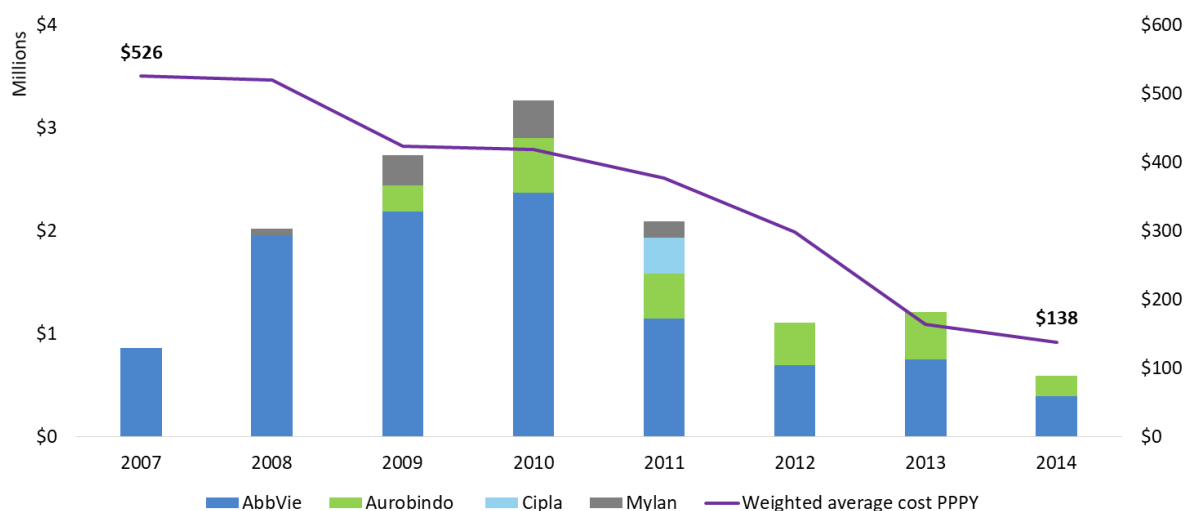
G.3.2. Project supply and pricing

Over the course of the Paediatric HIV/AIDS project, nearly 726,000 packs of LPV/r products were procured, with US\$13.9m of project funds being spent on the various formulations and dosages. While the project initially procured mostly formulations produced for adults

(200mg/50mg) and oral solutions, overall 62% of LPV/r products were the paediatric 100mg/25mg tablets.

Unlike a number of ARVs procured under the paediatric HIV/AIDS project, for many years LPV/r was supplied by the innovator company. However, as Figure G.5 below shows, generic suppliers accounted for a larger share of LPV/r procurement over time, which was coupled with reduced average treatment costs PPPY.

Figure G.5: Left axis: LPV/r project purchases by supplier (US\$m); Right axis: Weighted average treatment cost PPPY (US\$)



Source: CEPA analysis, based on project procurement tracker and GPRM database.

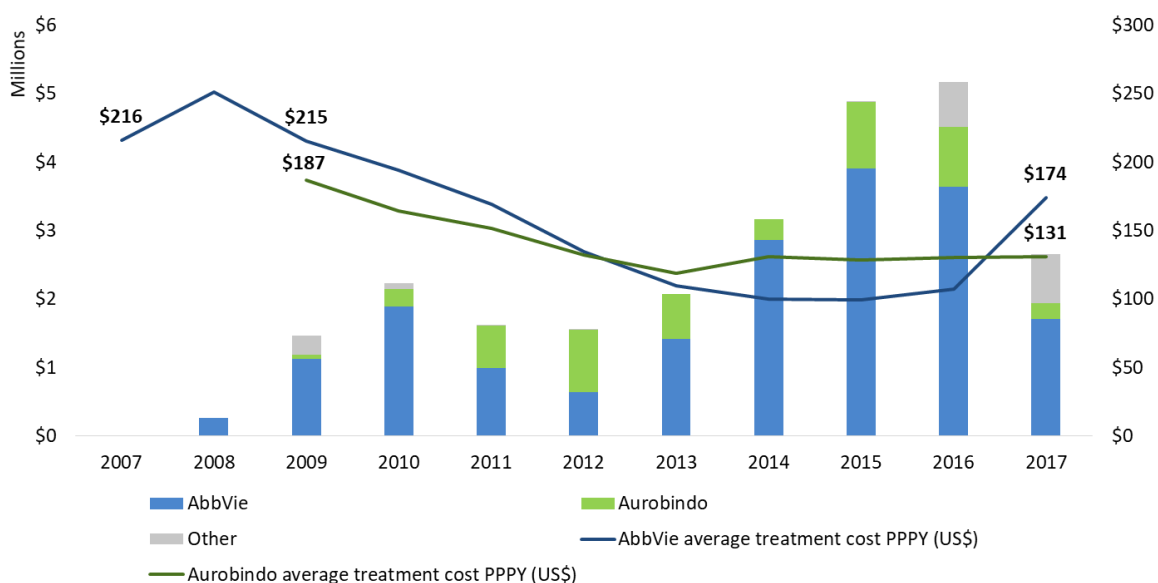
G.3.3. Supply and pricing in low and lower-middle income countries

