INDEPENDENT END OF PROJECT EVALUATION

SECOND-LINE HIV/AIDS PROJECT

UNITAID

PARTNER: CLINTON HEALTH ACCESS INITIATIVE (CHAI)

13 SEPTEMBER 2013

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All views represented in this evaluation are those of Dalberg and do not represent the views of UNITAID, partners, or other entities quoted herein.

Contents

List of Figures and Tables

Abbreviations

API	Active Pharmaceutical Ingredient
ART	Antiretroviral Therapy
ARV	Antiretroviral
CHAI	Clinton Health Access Initiative
FDA	Food and Drug Administration
FDC	Fixed Dose Combination
IDA	International Dispensary Association Foundation
MoH	Ministry of Health
MoU	Memorandum of Understanding
MSA/LTA	Master Supply Agreement / Long Term Agreement
MSF	Médecins Sans Frontières
N/A	Not applicable
PEPFAR	The U.S. President's Emergency Plan for AIDS Relief
PO	Purchase Order
PSM	Procurement and Supply Management Plan
R&D	Research and Development
SRA	Stringent Regulatory Authority
ToR	Terms of Reference
USD	United States Dollar
WHO	World Health Organization
WHO PQ	World Health Organization Prequalification Program

1 Context

1.1 Project Background

In 2006, WHO predicted that the need for second-line drugs would rise dramatically as patients increasingly developed resistance to first-line treatments. Depending on the switch rate, the number of people needing second-line treatment would range from 500,000 to 800,000 by 2010, up from a baseline of approximately 150,000 patients globally at the time. Before UNITAID intervened, there were only a limited number of suppliers, four branded manufacturers and only one generic in the second-line ARV market, and prevailing drug prices for low-income and lower-middle-income countries were prohibitive, roughly ten times higher than first-line treatment. Additionally, all formulations of second-line ARVs required cold chain transportation and storage, which posed a challenge for low-income countries with poor infrastructure. There was a great need for intervention in the second-line ARV market in order to promote the sustainable affordability, quality, and accessibility that comes from healthy competition among market actors.

UNITAID was established in 2006 and second-line HIV/AIDS was one of its first major interventions, along with the Pediatrics HIV/AIDS treatment project. UNITAID entered into a partnership with CHAI (the Clinton Health Access Initiative) for both the second-line ARV and pediatrics HIV/AIDS treatment projects. The Second-line HIV/AIDS project aimed to catalyze the development of the second-line ARV drug market. The main objectives of the project were to:

- Scale up access to quality-assured second-line treatments in 25 low and middle-income countries and first-line Tenofovir-based treatments in three countries,
- Facilitate price reductions for these drugs, and
- Ensure that countries transition to alternative funding by the project's end.

This project was large in size and scope: the project budget was USD $299,650,557 and its work involved a wide range of activities at the global and national level in 25 countries. Originally scheduled to take place between May 2007 and December 2008, the project ultimately wound up running until December 2012 as a result of three approved project extensions.

UNITAID financed the purchase of ARVs to be made available in the 25 countries and provided management and oversight of the project. CHAI was responsible for floating tenders, selecting suppliers and negotiating prices. CHAI also carried out upstream and downstream activities such as: forecasting needs in collaboration with each beneficiary country; submitting countries' orders; planning for receipt, clearance, storage, and distribution of drugs; and confirming the delivery of drugs in order to trigger payment to suppliers. CHAI consolidated all countries' orders four times a year (15th of March, June, September, and December). Individual orders were placed as well to meet emergency needs or to solve supply chain problems.

The UNITAID/CHAI model for this project included a procurement agent who was responsible for submitting purchase orders to suppliers selected by CHAI, ensuring pre-shipment testing, and ensuring delivery to beneficiary countries, as well as for processing suppliers' payments. The initial procurement agent, Missionpharma, was replaced in April 2009 by the International Dispensary Association Foundation (IDA) after the role was re-tendered upon project extension.

In addition to its procurement functions, CHAI was responsible for providing technical support to countries to increase the effectiveness of ordering, receipt, and use of project drugs as well as ensuring countries transitioned to alternative funding by the project's end.

1.2 Project Description

The goal of the Second-line HIV/AIDS project was to increase and maintain access to second-line treatment in beneficiary countries. Five outcomes collectively supported this goal: increasing the number of suppliers and products globally, increasing country access to second-line products, reducing product prices, ensuring a stable supply, and transitioning funding to alternative sources at project end. CHAI undertook 2-4 distinct activities through the course of this project to achieve each of the outcomes, as described below.

- **Increased number of quality-assured second-line ARV products and manufacturers**
  - CHAI engaged suppliers by providing demand forecasts for second-line ARVs across a number of countries so that suppliers would realize the market opportunity based on potential volumes
  - CHAI encouraged suppliers to submit their products to the WHO PQ program or other Stringent Regulatory Authority (SRA)
- **Increased number of quality-assured second-line ARV products in countries**
  - CHAI introduced the registration coverage criterion so that suppliers would compete on the basis of price and non price factors, encouraging products' registration prior to the tendering process
  - CHAI monitored dossier submissions by suppliers and national registration approvals
  - CHAI pursued getting waivers for unregistered products that were not SRA approved yet to bring these products earlier into the countries
- **Reduced price of second-line ARVs**
  - CHAI engaged with suppliers by providing demand forecasts for second-line ARVs across a number of countries so that suppliers would realize the market opportunity based on potential volumes
  - CHAI conducted "cost plus" negotiations with generic manufacturers during which CHAI helped them identify manufacturing cost savings that were ultimately passed on to the price
  - CHAI's tender process included volumes based on the pooled demand, so that suppliers would be encouraged to reduce prices based on high volumes
  - CHAI worked with countries to prepare them for uptaking ATV/r as soon as it was launched, since the price was expected to be much lower than LPV/r in the long run

- **Maintained the supply of second-line ARVs for beneficiary countries**
  - CHAI global team received ARV orders from the countries on a quarterly basis and placed the orders with the manufacturers selected in the tender
  - CHAI country teams monitored the supply levels and placed emergency orders to avoid stock outs
  - CHAI introduced the supplier performance criterion so that suppliers would compete on the basis of price and non price factors, encouraging suppliers to improve their lead times
- **Ensured transition funding for second-line ARVs**
  - CHAI coordinated with global partners to identify long-term funds and supported countries in securing these funds
  - CHAI provided further technical assistance to countries to forecast second-line ARVs and complete the PSM plans if transitioning to Global Fund grant to increase their likelihood of having a successful proposal

1.3 Objectives of the review

In early 2013, the UNITAID Secretariat initiated a final evaluation to assess the Second-line HIV/AIDS project. Dalberg Global Development Advisors, an international development consultancy, was selected to complete this review through a competitive bidding process. The purpose of the evaluation is to:

- Assess the performance and impact of the project over its lifetime, and
- Identify opportunities to improve the design or implementation of future projects.

2 Executive Summary

Objectives

The Second-Line Adult Anti-retroviral Treatments project (2L ARV) was a large and ambitious project undertaken to catalyze the development of the second-line ARV drug market. The main objectives of the project were to:

- Scale up access to quality-assured second-line treatments in 25 low and middle-income countries and first-line Tenofovir-based treatments in three countries,
- Facilitate price reductions for these drugs, and
- Ensure countries transitioned to alternative funding by the project's end.

Evaluation findings

Relevance: This project was highly relevant at the outset, remained so throughout the project, and the activities that were completed were highly aligned to the overall project objectives.

Effectiveness and Efficiency: Overall, the project was completed with a very high level of effectiveness though three project extensions were ultimately required.

Impact on Market Outcomes: A review of the available evidence and interviews with suppliers suggests that the project did have a meaningful influence on the market, notably by accelerating the pace of new market entrants, enhancing coverage for low-volume countries, deepening the range of products available at the country level, and contributing to price decreases.

Impact on Public Health Outcomes: The project contributed to increased access to second-line ARV treatments for people living in countries that previously did not have these life-saving drugs available. However, quantifying how much of the effect can be directly attributed to this project is challenging to measure.

Sustainability: After considerable effort, arrangements have been made to continue funding the delivery of 2L ARVs in each of the 25 participating countries.

Management: UNITAID and CHAI coordinated effectively on the project, with both parties fulfilling their expected roles and responsibilities.

Lessons learned and recommendations for the design of future initiatives

Insights for funding market interventions

Scale and scope mattes: Projects of this magnitude that aim to influence suppliers and countries simultaneously can offer unique benefits that would not be captured by a series of smaller and narrower projects, such as breaking vicious circles between demand and supply.

Take a long-term view: Motivating manufacturers to make multi-million dollar investments in production capacity and motivating national governments to invest scarce administrative time in regulatory changes requires a meaningful commitment from donors that sufficient funds will be made available over a long enough period to make these efforts worthwhile.

Insights for designing market interventions

Scan for synergies: The project yielded opportunities for even greater impact through synergies which could potentially be anticipated and included in the project design of future projects.

Align on an M&E framework that measures long-term system-wide impact. Given the complexities of any market-shaping initiative, stakeholders should agree on the overall goal and theory behind how the market will be changed and to what extent attribution can be identified, before aligning on initiatives and indicators.

Insights for implementing

Calibrate demand forecasts: Projects would benefit from building in sufficient time to calibrate their forecast methodology, or budgeting for in-country resources to assess demand and collect primary data for further forecast validation.

Establish clear roles and responsibilities: Ensure that UNITAID and partners are fully aligned on the scope of roles and responsibilities. In cases where implementing partners are held accountable to health outcomes, the ToR, budget, and timeline should reflect these added monitoring activities.

Collaborate with national authorities: Prioritize the signing of multiyear MoUs with beneficiary countries to minimize risks in future projects while minimizing administrative work.

Weigh procurement model trade-offs: Procurement models designs should explicitly consider the trade-offs between (i) managing procurement globally vs. strengthening national procurement systems, and (ii) incentivizing economies of scale vs. balancing supply dependency, to ensure alignment across stakeholders on the implications.

Plan early for transition: Recognizing that identifying and confirming transition funding for any donor-led project may take years, UNITAID and its partners could explore opportunities to engage other partners earlier, such as through co-funding.