Taking the 100mg+25mg dosage form of LPV/r, Figure G.6 below shows how supply and treatment costs have changed over time, based on data collected from the GPRM database.¹⁰³ As the figure shows, AbbVie have remained a dominant supplier of this commodity, while Aurobindo has remained the key generic supplier. Other suppliers that have been important in the market have included Cipla (particularly during the 2011-13 period) and Mylan in 2017. As regards prices, AbbVie has offered prices that are competitive with generic manufacturers, and these have declined by 20% between 2007 and 2017. However if the average cost PPPY is taken, prices have fallen by more than 50%. Aurobindo prices have fallen by 30% since it began supplying the market for this drug, although with the exception of 2017 these were higher than those offered by AbbVie. One thing to note is that, as with other ARVs analysed in this section Unitaid procurement accounted for a large amount of procurement of the paediatric version of this ARV, with more than 75% of procurement between 2008 and 2011 being accounted for by Unitaid funding.¹⁰⁴

¹⁰³ Given that the figure for wider supply only includes the 100mg/25mg dose of LPV/r, it is not fully comparable with the figure for project procurement, which includes the various formulations and doses.

¹⁰⁴ We have used the GPRM database as the single source for making this comparison, as opposed to comparing actual procurement data with wider procurement in the GPRM, given that figures differ slightly.

Figure G.6: Left axis: LPV/r 100mg+25mg supply (US\$m) by manufacturer; Right axis: Average treatment cost PPPY for low and lower-middle income countries (US\$)



Source: CEPA analysis, based on GPRM database.

To conclude, our assessment of the LPV/r market suggests that over time the market has matured with the introduction of paediatric-specific formulations that have been able to overcome cold storage constraints. In addition, prices have shown a generally decline over time, particularly for the 100mg+25mg oral tablets. While a number of suppliers have entered the market for 200mg +50mg and (to a lesser extent) the 100mg+25mg, the product innovator has maintained a relatively dominant position in the market, mostly on account of its significantly low price offering. Going forward, the introduction of the new smaller doses for infants will be an important addition, and it will be interesting to see whether the new licencing agreement signed between AbbVie and MPP will impact supply on the African market.

G.4. Abacavir (ABC) + Lamivudine (3TC)

G.4.1. Overview

ABC+3TC is another NRTI FDC that has been a key form of treatment used for treating CLHIV, both on the Paediatric HIV/AIDS project and more widely. ABC+3TC is seen as an efficacious combination, and the flexibility of the using this NRTI backbone with NNRTIs or PIs has meant it has formed the backbone of treatment regimens. Recent WHO recommendations have included ABC+3TC in first-line treatment for children under ten, and has been included as part of first and second-line treatment for HIV since 2006. In addition, the paediatric dosage of ABC+3TC (60mg+30mg) has been included in the IATT Optimal list since 2011. The product is also available in 120mg+60mg doses, and doses relevant for adults at 600mg+300mg.

ABC+3TC was first approved by the US FDA in August 2004 and by the European Medicines Agency in December 2004. In the US, ABC+3TC is sold under the brand name Epzicom and in

the EU as Kivexa. GSK are the innovators of the FDC, and since 2009 ViiV Healthcare has held the patent for this product. For both adult and paediatric regimens, price has been an issue for ABC+3TC, as over the years this has been double the price of AZT+3TC FDCs. As regards patents, GSK could not apply for basic patents related to ABC or 3TC in countries that did not grant patents on pharmaceuticals before the implementation of TRIPS, allowing Indian generic companies to supply either these medicines individually or in the FDC. However, in some countries, particularly China, GSK was able to apply patents and as a result higher prices were paid. In Ecuador, the government issued a compulsory licence on ABC+3TC in 2012 with the hope of reducing the price by 75%.¹⁰⁵

Table G.4 below summarises the list of supplier regulatory approvals and treatment costs PPPY for ABC+3TC. Note that we have only included approvals for the paediatric doses of 60mg+30mg, given that adult doses were not procured under the Paediatric HIV/AIDS project.

Table G.4: List of generic manufacturers for ABC+3TC 60mg+30mg

Company	Formulation	US FDA Approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Aurobindo	Oral tablet 60mg/30mg	2008	2009	US\$194
Mylan	Oral tablet 60mg/30mg	2012	2008	US\$219
Cipla	Tablet for oral suspension 60mg/30mg	2011	2014	US\$175
Mylan	Tablet for oral suspension 60mg/30mg	2014	Included due to US FDA approval	US\$96
Hetero	Oral tablet 60mg/30mg	2015	Included due to US FDA approval	US\$622 ¹⁰⁶

Source: US FDA and WHO PQ databases; MSF Untangling the Web in ARV Prices reports; GPRM.

G.4.2. Project supply and pricing

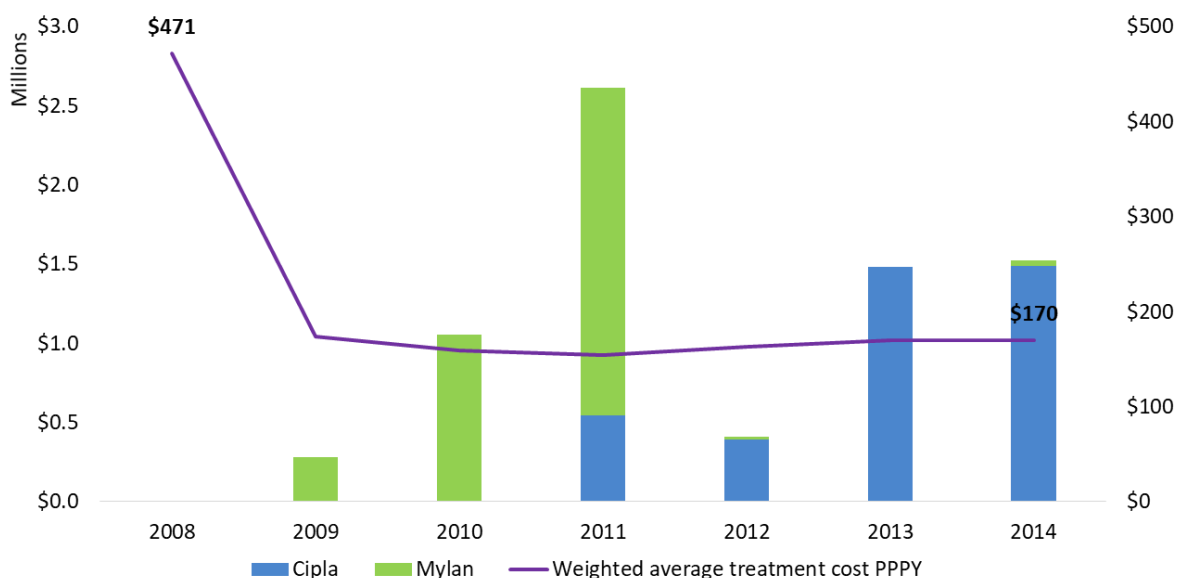
The Paediatric HIV/AIDS project procured more than 1.1m packs of the paediatric ABC+3TC tablets and costed nearly US\$7.4m. As Figure G.7 shows, supply on the Paediatric HIV/AIDS project was dominated by two suppliers – Matrix/Mylan and later Cipla, with overall supply being relatively equal between these two suppliers, although Matrix/Mylan were the initial supplier of the product before Cipla took over supply in later years. The change in supplier reflects the increase in dispersible versions of ABC+3TC over normal tablet versions, with Cipla

¹⁰⁵ MSF (2013), Untangling the Web of Antiretroviral Price Reductions.

¹⁰⁶ Based on entry in GPRM pricing database.

being the primary supplier of the former while Mylan was the primary supplier for the latter. This switch was made as a result of the product becoming eligible to supply the project in 2011, and the preference for dispersible tablets for children. CHAI was able to secure a significant reduction in treatment costs at the start of the project of nearly US\$300 PPPY, after which treatment costs remained relatively stable throughout the project.