2.1 Introduction

This is an independent final evaluation of the Second-Line Adult Anti-retroviral Treatments project (2L ARV) project. The evaluation was commissioned by the UNITAID Secretariat in July 2013 and conducted by Dalberg Global Development Advisors. The purpose of the evaluation is to 1) assess the performance and impact of the project over its lifetime; and 2) identify opportunities to improve the design or implementation of future projects.

Our evaluation builds upon a very comprehensive mid-term evaluation that was finalized in February 2012 by the Swiss Centre for International Health and the Swiss Tropical and Public Health Institute. This final evaluation does not go into detail on the operational and implementation issues identified in that review, but rather provides a higher-level assessment of the project's strategy and efficacy, in order to inform the design and implementation of future projects.

Evaluating market-shaping interventions is challenging because of the dynamic and complex nature of markets. Over the course of these projects, economic conditions change, key actors such as governments and manufacturers are influenced by factors outside the project's control, and new technologies have disruptive effects on the entire market. Therefore, our evaluation focuses on analyzing how the market evolved and then triangulating, based on quantitative analysis and repeated qualitative interviews with more than 20 stakeholders, the relevance, quality of management, effectiveness and ultimate impact and additionality of the project. More details on the methodology can be found in Annex 1.

2.2 Program Objectives

The Second-Line Adult Anti-retroviral Treatments project (2L ARV) was a large and ambitious project undertaken to catalyze the development of the second-line ARV drug market. The main objectives of the project were to:

- Scale up access to quality-assured second-line treatments in 25 low and middle-income countries [1]and first-line Tenofovir-based treatments in three countries[2],
- Facilitate price reductions for these drugs, and
- Ensure countries transitioned to alternative funding by the project's end.

This project was large in size and scope – the project budget was USD $299,650,557 and involved a wide range of activities at the global and national level in 25 countries. The project, originally scheduled to take place between May 2007 and December 2008, ultimately wound up running until December 2012 as a result of three approved project extensions.

[1] Benin, Botswana, Burundi, Cambodia, Cameroon, Chad, Cote d'Ivoire, D.R. Congo, Ethiopia, Ghana, Haiti, India, Kenya, Malawi, Mali, Mozambique, Namibia, Nigeria, Rwanda, Senegal, Tanzania, Togo, Uganda, Zambia, Zimbabwe

[2] Namibia, Uganda and Zambia

In its role on the 2L ARV project, UNITAID financed the purchasing of ARVs to be made available in the 25 countries and provided management and oversight of the project. The Clinton Health Access Initiative (CHAI) was selected to be the implementing partner to UNITAID. It organized rounds of tenders, negotiated with suppliers and contracted a procurement agent for order processing, pre-shipment testing and shipment to the respective countries.

2.3 Evaluation Findings

- **Relevance: This project was highly relevant at the outset, remained so throughout the project, and the activities that were completed were highly aligned to the overall project objectives**. In 2006 WHO predicted that the need for second-line drugs would dramatically rise as 1L patients developed resistance (at a compound rate of 40% between 2006 and 2010). There were only a limited number of manufacturers and only one generic supplier for drugs other than AZT, and the prevailing drug prices for low income countries were prohibitive. The project remained very relevant over the duration of the project – an estimated 50%-75% of the global market was procured through the project's tendering processes and therefore influenced by the project's efforts.

- **Effectiveness and Efficiency: Overall, the project was completed with a very high level of effectiveness.** Elements of the project that contributed the most to the project's effectiveness include: (a) offering direct assistance to manufacturers to lower aspects of their operating costs in exchange for agreeing to cost-plus negotiations for the ARV tenders; (b) providing assistance to manufacturers to overcome regulatory hurdles at the country level such as obtaining waivers for unregistered products; and (c) including non-price factors in the supplier selection process to encourage suppliers to meet the expected lead times and increase national registration of their products. In addition, the pooled demand model successfully encouraged suppliers to enter the market by sharing forecasts of global demand while also ensuring adequate volumes to sufficiently motivate manufacturers.

  There were mixed success rates of working with national authorities to sign MOUs and build country-level capacity to conduct quantification and forecasting at the country level. Additionally, by the end of the project all 25 beneficiary countries had successfully transitioned to alternative funding sources but the process took longer than anticipated. However, though transition extended beyond the initial project deadline of December 2008 through three project extensions, there was a tacit understanding that the original 18-month timeframe would not be sufficient and that project extensions would be needed.

- **Impact on Market Outcomes: While the project was not structured to directly measure attribution, a review of the available evidence and interviews with suppliers suggests that the project did have a meaningful influence on the market, notably by accelerating the pace of**

new market entrants, enhancing coverage for low-volume countries, deepening the range of products available at the country level, and contributing to price decreases. By December 2012, the number of second-line product suppliers had increased from 8 at project start to 15 at project end. In the same period, the number of WHO prequalified second-line products in the market increased from 11 to 35, and prices decreased by 15-60% for each of the formulations included in the project. By considering how the overall market evolved, examining CHAI's efforts in the 2L ARV project, and considering external factors that may have contributed to these trends, this final evaluation concludes that CHAI's efforts effectively accelerated growth of suppliers and products within the markets for 2L products, especially in low-volume countries, and had a meaningful influence on the overall reductions in the price of 2L drugs. The project also had beneficial indirect effects on the use of Tenofovir as a more cost-effective first-line treatment. While there was some positive momentum in the 2L market at the outset of the project, the interventions were helpful in accelerating the rate of entry of new suppliers and products.

- **Impact on Public Health Outcomes: The project contributed to increased access to second-line ARV treatments for people living in countries that previously did not have these life-saving drugs available**. However, quantifying how much of the effect can be directly attributed to this project is challenging to measure. Patient uptake estimates were based on a variety of methodologies and had varying degrees of accuracy depending on the sophistication of in-country public health data systems. Available evidence and interviews with stakeholders suggests that the achievements of the project included: (i) an increase in the availability and ultimately the uptake of ATV/r, which allows for simple delivery and storage as well as improved patient adherence; and (ii) an increased access to drugs for patients in low volume countries where UNITAID was the only donor for HIV/AIDS commodities.

- **Sustainability: After considerable effort, arrangements have been made to continue funding the delivery of 2L ARVs in each of the 25 participating countries.** Of the 25 countries that were included in the project, all 25 had transitioned to alternative funding by project end in 2012. The transition funding secured will maintain patient treatments that were funded by UNITAID during the lifetime of the project. Other outcomes, such as lower price levels, will need sustained monitoring to verify that price levels remain sustainably affordable through supplier competition and increased volumes such that further interventions are not needed.

- **Management: UNITAID and CHAI coordinated effectively on the project, with both parties fulfilling their expected roles and responsibilities**. Selection of CHAI as a partner also yielded synergistic efficiency benefits due to their simultaneous implementation of the Pediatric HIV/AIDS Treatment Project and other non-UNITAID funded country-based projects. The project extensions were due not to any shortcomings in coordination but rather to a tacit understanding between CHAI and UNITAID that the original 18-month initial project timeline was insufficient to accomplish the project outcomes. Other factors supporting the need for extensions include

delays in the launch of ATV/r and the time required to secure alternative funding for the 25 beneficiary countries, which seems reasonable and appropriate in light of how the external environment evolved.

2.4 Lessons learned and recommendations for the design of future initiatives

The ultimate goal for market interventions such as 2L ARV is to achieve sustainable affordability, quality, and accessibility offered by healthy competition among market actors. This particular project offers several lessons about how to fund, design and implement effective market shaping interventions.

Insights for funding market interventions

- **Scale and scope matters.** This project was notably ambitious in targeting an initial 27 countries for market interventions aimed at achieving five distinct outcomes, and some decisions – particularly on geographic scope – were controversial at the time. Yet projects of this magnitude that aim to influence suppliers and countries simultaneously can offer unique benefits that would not be captured by a series of smaller and narrower projects. The "vicious cycle" wherein suppliers will lower prices only once they are shown sufficient demand and countries will demand products only once they become affordable can be broken by instilling in both sides confidence in the actions of the other. Additionally, low-volume countries that might otherwise be viewed as unattractive by suppliers can become more attractive markets for entry when they are pooled with higher-volume countries.

- **Take a long-term view.** This project was originally scoped for 18 months, but it soon became apparent that sustained effort would be required in order to fully achieve the intended outcomes. Motivating manufacturers to make multi-million dollar investments in production capacity and motivating national governments to invest scarce administrative time in regulatory changes requires a meaningful commitment from donors that sufficient funds will be made available over a long enough period to make these efforts worthwhile.

Insights for designing market interventions

- **Scan for synergies.** The project yielded opportunities for even greater impact through synergies which could potentially be anticipated and included in the project design of future projects. One example was in the price reductions for Tenofovir, which ended up increasing its use as a first-line drug as well as second-line, and another was the synergies with the Pediatric HIV/AIDS project. While there will always be unexpected benefits to any implementation, teams can be encouraged to think broadly about potential linkages during the design phase.

- **Align on an M&E framework that measures long-term system-wide impact.** Project teams and funders seek a framework to learn from and improve the project while it is ongoing, and to track the longer-term changes to the market even after the project has closed down. Given the

complexities of any market-shaping initiative, stakeholders should agree on the overall goal and theory behind how the market will be changed and to what extent attribution can be identified, before aligning on initiatives and indicators. And to truly measure changes to the market, investing in a substantial M&E effort across countries and extending that effort for a number of years would be needed.

Insights for implementing

- **Calibrate demand forecasts.** The higher level of uncertainty in nascent or fragmented markets makes forecasting particularly difficult. Additionally, the uncertainty of long-term funding commitments can influence a country's forecasts upwards in an attempt to secure more funding in the shorter term. Nonetheless, the 2L ARV forecasts improved over time as additional data was gathered and calibrated. Future projects would benefit from building in sufficient time to calibrate their forecast methodology, or budgeting for in-country resources to assess demand and collect primary data for further forecast validation.

- **Establish clear roles and responsibilities.** Ensure that UNITAID and partners are fully aligned on the scope of roles and responsibilities, particularly for activities related to tracking and reporting on public health impact. In cases where implementing partners are held accountable to health outcomes, the ToR, budget, and timeline should reflect these added monitoring activities.