Figure G.7: Left axis: ABC+3TC project purchases by supplier (US\$m); Right axis: Weighted average treatment cost PPPY (US\$)



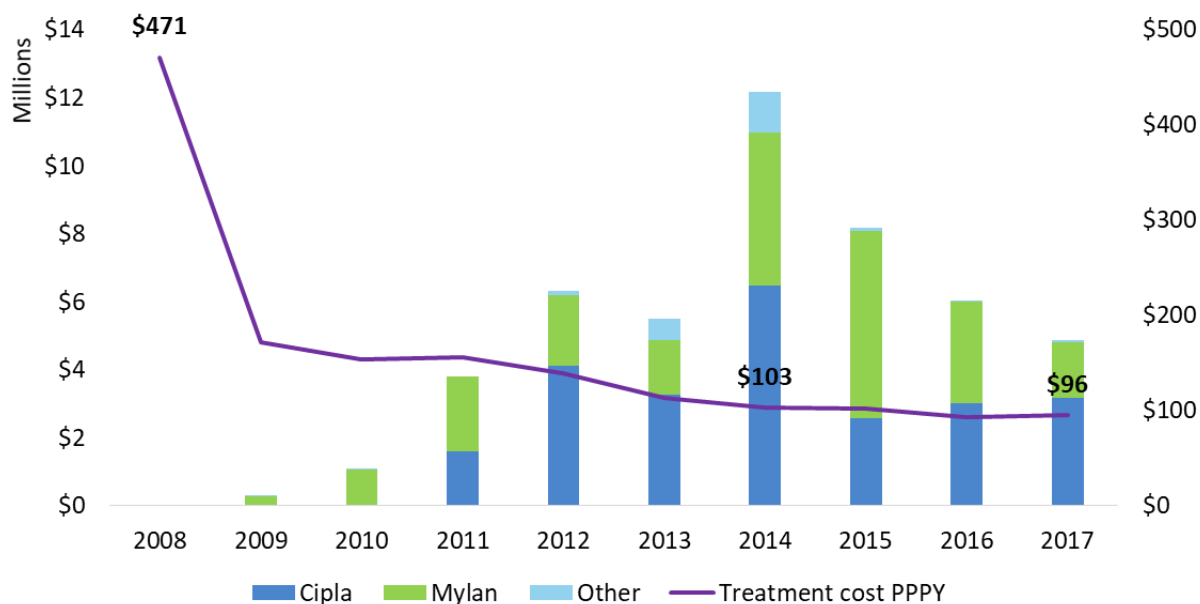
Source: CEPA analysis, based on project procurement tracker and GPRM database.

This suggests that despite a number of suppliers being US FDA or WHO PQ approved, these suppliers were able to keep a competitive position for this product, and priced in a way that allowed them to remain competitive, given that pressures to reduce prices below the US\$170 PPPY mark were relatively limited.

G.4.3. Supply and pricing in low and lower-middle income countries

In terms of wider supply, Figure G.8 shows that the market for this commodity has been dominated by the two main suppliers of the Paediatric HIV/AIDS project, while competition from other suppliers has been relatively limited, despite competitors obtaining regulatory approvals. Between 2008 and 2010, ABC+3TC procurement was solely undertaken with Unitaid funding (and accounted for 70% in 2011), highlighting the important role the project had on bringing this product to these markets. As regards prices, the figure shows that prices have been able to fall considerably, with average cost of treatment falling by US\$376 PPPY between 2008 and 2017. Another interesting observation is that relative to the wider market, PPPY prices were somewhat higher on the Unitaid project, especially between 2012 and 2014 when funding was mainly being transitioned.

Figure G.8: Left axis: ABC+3TC supply (US\$m) by manufacturer; Right axis: Average treatment cost PPPY for low and lower-middle income countries (US\$)



Source: CEPA analysis, based on GPRM database

G.5. Efaviranz (EFV)

G.5.1. Overview

EFV is a NNRTI that is often used with NRTIs in FDCs or as a single medication for treating HIV. The ARV comes in a variety of doses and formulations, with the most common doses for paediatric use being 200mg and 50mg tablets or capsules (with 600mg doses being used to treat adults). EFV was initially approved by the US FDA in 1998, and is sold under the brand name Sustiva by both BMS and Merck and Co, who jointly hold the rights to sell the product in different countries.¹⁰⁷ The original approval of the drug was for treatment of adults and children aged three and above and weighed at least 10kg. However, in 2013 BMS was awarded a patent by the US FDA for infants aged three months to three years and weighing at least 3.5kg. EFV has formed part of WHO first-line treatment guidelines for children older than three years, and the 200mg scored tablet has been part of the optimal IATT list since 2011. However, going forward it is likely that should paediatric dolutegravir (DTG) become available (which is one of the products being supported under Unitaid's Optimal ARVs grant), EFV usage is likely to decline.

Since coming onto the market, a number of generic manufacturers have received US FDA or WHO PQ approval. Despite several suppliers on the market, only one has been approved for the preferred scored version of the 200mg. The generic suppliers that have been approved

¹⁰⁷ BMS holds the rights to EFV and related products in the US, Canada, the UK, Germany, France, Italy, Spain and Ireland, while Merck holds the rights to sell the product in other European countries and other countries not covered by BMS.

by the US FDA or WHO PQ are summarised in the table below (note that we have excluded 600mg approvals from this table).