- **Collaborate with national authorities.** Prioritize the signing of multi-year MoUs with beneficiary countries to minimize risks in future projects while minimizing administrative work. More MoUs can be secured by considering stronger incentives, increasing implementer resources in country, or engaging countries earlier in the process.

- **Weigh procurement model trade-offs.** The design of the procurement model for 2L ARV prioritized centralized procurement and higher volumes over further capacity building and potential supply dependency. While 2L ARV procurement was effective and ultimately successful in incentivizing new market entry, future designs should explicitly consider the trade-offs of their choices in this area, to ensure alignment across stakeholders on the implications.

- **Plan early for transition:** Recognizing that identifying and confirming transition funding for any donor-led project may take years, UNITAID and its partners could explore opportunities to engage other partners earlier, such as through co-funding.

3 Log Frame

The overall logic behind the Second-line HIV/AIDS project's design can be explained in a Log Frame. The Log Frame below is a synthesis of the 2011 and 2012 project log frames and additional project documentation on actions and indicators for the 2008-2010 period[3].The Log Frame explains how each activity CHAI performed over the course of the project contributed to outcomes supporting the project's ultimate impact.

We recognize that a Log Frame is inherently limited and cannot capture the full complexity of a market dynamics intervention, since it attempts to describe in a linear manner what is in reality a set of non-linear relationships and feedback loops.

- **One activity might affect multiple goals**. For example, increasing the number of suppliers will help in achieving both increased competition and greater supply sustainability, and might increase national availability[4] and product adaptability.

- **There are synergies and complementarities between goals.** For example, ensuring sustained funding will also benefit affordability and supply sustainability, as manufacturers have more incentive to enter / not exit a market, and might be able to reduce the risk premiums in their prices[5].

Section 4.2 describes the effectiveness of each of the activities described in the Log Frame below, and Section 4.3 evaluates the contribution to market and public health impact.

[3] Concretely, the Log Frame includes one activity from the 2008-2010 project agreements that is not explicitly included in the log frames of 2011-2012: "Engage and negotiate with industry to stimulate an increase in the availability of relevant drugs of assured quality and collaborate with the Pre-qualification Program of WHO/UN and/or stringent regulatory authority to encourage prequalification"

[4] Increase national availability if number of countries with registered products increases

[5] Manufacturers reduce price if they are assured that they can spread the amortization of their fixed costs over a longer time period

Figure 1. Log Frame for Second-line Adult HIV/AIDS project

Impact	Increase and maintain access to second-line treatment in beneficiary countries				
Outcomes	Better-adapted, quality-assured second-line ARVs are continuously supplied to beneficiary countries at lower prices				
	1) Global availability: Increase number of quality-assured second-line ARV products and manufacturers globally	**2) National availability:** Increase number of quality-assured second-line ARV products in countries	**3) Affordability:** Reduce the price of second-line ARVs	**4) Delivery**: Maintain the supply of second-line ARVs for beneficiary countries	**5) Sustainability:** Ensure transition funding for second-line ARVs
Outputs	• Number of new suppliers with US FDA or WHO PQ approval for second-line ARVs • Number of new quality-assured products	• Number of products and suppliers registered per country • Number of waivers applied/obtained per country	• Prices paid for second-line ARVs ordered through the UNITAID Project • CHAI ceiling prices for second-line ARVs	• Number of MOUs signed • Volumes and value of second-line ARVs ordered and delivered • Number and value of emergency orders	• Number of countries successfully transitioned • Number of post-transition emergency orders
Activities	• Incentivize supplier market entry by providing market intelligence on second-line ARV demand • Help suppliers enter the market by encouraging them to submit their products' dossiers to an SRA (WHO PQ or FDA)	• Incentivize suppliers to register products in countries by adding a registration coverage criterion in CHAI's supplier selection process • Support national registration approval by monitoring suppliers' dossier submissions to the national authorities • Work with national authorities to obtain waivers for unregistered products that are not SRA approved yet	• Incentivize supplier market entry by providing market intelligence on second-line ARV demand • Negotiate prices with eligible suppliers • Coordinate with countries in the project to pool their second-line orders • Support uptake of ATV/r as lower-cost alternative to LPV/r • Procure TDF formulations for first-line use in Namibia, Uganda, and Zambia to incentivize volume-based price reductions	• Procure second-line ARVs for beneficiary countries on a quarterly basis • Monitor supply levels and place emergency orders to avoid stock-outs • Incentivize suppliers to deliver products in the agreed time by adding a supplier performance criterion in CHAI's supplier selection process	• Coordinate with global partners to identify long-term funds and support countries in securing these funds • Provide further technical assistance to countries to forecast their second-line ARV needs and to support procurement planning if transitioning to Global Fund grants

4 Lessons learned and recommendations for the design of future initiatives

Final evaluations provide the opportunity to draw out lessons learned for future projects. The 2L ARV project was a very large, ambitious and ultimately successful project. The project should yield new insights to benefit UNITAID and other actors focused on market dynamics in global health.

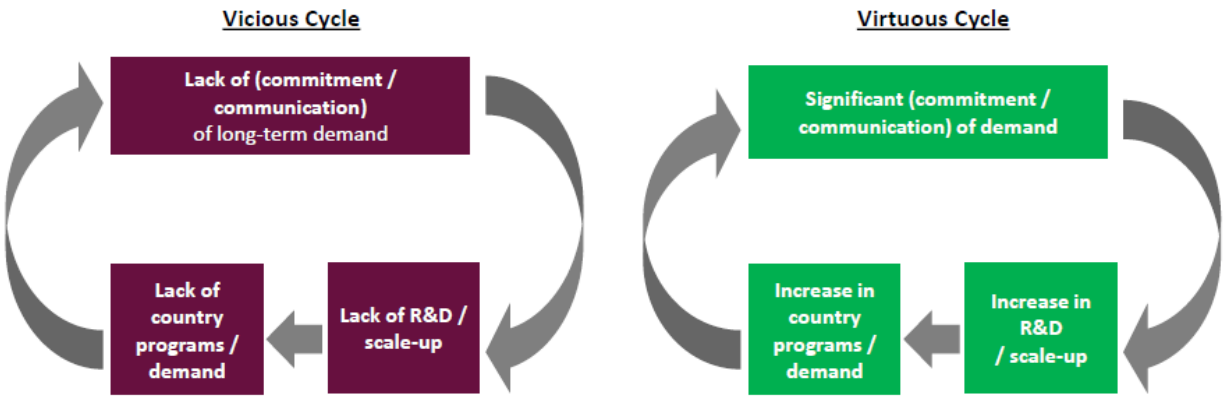
4.1 Insights for funding market interventions

4.1.1 Scale and scope matters

Large-scale and multi-faceted interventions yield a host of added direct and indirect benefits above what might be possible with a series of smaller initiatives. The 2L ARV project incorporated scale and scope in two ways: 1) by working across multiple segments of the value chain, and 2) by targeting a large group of diverse countries for 2L orders. This allowed the project to capture benefits that would not have materialized if UNITAID had approached specific market barriers independently with a series of smaller, piecemeal interventions.

- **Extending project scope across the value chain**
  2L ARV had an ambitious scope, as demonstrated by the number and type of activities included as well as the engagement across multiple levels of the supply chain: directly with manufacturers, with procurement agents, and with countries. By covering many bases at one time, the 2L ARV project could short-circuit the "vicious cycles" that can so commonly manifest where there are market shortcomings. For examples, suppliers cited lack of demand for low volumes and higher prices as reasons why they did not enter a market, and countries could similarly cite lack of availability and affordability as the rationale for not investing in the diagnostics and education needed to spur demand. Both suppliers and countries were waiting for the other to act. Market interventions that are aimed at different segments of the value chain simultaneously and applied with multiple levers against the confluence of barriers, can yield more traction against these barriers that any single focused intervention might not be able to yield by demonstrating to each side – whether suppliers or countries – that the results they need from the other side are coming soon.

Figure 2. Vicious and virtuous market cycles, from Dalberg's market shaping framework



- **Realizing benefits from geographic scale**

  Access for some of the countries with greatest needs might require scale. 2L ARV was broad in its reach and initially targeted 27 countries, of which 25 participated. The low-volume countries in this group might not have gotten affordable access to 2L ARVs if not for the opportunity to pool their demand with that of the larger countries. For example, manufacturers expressed less interest in registering their products in low-volume countries due to the low return on investment, and would not have done so without the incentives and support offered through this project. The decision to use such a large group of countries was controversial at the time, as was the decision to include low-volume countries at all. While the size and makeup of the country pool did contribute some new project management challenges, such as in reconciling procurement processes across such different countries or getting MoUs signed in countries where CHAI had limited presence, ultimately the result was greater impact by extending access to a broader set of countries and beneficiaries.

Given this learning, it is worth asking whether 2L ARV project could have been even more ambitious on scope and gone one step further through in-country efforts to improve the distribution and monitor patient uptake. For example, UNITAID and CHAI could have monitored product delivery to hospitals or aided with education and diagnosis within hospitals to identify patients failing on 1L treatment. Supporting diagnosis would have provided a new source of primary data for the demand forecasts while increasing patient uptake, though additional staff resources might have been needed. By extending the scope to in-country activities, UNITAID and CHAI would also have realized improved measurement of health outcomes, though we recognize that it is an expansion of UNITAID's core market-shaping mission. Finally, the 2L ARV project could have benefited from even greater synergies with the Pediatric HIV/AIDS Treatment project, whose activities did extend in-country.

4.1.2 Take a long-term view

Market transformation requires projects with time horizons of 3-5 years, for three reasons:

- **Instilling confidence in market actors.** In the case of the 2L ARV project, suppliers wanted to have confidence in their knowledge of the market before committing to investments, such as for additional production capacity. Programs that can signal continuity by offering assurance that the incentives offered will persist year-to-year, will likely see greater responsiveness from suppliers. One interviewee noted that CHAI realized big gains in the tender process with suppliers when they were able to communicate details of the following year's process as well, such as the inclusion of non-price factors as criteria in the tender process. These benefits were only possible to capture once project extension agreements provided that visibility to suppliers. As one interviewee described of multi-year extensions, "While challenging, it is important to give the market that kind of predictability."

- **Letting interventions play out and markets mature.** The total project impact is dependent on many individual interventions coming together, particularly for projects with 2L ARV's scale and scope. Individual interventions can also take more time to organize and show observable results, such as those that involve coordinating with national governments or establishing new processes like pooled demand procurement.

- **Scaling the learning curve**. It takes time to build understanding and credibility with all actors, and to collect or develop needed information in markets where accurate hard data may be lacking.

4.2 Insights for designing market interventions

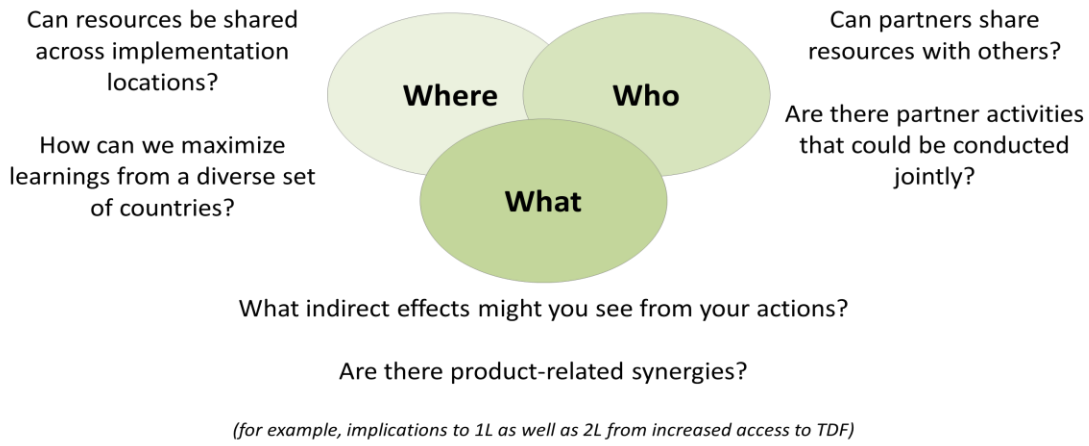
4.2.1 Scan for synergies

Though 2L ARV was extensive in scope, UNITAID and CHAI nonetheless identified opportunities outside the project scope to yield yet greater impact and efficiencies. The price reductions for Tenofovir as a first-line drug offer one example. CHAI procured TDF for 1L use in three countries in order to generate greater volumes that would drive down the price for TDF in 2L regimens of other countries. However, interviewees called out the unintended positive benefit to the 1L market as one of the major outcomes for this project: the resulting decrease to TDF prices and increase in their volume resulted in (WHO) recommending TDF as one of the preferred – and more affordable -- first-line treatment options.

The often-cited synergies between the Pediatric HIV/AIDS project and 2L ARV serve as another example. The CHAI country teams supported both projects, and with the Pediatric project continuing through December 2013, CHAI retained funding for staff who could support 2L ARV as well in transitioning or assessing final impacts even after the 2L ARV deadline. As one interviewee described, CHAI didn't need additional UNITAID funding to have a post-project on-the-ground presence: "CHAI was still there despite the program ramping down; they didn't need UNITAID to keep someone there to keep the lights on."

While there will always be unexpected benefits and challenges that crop up in any implementation, project design teams can be encouraged to consider a wide range of complementarities and account for them in the project design in order to better monitor and support additional outcomes, or at a minimum to realize greater project efficiencies.

Figure 3. Framework for considering project linkages and synergies



4.2.2 Align on an M&E framework that measures long-term system-wide impact

This project sought an M&E framework to serve two discrete functions: 1) testing, learning and adapting aspects of the project during implementation, and 2) tracking long-term market changes. To accomplish both, the project needed a Log Frame linking activities to outcomes and impact, with clear and comparable indicators to track over time. Stakeholders should agree on the overall goal and general theory behind how the market will be changed in a complex market-shaping project such as 2L ARV, where outcomes can be hard to measure and attribution difficult to ascertain.

To learn and adapt based on the project's performance, it is imperative that teams rigorously monitor how conditions are evolving, act quickly to adapt to changing circumstances, and effectively coordinate among one another to implement those changes. These short feedback loops will allow for real-time improvements in response to project setbacks. CHAI notably did identify a number of opportunities for real-time improvements which were then shared with UNITAID.

Tracking long-term market changes requires a substantial M&E effort, building off of national information management systems, to capture baseline information and track progress during and ideally for some years after the project closes down. A parallel effort could even contribute to bolstering national systems and building in-country capacity for information management which is often lacking. While the budget for such an effort could be sizeable, it would justify the tremendous investment in

market shaping initiatives such as this while also producing learnings to refine the design of future projects.

As one interviewee noted in recommending a longer timeframe for impact capture, “If you're going to do a market project, impact doesn't end when the project ends. It should just be beginning."

The 2L HIV/AIDS project developed comprehensive log frames in 2011 and 2012. In section 3, a combined log frame reflecting the entire project is shown. The log frame includes the most relevant indicators used in the project to measure the outcomes. In addition to those, we propose below a set of indicators that would help better reflect project outcomes as well as the ultimate impact to public health:

Outcome	Selected Log Frame indicators	Suggested additional or updated indicators
Increase number of quality-assured second-line ARV products and manufacturers globally	• Number of new suppliers with US FDA or WHO PQ approval for second-line ARVs • Number of new quality-assured products	• Number of suppliers with US FDA or WHO PQ approval (branded and generic companies) per formulation over time • Number of new formulations over time • Number of new products per formulation over time
Increase number of quality-assured second-line ARV products in countries	• Number of products and suppliers registered per country • Number of waivers applied/obtained per country	• Number of newly registered 2L ARV products per country • Number of new products that are pending SRA approval delivered per country
Reduce the price of second-line ARVs	• Prices paid for second-line ARVs ordered through the UNITAID Project • CHAI ceiling prices for second-line ARVs	
Maintain the supply of second-line ARVs for beneficiary countries	• Number of MOUs signed • Volumes and value of second-line ARVs ordered and delivered • Number and value of emergency orders	• Number and value of stock outs at national level • Volume and value of expired/lost drugs
Ensure transition funding for second-line ARVs	• Number of countries successfully transitioned • Number of post-transition emergency orders	
Public health outcome	• Estimated number of patients on second-line ARV treatment	• Number of new patients switched to second-line treatment • Percentage of patients with good adherence to second-line treatment • Survival at 6, 12 and 24 months after initiation of second-line treatment

4.3 Insights for implementing

4.3.1 Calibrate demand forecasts

Market dynamics interventions need to account for and manage the uncertainty inherent in markets, particularly those that are more informal or volatile. For the 2L ARV project, the market for second-line products in these countries was essentially nonexistent in 2006. Visibility into future demand was described as very poor in the early stages of the project. The dependency on first-line failure was another complicating factor: forecasting for second-line is a derivative of how many people fail first-line treatment. As one interviewee stated in describing their lack of historical data or beneficiary information on which to base forecasts, "While I don't want to call it guessing, we did collect a lot of information about expectations." Several interviewees called out the extent to which the forecasts improved over time as they gathered and calibrated information data. At the same time, the players in the market were new, and potentially found it difficult to interpret and deal with shifting and incorrect forecasts. At least one manufacturer shared that his company had overinvested in capacity as a result of a 2L ARV forecast.

In designing future market shaping projects, a longer timeline would build in flexibility for the project team to learn from early mistakes and calibrate the forecast methodology. Another option is to scope for in-country resources to more closely assess demand and collect the primary data needed to develop or further validate these forecasts, or even to invest in building capacity for improved information management infrastructure to benefit forecasts as well as other market data needs.

4.3.2 Establish clear roles and responsibilities

Ensure that UNITAID and partners are fully aligned on the scope of roles and responsibilities, particularly for activities related to tracking and reporting on public health impact. In cases where implementing partners are held accountable to health outcomes, the ToR, budget, and timeline should reflect these added monitoring activities.

4.3.3 Collaborate with national authorities

In some years CHAI was not able to obtain signed MoUs with all of the beneficiary countries due to a range of political and administrative challenges, which creates risk in case official or technical problems arise. To minimize this risk in future projects, implementers could consider: (i) introducing stronger incentives for national authorities to sign the MoU; for example, by making it a requirement for procurement (the MoU was not required for procurement in 2L ARV), (ii) increasing implementer resources on the ground to more directly prioritize MoU signing; and (iii) engaging beneficiary countries on the MoUs earlier in the process.

4.3.4 Weigh procurement model trade-offs

The procurement model used for 2L ARV reflected choices made against two sets of potential tradeoffs:

- Managing procurement globally vs. strengthening national procurement systems
- Incentivizing economies of scale vs. balancing supply dependency

CHAI chose to pool countries' demand and outsource the procurement process, which in a nascent market helped encourage suppliers to enter the market, but with the consequence of limiting country-level ownership. Similarly, procurement of large volumes from a few suppliers (primary and secondary) enabled the project to achieve better prices in the short-term but increased supply dependency and could have caused risks in the long-term. For future project designs, teams should similarly weigh these trades-offs and align with stakeholders on the implications.

4.3.5 Plan early for transition

Recognizing that identifying and confirming transition funding for any donor-led project may take years, UNITAID and its partners could explore creative opportunities to engage other partners earlier, such as through co-funding, in addition to ensuring that the project length is sufficiently long from the beginning.

5 Findings

The 2L ARV findings below have been organized into four categories: relevance, effectiveness and efficiency, impact and sustainability, and management. Figure 4 below presents a high-level summary of key the findings and review ratings for each of these categories. In "Efficiency & Effectiveness" we assess the individual activities undertaken under 2L ARV, and in "Impact & Sustainability" we evaluate the contribution of these activities to the intended outcomes, market impact, and ultimately health impact.