Table G.5: Approval of generic manufacturers for EFV

Manufacturer	Formulation and dose	US FDA approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Aurobindo	Oral tablet 50mg Oral tablet 100mg Oral tablet 200mg	2005	Included due to US FDA approval	50mg: US\$80 ¹⁰⁸ 100mg: Not available 200mg: US\$438
Cipla	Oral capsule 200mg	2009	No approval	US\$146
Mylan	Oral tablet 50mg Oral tablet 100mg Oral tablet 200mg	2009	Included due to US FDA approval	50mg: US\$66 100mg: US\$60 200mg: US\$25
Strides	Oral tablet (scored) 200mg	2010	2009	US\$128
Micro Labs	Oral capsule 50mg Oral capsule 200mg	2012	No approval	50mg: US\$90 200mg: US\$61
Micro Labs	Oral tablet 50mg Oral tablet 100mg Oral tablet 200mg	2018	No approval	Not available

Source: US FDA and WHO PQ databases; MSF Untangling the Web in ARV Prices reports; GPRM.

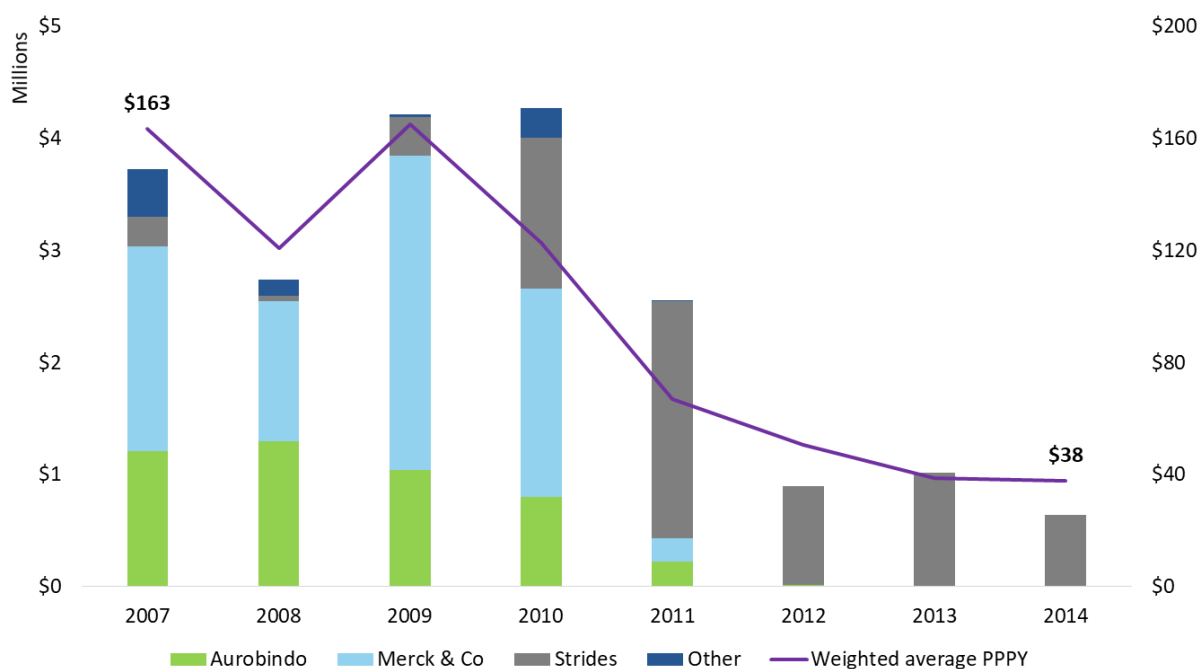
G.5.2. Project supply and pricing

EFV was among the key ARVs procured under the Paediatric HIV/AIDS project, with nearly 2.35m of the different EFV formulations and dosages being procured worth more than

¹⁰⁸ This PPPY estimate is based on prices quoted by MSF for two tablets costing US\$0.11 taken daily for 365 days, given that the PPPY cost is not quoted in their report.

US\$20m by the end of the project, or 13% of the value of commodity procurement. The majority of EFV procurement was the 200mg tablets, which accounted for US\$13m in costs. The project was also able to achieve significant reductions in treatment costs PPPY, as shown in Figure G.9 below. The figure also shows that initially a significant amount of EFV was sourced from Merck & Co, before a greater share of procurement transitioned to generic suppliers, with Aurobindo being the main supplier in early years while Strides was the main supplier during the later years of the project, given the preference for the scored version of the 200mg tablet.