Figure 4. Summary of findings

Dimensions	Rating	Comments
Relevance	**High**	+ Limited number of suppliers for second-line ARVs (other than AZT)[6] in 2006: 4 branded manufacturers and only one generic + Of the 6 WHO prequalified second-line ARVs (other than AZT)[7] in 2006, 4 were only offered by a single supplier + High 2L ARV prices in 2006, from USD $1000 in low-income countries to USD $4000 in middle-income, were approximately 10x higher than for 1L treatments + In 2006, formulations required a cold chain and were not appropriate for resource-limited settings
Effectiveness and efficiency	**Medium-High**	- Three project extensions required to meet transition funding objective; only one extension was at no-cost + From 2007 – 2010, 16 of 18 project actions[8] were successfully completed; the only exceptions were in signing MoUs with beneficiary countries and in development of a transition plan + For 2011 – 2012, 9 of 13 project activities[9] supporting the Log Frame were successfully completed as planned; the other three were completed but either there was insufficient evidence to determine effectiveness or it was not completed within the expected timeframe. The exceptions were: • The timeliness by which 25 beneficiary countries ultimately secured transition funding with CHAI support • The support for national registration approval, and the ability to avoid stock outs, neither of which could be validated due to a lack of documentation
Impact and sustainability	**Medium-High**	All five project outcomes in the Log Frame were realized over the project timeline of 2007 – 2012, however, direct attribution to the project is hard to ascribe since there were other external factors at play: + **Global availability:** The number of WHO and FDA quality-assured manufacturers increased from 8 to 15. Additionally, formulations increased from 8 to 11, and WHO prequalified products from suppliers increased from 10 to 35 + **National availability:** Expanded 2L ARV access in countries, particularly those

[6] Other than Zidovudine 300mg (AZT), which would add three additional generic manufacturers but was not included in 2L ARV other than in 2009 on an exception basis

[7] Again with the exception of Zidovudine 300mg which was offered by Cipla as well as the three generic suppliers

[8] Project actions were tracked before the 2011 log frame was created

[9] Although the Log Frame contains 14 activities since it reflects the entire project; one of the activities was not explicitly included in the 2011 and 2012 log frames; therefore we have not evaluated this activity (dossier submission to SRAs) for 2011 and 2012

		with low volumes: for example, Haiti had access to 2 formulations in 2008 and 6 in 2010 + **Affordability:** Product prices decreased by 15% to 70% of their price at project start + **Supply stability:** Share of non-pooled / emergency orders by volume decreased from 31% in 2008 to 11% in 2010 and to 0% in 2011[10] + **Funding:** 25 countries successfully transitioned to non-UNITAID funding by 2012 However, we do call out one risk to longer-term sustainability: - A sustainability risk arises from the continued lack of in-country support[11] for diagnosis and training needed to identify patients needing second-line treatment
Management	**Medium-High**	+ UNITAID and CHAI worked very effectively together after an initial learning period + UNITAID and CHAI collaborated well in adjusting the project plan to reflect market needs and interim learnings + Reporting and M&E frameworks improved significantly, partly in response to the mid-term; the project lacked a log frame until 2011 - Responsibility for patient uptake as an outcome was a source of tension

5.1 Relevance

Final review rating: High[12]

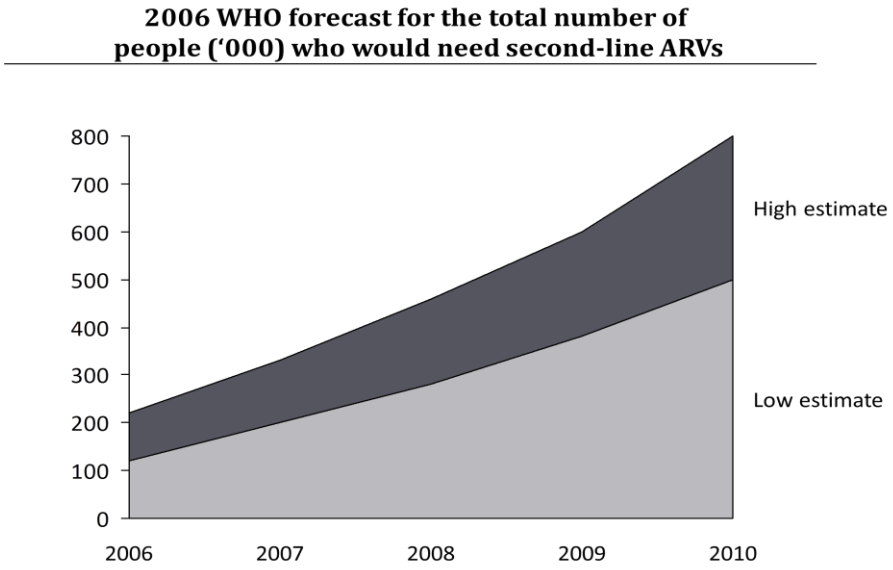
The Second-line HIV/AIDS project had an ambitious goal: to dramatically expand the market for second-line ARVs. In 2006, WHO predicted that the need for second-line drugs would dramatically rise as patients began developing resistance to first-line treatments. Depending on the switch rate between 1L and 2L, the number of people needing second-line treatment would range from 500,000 to 800,000 by 2010, up from a baseline of approximately 150,000 patients globally at the time. However, there were only a limited number of suppliers and almost no generic manufacturers in the 27 countries proposed for project inclusion, and prevailing drug prices for these countries were prohibitive. As a result, a project to expand access to and lower prices for the predicted wave of patients needing second-line ARVs in low- and middle-income countries was highly relevant.

[10] 2012 showed 100% emergency orders since it was a project extension exclusively to cover emergencies while countries transitioned to other funding sources

[11] In-country support was outside the scope of the 2L ARV project

[12] Findings constitute a combined qualitative and quantitative assessment of the different areas under review. A "high" rating indicates that all or most goals in an area have been achieved; a "medium" rating indicates that a significant portion of goals has been achieved, but that some important gaps exist. A "low" rating indicates that the majority of goals in an area have not been achieved.

Figure 5. 2006 WHO second-line ARV forecast



Source: World Health Organization, "Prioritizing Second-Line Antiretroviral Drugs for Adults and Adolescents: a Public Health Approach", 2007

5.1.1 Limited number of suppliers in the second-line ARV market

Suppliers, particularly generic manufacturers, had few incentives to produce second-line drugs. As seen in Figure 5, only branded companies were selling second-line drugs with the exception of Zidovudine and Didanosine. Of the seven second-line ARVs, four were only offered by a single supplier, meaning there was no competition to lower the price.

Additionally, as was reinforced by interviewees who were involved in the project from the beginning, overall demand appeared low but was not well-known, the entire market was fragmented so visibility into longer-term demand was especially challenging, and there was no donor funding for the second-line market.[13]

[13] CHAI, "Engaging the ARV Marketplace to Optimize Outcomes for Patients", 2006

Figure 6. Manufacturers of SRA approved second-line ARVs prior to 2007[14]

Drug	Manufacturer (s)
Abacavir 300mg	ViiV HealthCare
Didanosine 200 mg	Bristol-Myers Squibb, Barr Pharmaceuticals
Didanosine 400 mg	Bristol-Myers Squibb, Barr Pharmaceuticals
Lopinavir + Ritonavir 200/50mg	Abbott Laboratories
Tenofovir + Emtricitabine 300/200mg	Gilead Sciences, Inc.
Tenofovir 300mg	Gilead Sciences, Inc.
Zidovudine 300mg	ViiV HealthCare, Combino Pharm S.L., Cipla Ltd, Ranbaxy Laboratories Ltd

5.1.2 Second-line ARV prices were very high, particularly when compared to first-line regimens

Second-line treatment was approximately ten times the cost of first-line treatment[15], with prices ranging from USD $1,000 per patient annually in low-income countries to USD $4,000 in middle-income countries. In 2006, WHO estimated that second-line treatment would represent 90% of the total cost for HIV/AIDS treatment in 2011 if prices remained at the same level as in 2006. [16]

5.1.3 Formulations were not appropriate for resource-limited settings

All formulations prior to 2007 required cold chain transportation and storage, which posed a challenge for low-income countries with poor infrastructure.

5.2 Effectiveness and Efficiency

Final review rating: ***Medium-High***

In this section we review whether project activities were completed on time and on budget, and how successfully they supported the project outcomes.

[14] Note that while Zidovudine is included in the table because some countries used it for second-line treatment, it was only included in this project as an exception for one year and was not a focus of the project

[15] The regimen used for the baseline calculation was (TDF or ddI) + (3TC or ABC) + LPV/r (source: CHAI 2009 project proposal)

[16] WHO, "Prioritizing Second-Line Antiretroviral Drugs for Adults and Adolescents: a Public Health Approach", 2007

5.2.1 The project did not meet the original time and budget expectations; three extensions were required

All project plan activities were completed, but not by the original project timeline of December 2008. However, there was a tacit understanding between CHAI and UNITAID that the original 18-month initial project timeline was insufficient to accomplish the project outcomes. Three extensions were granted that carried the project forward to December 2012. The first two extensions, in 2009 and 2010-2011, were intended for two purposes:

- To accelerate market uptake of ATV/r, viewed as a critical new product
- To ensure that countries successfully transitioned to alternative funding so that patient continuity of treatment was not compromised

The 2012 no-cost extension allowed any unspent 2011 funds to carry over into 2012 with the aim to reduce the risks inherent in the funding transition process. Further discussion of the project extensions and transition planning are found in this section under Efficiency, in the Management section, and in Recommendations.

The project plan activities were ultimately completed under budget, though the budget did need to be increased in the first and second extensions.

Table 1. 2L ARV budget commitments and disbursements for 2007 – 2012

Year	Budget (Million USD)	Budgeted disbursement to CHAI (Million USD)
2007	35.90	35.90
2008	64.33	88.22
2009	73.40	27.04
2010	78.50	61.12
2011	39.40	22.53
2012	8.11	17.52
Total	299.65	252.33

Source: UNITAID financial records

The MoU budget commitment for the entire project (including extensions) was USD $299,650,557 and the project disbursement was USD $252,329,444. The project was completed approximately 16% below budget.

There were several justifications for committing more funds than were ultimately necessary. If the supply or availability of ARVs were to be discontinued due to a lack of funding, the health consequences would be disastrous for patients whose treatment was interrupted. Given the significant uncertainties inherent in the project, particularly around the timing of securing long-term transition funds, it made sense to provide leeway in the budget commitment to ensure that no supply discontinuations occurred.

However, future projects would benefit from learning from early mistakes and calibrating the budgeting methodology. The 2L project adjusted its financial systems to make disbursements based on actual needs, but it maintained the tendency to commit more funds in each new MoU than it was ultimately necessary to disburse. The funds committed but not disbursed had an opportunity cost. Had it been realized sooner that need was not in line with the original allocation, the funds could have been re-allocated to additional activities to help advance the 2L project objectives, for instance, in-country support or M&E activities, or to new projects such as HIV diagnostics to support patient uptake (a project on HIV diagnostics was ultimately undertaken in 2012).

5.2.2 The large majority of project activities were successfully completed

Our assessment of the project activities is broken into two sections based on the documentation available. In the first section, which covers 2007 – 2010, we summarize the completion rates of *actions* – separate from the Log Frame activities - that were specified in the project plan. These actions were not connected to a Log Frame, as the first log frame for 2L ARV was not developed until 2011. In the second section which covers 2011 and 2012, we summarize the extent to which CHAI achieved the activities that supported each of the five outcomes in the Log frame (see Section 2). The Log Frame is intended to represent the objectives of the entire project, and in particular consolidates the separate log frames that were developed for each of 2011 and 2012. The project Log Frame activities for 2008 – 2010 are below. Note that the activity set was defined in annual agreements between UNITAID and CHAI and so there were minor differences (noted below) in the set of activities between each year. The summary of the midterm assessment for this period conducted by the Swiss Tropical and Public Health Institute is included in Annex 8.

The 2007 annual report did not include a table detailing progress against activities. The 2007 narrative report included tracking towards the following three indicators:

- MoU agreements signed with beneficiary countries: 24 out of 25 (96%)
- MSA signed with all four suppliers: Matrix, Cipla, Aurobindo and Aspen
- Selection of procurement agent: agreement signed in August 2007

Table 2. 2L ARV budget commitments and disbursements for 2007 – 2012.

	Actions	2008	2009	2010	Overall assessment
1	**Beneficiary selection process**	Completed	Completed	Completed	✓
2	**Project strategy addressing the needs of the Project**	Not available	Completed	Completed	✓
3	**Procurement strategy addressing the needs of the Project**	Completed	Completed and approved by WHO CRC on November 20, 2008 and renewed annually	Completed and approved by WHO CRC on November 20, 2009 and is renewed annually	✓
4	**Estimation of drug regimens and forecasts with countries**	Completed	Completed September 2008 and updated through April 2009	Completed September 2009 and Updated January 2010 and August 2010	✓
5	**ARV Supplier selection**	Completed	Completed March 2009	Completed March 2010 and May 2010 for ATV/RTV	✓
6	**MoU agreements (or Amendments) Signed with Relevant Authority of Beneficiary Programs***	24 of 25 participating Countries signed MoUs (96%)	17 of 25 participating Countries signed MoUs (68%)	12 of 18 participating Countries signed MoUs (67%)	✗
7	**Joint Activities with industry to stimulate an increase in the availability of relevant drugs**	Ongoing	Ongoing	Ongoing	✓
8	**CHAI's Procurement Management and Technical Assistance**	Not available	Ongoing per Project Agreement	Ongoing per Project Agreement	✓
9	**Selection of procurement agent***	Completed for 2009 & 2010	Selection completed	Not applicable	✓

			February 2009 Transition began March 2009 and completed June 2009		
10	**Quarterly estimates and delivery schedules**	Ongoing as scheduled on a quarterly basis	Completed Q1-Q2 2009	Completed Q1-Q2 2010	✓
11	**Placement of Purchase Orders and Delivery of Products**	Ongoing as scheduled on a quarterly basis	Ongoing as scheduled in March, June, September and December, on a quarterly basis	Ongoing as scheduled in March, June, September and December, on a quarterly basis	✓
12	**CHAI's Procurement Management, Project Support**	Board approval completed Management is ongoing as scheduled	Not applicable	Not applicable	✓
13	**Reporting**	Agreement on report contents completed. Ongoing on a semi-annual and annual basis as set forth in Schedule	Semiannually	Semiannually	✓
14	**Procurement planning**	Completed	Completed January 2010	Completed. Process commenced for 2011 in November 2010 after Board of UNITAID approved 2011 funding	✓
15	**Sign Master Supply Agreements (MSA) with all Suppliers***	Not available	Signed required MSA with suppliers (with branded companies procured under the "Access	Signed required MSA with suppliers (with branded companies procured under the "Access prices")	✓

			prices")		
16	**Signature of legal agreement between UNITAID & CHAI and Project Plan approved**	Not available	Completed June 2009	Completed December 2009	✓
17	**First Funds disbursed by UNITAID to CHAI**	Not available	Completed December 2008 Final funds disbursed November 2009	Completed December 2009 Final funds disbursed September 2010	✓
18	**Transition/ Exit time**	Not available	8 countries are expected to transition after 2009	11 countries have completed transition	✕
* Indicates activity progress referenced in 2007 narrative reports. Summary of 2007 progress precedes this table.					

Table 3. Performance of project activities against the Log Frame

Note: these activities are from the Log Frame included in Section 2, which represents a consolidation of the 2011 and 2012 log frames and additional project documentation on actions and indicators for the 2008-2010 period[17]*. The performance indicated is a summary based on the indicators in the log frames.*

Outcome	Activity	Perfor-mance	Evidence
Increase number of quality-assured second-line ARV products and manufacturers globally	Incentivize supplier market entry by providing market intelligence on second-line ARV demand	Good	• Generally positive manufacturers' feedback on the value of the market intelligence shared by CHAI • Global demand forecasts created based on the country beneficiaries' forecasts, once calibrated so that accuracy was improved
	Help suppliers enter the market by encouraging them to submit their products' dossiers to an SRA (WHO PQ or FDA)	Not applicable	• Not applicable for 2011 and 2012
Increase number of quality-assured second-line ARV products in countries	Incentivize suppliers to register products in countries by adding a registration coverage criterion in CHAI's supplier selection process	Very Good	• Registration coverage criterion added in 2009 • Positive manufacturers' feedback on the benefits of this criterion
	Support national registration approval by monitoring suppliers' dossier submissions to the national authorities	N/A	• Limited evidence
	Work with national authorities to obtain waivers for unregistered products that are not SRA approved yet	Very Good	• Presence in-country of second-line drugs pending SRA approval for which countries would otherwise have to wait for SRA approval • Positive feedback from country offices on CHAI's contribution to achieve waivers

[17] Concretely, the Log Frame includes one activity from the 2008-2010 project agreements that is not explicitly included in the log frames of 2011-2012: "Engage and negotiate with industry to stimulate an increase in the availability of relevant drugs of assured quality and collaborate with the Pre-qualification Program of WHO/UN and/or stringent regulatory authority to encourage prequalification"

			• Annual reports' statements on the role of CHAI staff in obtaining waivers
Reduce price of second-line ARVs	Negotiate prices with eligible suppliers, including assistance reducing their manufacturing costs	Very Good	• Most generic suppliers engaged in cost-plus negotiations which entailed discussions on price reductions (eg, Aurobindo, Cipla, Hetero, Matrix and Ranbaxy in 2010)
	Coordinate with countries in the project to pool their second-line orders	Very Good	• All 25 original countries included in pool through 2009 (dropping to 18 in 2010 and 15 in 2011), allowing for calculating aggregated demand
	Promote use of ATV/r as lower-cost alternative to LPV/r	Very Good	• ATV/r increasingly included in national forecasts and Global Fund procurement plans • Increase in ATV/r product volumes bought by the program
	Procure TDF formulations for first-line use in Namibia, Uganda, and Zambia to incentivize volume-based price reductions	Very Good	• Large TDF volumes procured for these countries (50-75% of total volume)
Maintain the supply of second-line ARVs for beneficiary countries	Procure second-line ARVs for beneficiary countries on a quarterly basis	Good	• For countries that placed orders, at least 70% of the orders were placed on a quarterly basis except in 2007 during project launch, and in 2012 which was entirely for emergency orders • MoUs not signed with 100% of countries, posing fraud risks
	Monitor supply levels and place emergency orders to avoid stock-outs	N/A	• Data available for emergency orders but not for stock-outs so could not verify that stock-outs were avoided
	Incentivize suppliers to deliver products in the agreed time by adding a supplier performance criterion in CHAI's supplier selection process	Very Good	• Registration coverage criterion added in 2009 • Positive manufacturers' feedback on the benefits of this criterion

Ensure transition funding for second-line ARVs	Coordinate with global partners to identify long-term funds and support countries in securing these funds	Fair	• Long-term funds ultimately identified but required three project extensions to be completed
	Provide further technical assistance to countries to forecast their second-line ARV needs and to support procurement planning if transitioning to Global Fund grants	Good	• Evidence from annual reports: CHAI deployed resources to work with national teams on preparing high quality proposals for the Global Fund • Additional details from country offices on CHAI's technical assistance role

5.2.2.1 Market intelligence, procurement techniques and inclusion of national registration criterion were the main successful activities

Stakeholders highlighted three success factors that contributed to complete the activities successfully:

- Market intelligence of second-line ARV demand and deep knowledge of manufacturers' business models earned CHAI the credibility to influence markets. Interviewees acknowledged the value of CHAI's engagement in providing the market's first efforts at visibility into long term demand, though they acknowledged some problems with forecast accuracy, particularly in the early years of the project.
- Procurement techniques were innovative and effective. The tenders conducted for the project included aggregated drug volumes from the beneficiary countries and allowed suppliers to express their willingness to engage in cost plus negotiations.
- Inclusion of non-price factors in the tender process tackled the constraints of conducting procurement in low volume countries and increased competition among suppliers.

5.2.2.2 Transition planning began in 2008 and did not fully account for the level of effort required to secure funding for the 25 beneficiary countries

Transition was not completed until 2012 and the project had to be extended three times to ensure continuity of patient treatment. Interviews indicate that there was not a formal transition strategy in place at the beginning of the project. Major efforts were put in place toward the end of the project to secure funding and train health authorities on forecasting and supply chain management. However, transition should have been prioritized since the beginning of the project.

5.2.2.3 Collaboration with national authorities was effective but MoUs were not signed for all beneficiary countries

In 2007, 2008, and 2011 over 90% of participating countries signed a MoU; however, in 2009, 2010 and 2012 less than 70% of participating countries did so. The lack of signed MoUs represented a risk for the project. In all countries, CHAI relied on national authorities' capacity to prevent theft or diversion from occurring. MoUs were used to ensure a commitment from the national authorities to safe and secure storage and distribution of drugs to the intended destinations and to conduct efforts to prevent, detect and prosecute any diversion of these drugs. In addition, countries signing MoUs would commit to (i) collaborate with the project for quantification and reporting exercises, and (ii) provide UNITAID-financed products free of charge to patients.