Figure G.9: Left axis EFV project purchases by supplier (US\$m); Right axis: Weighted average treatment cost PPPY (US\$)

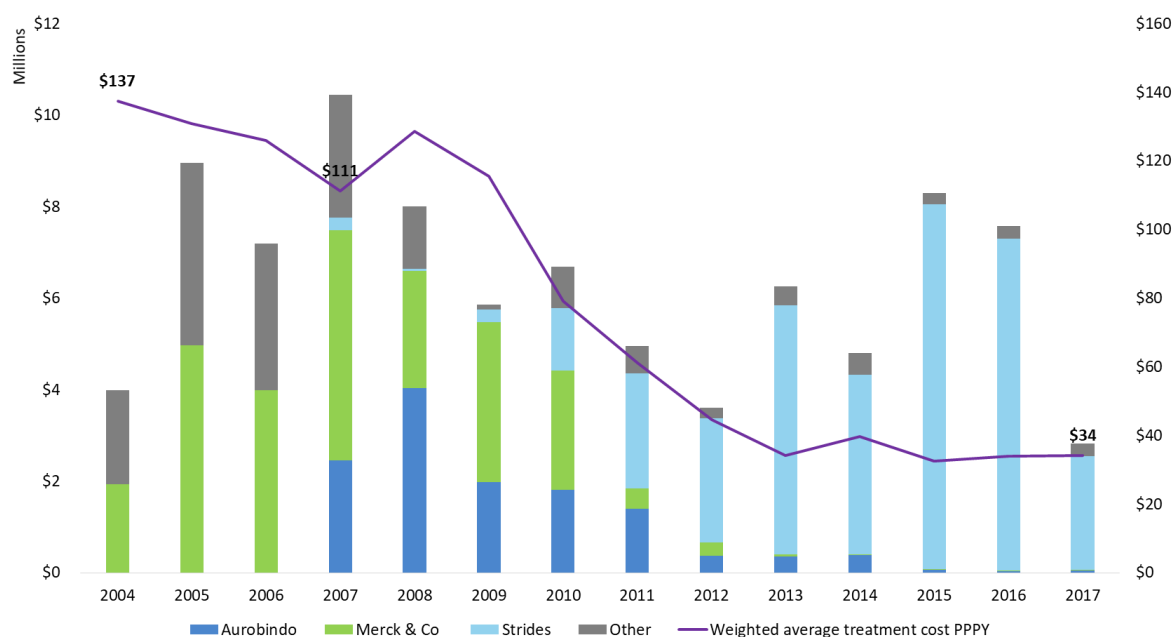


Source: CEPA analysis, based on project procurement tracker and GPRM database.

G.5.3. Supply and pricing in low and lower-middle income countries

The decline EFV prices (for doses used for paediatric treatment) aligned closely with the implementation of this project, as shown in Figure G.10 below. The figure also shows that supply in low and lower-middle income countries has mainly reflected the supply base of the project, with Strides being the major supplier of EFV in recent years. It should be noted that up until 2012 the project accounted for a large proportion of EFV procurement for paediatric doses. For example, in 2009 and 2010 the project accounted for over 70% of donor procurements of the 200mg and 50mg of EFV. Since the first year of the project, the weighted average treatment cost PPPY has fallen by 70% for EFV, highlighting the considerably progress made with regards to ensuring affordability.

Figure G.10: Left axis: EFV supply (US\$m) by manufacturer; Right axis: Weighted average treatment cost PPPY for low and lower-middle income countries (US\$)



Source: CEPA analysis based on GPRM database

G.6. Nevirapine (NVP)

G.6.1. Overview

NVP is a key NNRTI that has been used for treating HIV among adults and children, forming a key part of key FDCs such as AZT+3TC+NVP mentioned previously as well as d4T+3TC+NVP, which until recently was a key FDC used for treating HIV. NVP is available in a wide range of formulations and dosages, with treatment for children often being in either 50mg or 200mg doses (the latter also being used for treating adults), with the 50mg being available as a tablet or in syrup form. Historically, NVP has formed part of WHO recommendations for first-line treatment of children of all ages. However, in 2013 WHO recommended that LPV/r be used as part of first-line treatment alongside NRTIs for children under three, while EFV has been recommended for children older than three, given that both have shown greater efficacy than NVP for treating children. As a result, it is expected that health programmes will phase out the use of NVP going forward.

NVP was first approved by the US FDA in 1996, and the innovator company was Boehringer Ingelheim and was sold under the brand name Viramune, which expired in 2012. While originator prices for NVP have reduced in recent years, supply in low income countries has been made by generic companies given that they have offered significantly lower prices. Organisations such as MSF have previously criticised Boehringer Ingelheim for not including versions used specifically for children, stating in 2008 that it costed more to treat a 10kg child

with NVP than an adult due to Boeringher Ingelheim excluding paediatric formulations of NVP from its donation programme for PMTCT.¹⁰⁹

Generic competition for the 200mg dose of NVP is relatively extensive, given the historical importance of NVP in HIV treatment programmes, while several companies have also obtained regulatory approval for paediatric versions. The table below includes regulatory approvals of generic producers for forms of NVP specific to children (i.e. excluding the 200mg approvals, given that this has been obtained by a wide range of generic companies).

Table G.6: Approval of generic manufacturers for NVP

Manufacturer	Formulation and dose	US FDA approval	WHO PQ	Treatment cost PPPY when first approved by FDA/WHO PQ
Aurobindo	Oral suspension 50mg/5ml	2005	Included due to US FDA approval	US\$135
Cipla	Oral suspension 50mg/5ml	2017	2009	US\$77
Cipla	Tablet for oral suspension 50mg 100mg	2012	2014	50mg: US\$53 100mg: No data available
Aloegen	Extended release oral tablet 100mg	2012	Not approved	No data available
Micro Labs	Oral tablet 20mg 50mg 100mg	Not approved	2014	20mg: No data available 50mg: US\$30 100mg: No data available
Mylan	Extended release oral tablet 100mg	2015	Not approved	Not available
Aurobindo	Extended release oral tablet 100mg	2016	Not approved	Not available

US FDA and WHO PQ databases; MSF Untangling the Web in ARV Prices reports; GPRM.

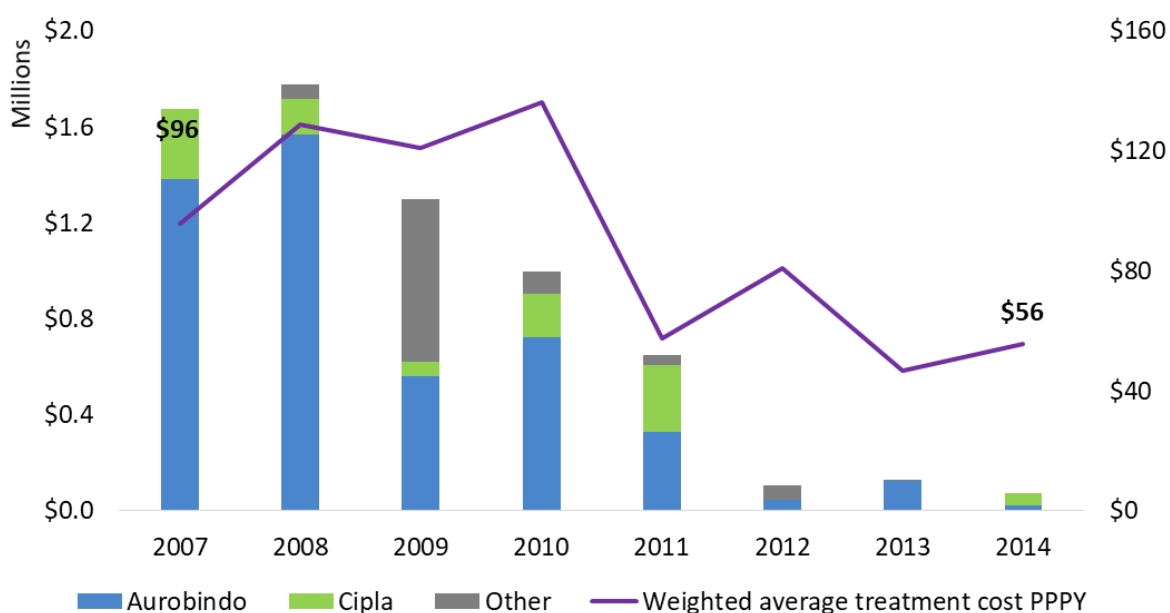
G.6.2. Project supply and pricing

Nearly 3m NVP packs were procured as part of the Paediatric HIV/AIDS project, accounting for US\$6.7m of total commodity spending. The 50mg/ml syrup version of the ARV accounted for more than two thirds of NVP procurement both in quantity and value, with the 200mg

¹⁰⁹ MSF (2008), Untangling the Web of ARV Price Reductions.

dose also accounting for a significant amount of procurement (520k packs, equivalent to 18% of total commodities and 26% of total value) while the 50mg dispersible tablets accounted for almost all NVP procurement in 2013 and 2014 (noting these were years with lower levels of procurement overall). As shown in the figure below, Aurobindo was often the main supplier for NVP tablets, while Cipla also played an important role over the years. As regards prices, while they varied and were relatively high during the initial years of the project, in later years prices were considerably lower. However, it is unclear why prices for NVP were so high in the early years of the project, given that this single formulation ARV is among one of the cheaper ARVs in the market.