It is important to note that there was no reported violation of the terms of the MoU in those countries that did not sign the yearly MoU during the project. There are also indications that country representatives found the process of signing the same form every year to be somewhat redundant, which contributed to the low participation in some years.We recognize that CHAI's work with national authorities extended beyond the MoU terms, and stakeholders agreed that a major contributor to the project success was the in-country presence of CHAI and its ability to provide technical assistance to ministries of health related to national treatment policies and quantification exercises. CHAI worked with countries to help prepare them to meet the transitioning challenges by providing training and reference materials. In some cases, a local MoH resource was seconded to follow the CHAI team through the forecasting and order processes.

On the other hand, procurement was done by the CHAI global teams, which while effective, produced the resulting disadvantage that it did not enable the building of technical capability for managing procurement systems in the beneficiary countries. CHAI global teams issued the tenders and managed the supply selection process; which allowed the project to gain scale and exert bargaining power with suppliers. However, this process did not involve national authorities, which limited the extent to which the national technical capability was built.

CHAI was also implementing the UNITAID Pediatric project and other donors' programs. Consequently, it is difficult to assess the depth of CHAI's relationship with the national authorities while looking at 2L ARV in a vacuum.

5.2.2.4 Certain activities could not be assessed due to limited evidence

We found it difficult to assess the quality of two activities due to lack of solid data: 1) We only have anecdotal evidence from interviews that indicate that CHAI supported national registrations; and 2) although annual reports include data on the number of non-pooled orders, we were not able to locate documentation of stock-out numbers directly to see if the quantity decreased over time.

5.3 Impact and sustainability

Final review rating: Medium-high

In this section, we take stock of how the project made progress toward its intended outcomes and impact. We also reflect on the extent to which the progress that has been made is likely to be sustained in the future.

To recap, the project aimed to achieve five overall outcomes as illustrated in the Log Frame below *(added details in Section 2)*:

Figure 7. Log Frame for Second-line Adult HIV/AIDS project

Impact	Increase and maintain access to second-line treatment in beneficiary countries				
Outcomes	Better-adapted, quality-assured second-line ARVs are continuously supplied to beneficiary countries at lower prices				
	1) Global availability: Increase number of quality-assured second-line ARV products and manufacturers globally	**2) National availability:** Increase number of quality-assured second-line ARV products in countries	**3) Affordability:** Reduce the price of second-line ARVs	**4) Delivery**: Maintain the supply of second-line ARVs for beneficiary countries	**5) Sustainability:** Ensure transition funding for second-line ARVs
Outputs	• Number of new suppliers with US FDA or WHO PQ approval for second-line ARVs • Number of new quality-assured products	• Number of products and suppliers registered per country • Number of waivers applied/obtained per country	• Prices paid for second-line ARVs ordered through the UNITAID Project • CHAI ceiling prices for second-line ARVs	• Number of MOUs signed • Volumes and value of second-line ARVs ordered and delivered • Number and value of emergency orders	• Number of countries successfully transitioned • Number of post-transition emergency orders
Activities	• Incentivize supplier market entry by providing market intelligence on second-line ARV demand • Help suppliers enter the market by encouraging them to submit their products' dossiers to an SRA (WHO PQ or FDA)	• Incentivize suppliers to register products in countries by adding a registration coverage criterion in CHAI's supplier selection process • Support national registration approval by monitoring suppliers' dossier submissions to the national authorities • Work with national authorities to obtain waivers for unregistered products that are not SRA approved yet	• Incentivize supplier market entry by providing market intelligence on second-line ARV demand • Negotiate prices with eligible suppliers • Coordinate with countries in the project to pool their second-line orders • Support uptake of ATV/r as lower-cost alternative to LPV/r • Procure TDF formulations for first-line use in Namibia, Uganda, and Zambia to incentivize volume-based price reductions	• Procure second-line ARVs for beneficiary countries on a quarterly basis • Monitor supply levels and place emergency orders to avoid stock-outs • Incentivize suppliers to deliver products in the agreed time by adding a supplier performance criterion in CHAI's supplier selection process	• Coordinate with global partners to identify long-term funds and support countries in securing these funds • Provide further technical assistance to countries to forecast their second-line ARV needs and to support procurement planning if transitioning to Global Fund grants

There are a number of challenges to analyzing the outcomes and impact of market shaping interventions. They are, by definition, efforts to shape dynamic sectors that have many different actors and influencers. Throughout a market's evolution, events occur that could neither be anticipated in advance, nor effectively mitigated during the course of a project: new companies enter and leave, the

global economy rises and falls, new technologies emerge and others become quickly obsolete. The final challenge is that there are no meaningful counterfactuals – the second-line market for ARVs is a very unique market. The 2L ARV project affected the entire global market for these drugs.

As a result, we have used the following approach for assessing how the project contributed to overall market outcomes and impact. The intended outcome areas of the project were: (i) global availability, (ii) national availability, (iii) affordability, (iv) delivery, and (v) sustainability. For each of the five outcome areas we consider and discuss:

- **Market observations.** Consider how the overall market evolved. We analyze the changes in the market that occurred before, during and after the interventions
- **Relevant project contributions.** Discuss the activities undertaken throughout the course of the project that could have contributed to these changes in the market
- **2L ARV additionality.** Consider the other external factors that may have contributed to these trends, and then make a determination, based on triangulation of the evidence gathered in the evaluation process, about how additional the project's efforts were towards shaping the overall market trends

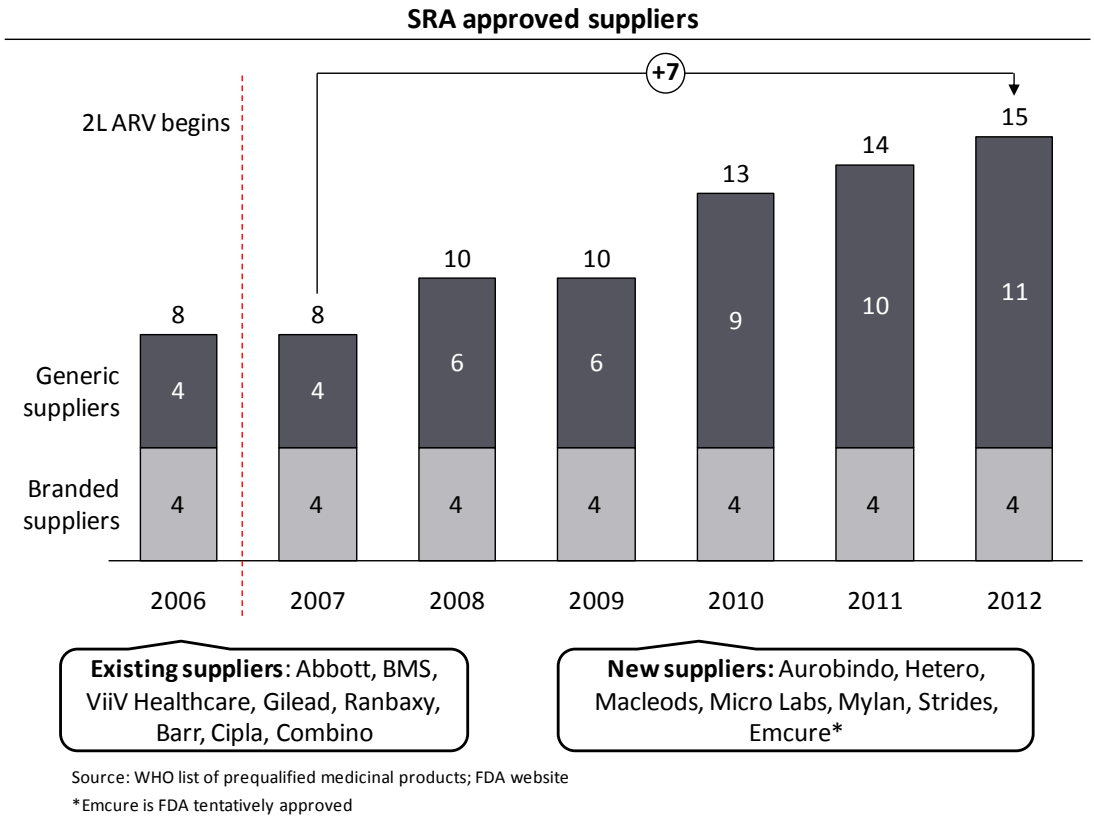
The market for second-line drugs was small and nascent when the project started in 2007, and the 2L ARV project ambitiously attempted to influence multiple aspects of the market system simultaneously: supplier entry, national coverage, and price levels. Each of these was subject to other factors in the market. However, our interviews with manufacturers indicate that the project actions undertaken did play a critical role in influencing supplier entry.

5.3.1 Outcomes 1 and 2: Global and National Availability

Market observations:

Throughout the duration of the project, the number of suppliers increased from 8 to 15.