Figure G.11: Left axis: NVP project purchases by supplier (US\$m); Right axis: Weighted average treatment cost PPPY (US\$)

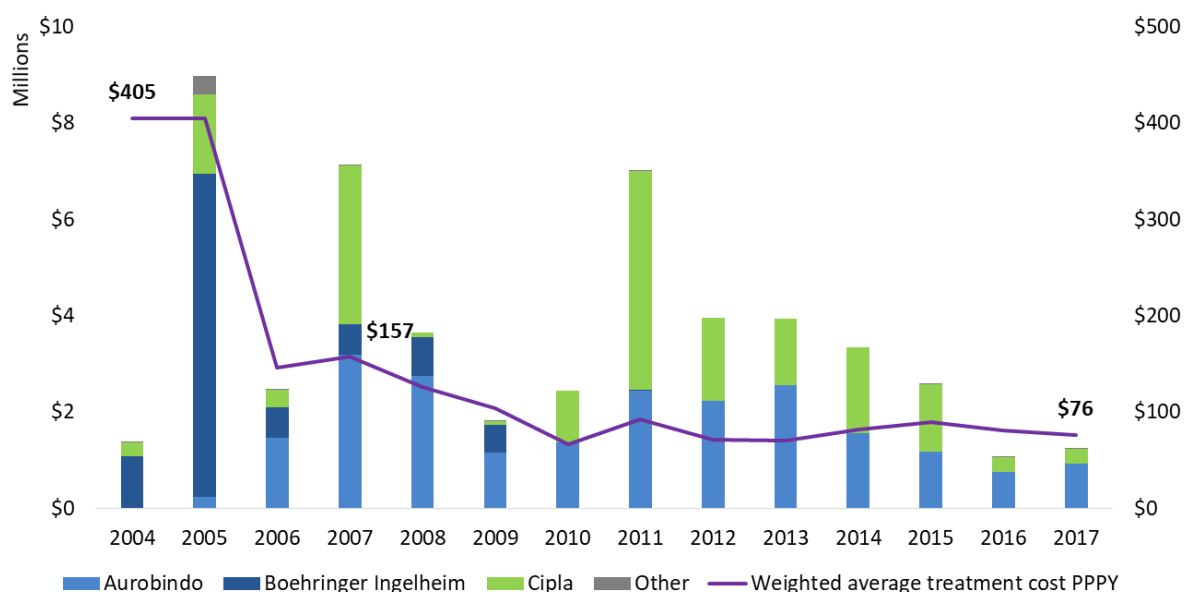


Source: CEPA analysis, based on project procurement tracker and GPRM database

G.6.3. Supply and pricing in low and lower-middle income countries

For analysing wider impact, we have excluded the 200mg tablet from the analysis, given that this formulation is mainly used in the adult market and has been procured in significantly quantities, and as such the project has been less focused on increasing access to this product. Therefore, only paediatric formulations (the 50mg tablets and the oral suspension) are included. As shown in the figure below, both Aurobindo and Cipla have been key suppliers both on the project and more widely in these market, although it should be noted that Unitaidd procurement accounts for a considerable amount of the procurement shown below. For example, for the oral suspension, Unitaidd accounted for at least 60% between 2006 and 2011, and was 93% in 2008. Between 2004 and 2009, Boehringer Ingelheim were a key supplier of these commodities, although since then supply has been provided solely by generic companies. As regards prices, significant decreases were experienced between 2004 and 2006, with relatively more gradual declines taking place over the period.

Figure G.12: Left axis: Paediatric NVP supply (US\$m) by manufacturer; Right axis: Weighted average treatment cost PPPY for low and lower-middle income countries (US\$)



Source: CEPA analysis, based on GPRM database.

This analysis shows that generic suppliers have been able to enter the market for paediatric NVP, although this has been dominated by Cipla and Aurobindo. Given that prices have been able to fall significantly and remained lower for a number of years, coupled with the small size of the paediatric market, the number of suppliers is likely to have been appropriate. Going forward, supply of NVP and FDCs including the ARV is likely to decline as a result of WHO guidelines and the IATT list favouring either PIs and/or other NNRTIs.