Figure 8. Number of SRA-approved manufacturers for 2L ARV products between 2006 - 2012



Source: WHO list of prequalified medicinal products; FDA website

*Emcure is FDA tentatively approved

Terminology: For the purpose of this report, formulation refers to a medicinal preparation according to a specific procedure/formula and administered in a specific form, and product refers to the manufacturer version of a formulation

Over the same timeframe, manufacturers introduced three new formulations and 25 new products. The number of WHO prequalified products increased from 10 products for 8 formulations in 2006 to 35 products for 11 formulations in 2012.[18] In addition, Abbott introduced heat-stable LPV/r[19] in 2007, which was the first heat-stable fixed dose combination in the market. By the end of the project, 10[20] of the 11 formulations available were supplied by more than one manufacturer, thus promoting a more competitive market. As one example, LPV/r 200/50mg was only supplied by Abbott before the project began. As of 2012, Mylan (WHO prequalified), Aurobindo and CIPLA (FDA approved) had also launched products based on this formulation. The expansion in the number of products was driven by both new

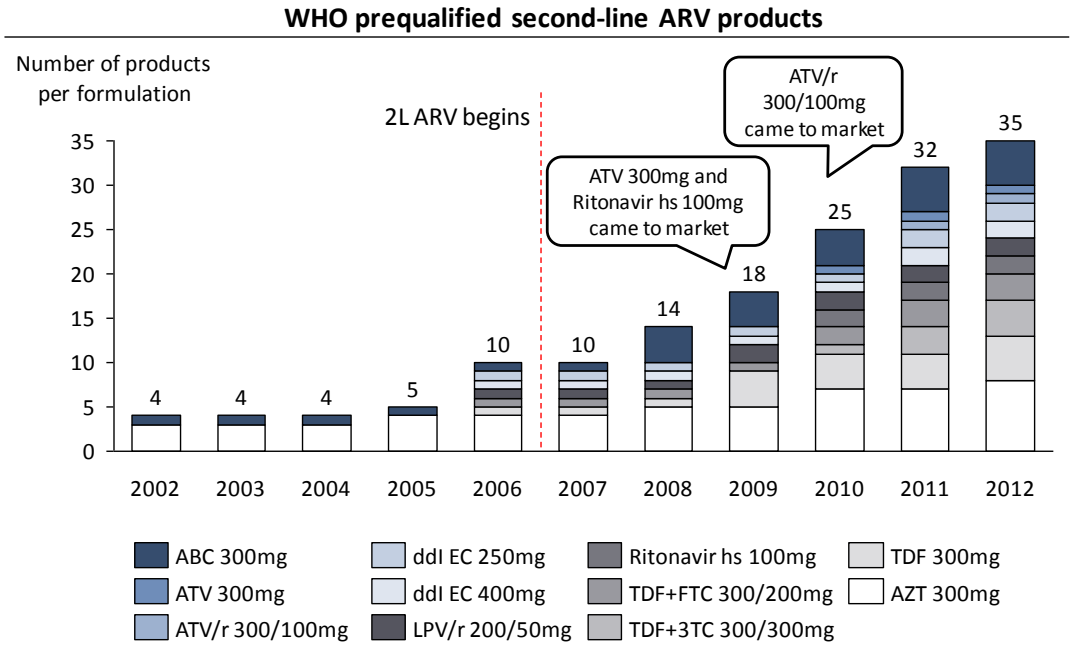
[18] Tenofovir + Lamivudine was WHO PQ in 2010, but is not listed as new formulation as it was already in the market

[19] We do not consider heat-stable LPV/r a new formulation since it did not prequalify for patent protection in some countries

[20] ATV 300mg and ATV/r 300/100mg have one WHO prequalified manufacturer (Mylan) but for ATV 300 mg there is a FDA approved manufacturer (Emcure)

second-line ARV suppliers entering the market (such as Strides with TDF 300mg) and by existing second-line ARV suppliers expanding their portfolio of quality-assured products, such as when Cipla added TDF+FTC 300/300mg.

Figure 9. WHO prequalified second-line products procured under the project



Source: WHO list of prequalified medicinal products

Relevant project contributions:

The most effective contribution that 2L ARV made towards encouraging manufacturers to enter the market was the production of demand forecasts and facilitation of pooled demand. We interviewed three manufacturers that represent approximately 80% of the 2L market share, including both branded and generic manufacturers. They stated that the increased transparency and understanding of the market volume were key to their investment decision-making processes. As one manufacturer noted, "We decided to invest in second-line ARVs when we learnt that market volume was there. CHAI's market knowledge and forecasts were the main contributors to our investment assessment."

Elements of the procurement process, such as including a criterion related to how many countries a manufacturer had registered products, also helped to create incentives for manufacturers to increase market coverage.

CHAI's efforts to encourage manufacturers to register their products with an SRA or with national authorities received more mixed reviews from manufacturers. The manufacturers interviewed did not

cite the process as a constraint to entering markets, and in fact at least one supplier interviewed stated that they had no problem completing the SRA submission documents.

Project country teams emphasized the value of CHAI's support in obtaining waivers for unregistered products that were not WHO prequalified or FDA approved but that nonetheless met the quality requirements specified in the procurement process. This alternative process allowed countries to access drugs for which they otherwise would have to wait up to two years. One of CHAI's team members stated that "the project's main benefit was to bring products to national markets in a timely fashion. Other donors like PEPFAR require products to be SRA approved; UNITAID, by procuring products that are still pending approval and meet all the quality criteria, and by obtaining waivers for national registration, could bring products to the country 2 to 3 years earlier." Examples of products brought in-country prior to an SRA approval are TDF+FTC 300/200mg procured from Cipla in 2009, or Ritonavir hs 100mg procured from Matrix in 2010.

2L ARV additionality:

Considering the full range of market trends, it is reasonable to conclude that CHAI's efforts effectively accelerated growth of suppliers and products within the 2L markets, especially in low-volume countries. CHAI's actions encouraged additional suppliers to enter the market or to produce additional 2L products, but it is important to note that there were additional signals in the market that demand for 2L products would be increasing, such as WHO forecasts on the number of patients expected to fail first-line treatment or the entry of major donors such as PEPFAR and the Global Fund into the HIV/AIDS space.

In our estimation, based on interviews with stakeholders and our review of market trends, in the absence of CHAI's efforts suppliers would likely have produced second-line products and introduced them to major markets such as Kenya or Nigeria, but the market beyond would have remained fragmented. Evidence also indicates that the project had an impact by increasing the access to more affordable second-line ARVs within low-volume countries (eg, those with fewer than 1500 patients seeking second-line treatment). By the end of the project, 2L ARV suppliers offered products in a wider range of countries, including low-volume countries, though the latter are generally less attractive to suppliers given the high registration fees and complex registration processes weighed against the likely returns. For instance, in 2008, DRC and Chad had fewer than 200 patients seeking second-line treatments. Without this intervention, suppliers would have had far less incentive to introduce their products to these countries.

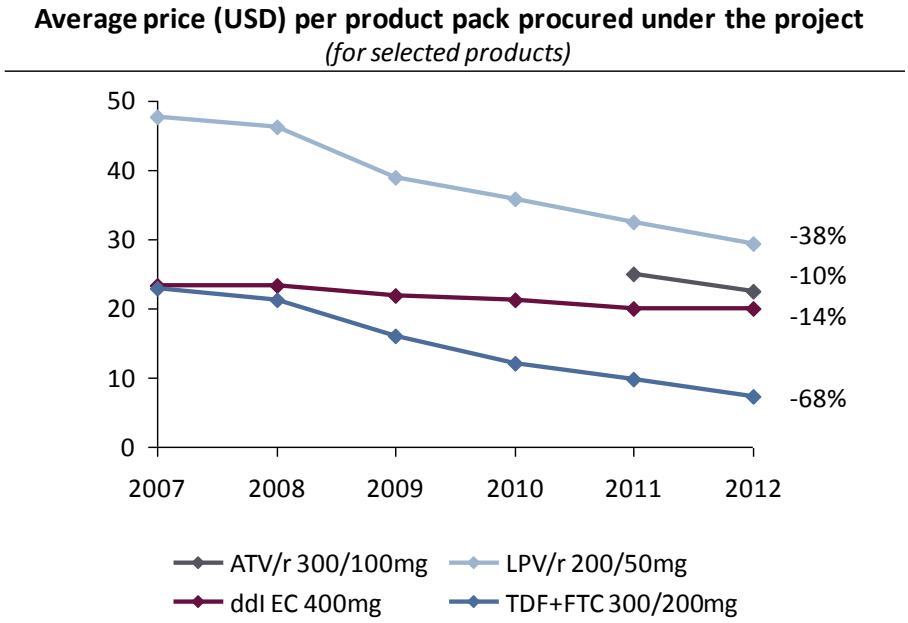
5.3.2 Outcome 3: Affordability

For affordability we note the absolute price decrease realized but do not assess whether individual country governments, much less the end beneficiaries, would be able to afford treatment at the reduced price[21].

Market observations:

CHAI prices for the 10 formulations[22] included in this project decreased ~15 – 70% between 2007 and 2012. The largest price decreases were for the three TDF formulations that can be used for 1L or 2L treatments.

Figure 10. CHAI negotiated price evolution during the project



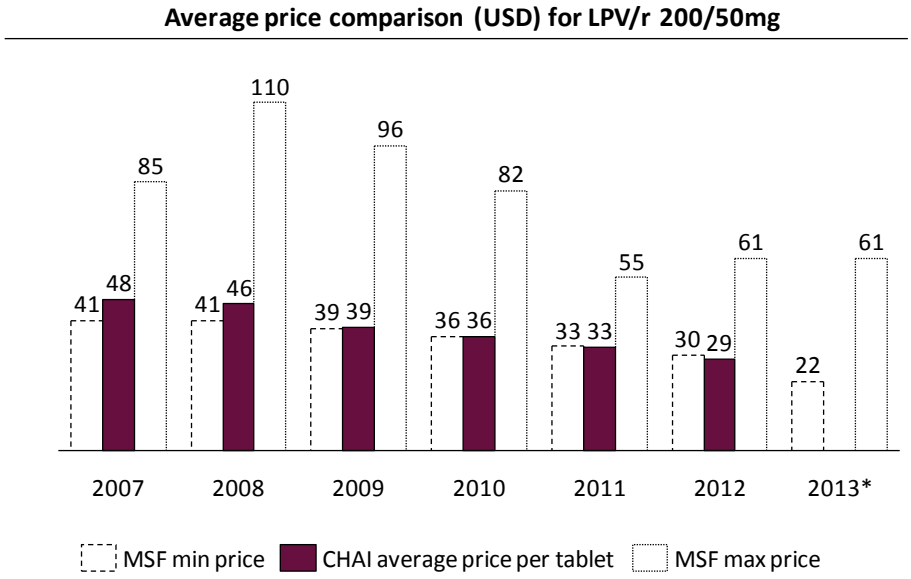
Source: CHAI order tracker

CHAI's negotiated prices for LPV/r were near the lowest recorded market prices in any given year.

[21] The 2009 project plan proposed that prices be reduced on average from USD $1000 per patient to USD $500, which while a substantial improvement, would ultimately need to be considered in the context of donor funding available and per capita income in country to be considered affordable. The World Bank defines low income countries as those with Gross National Income (GNI) per capita less than USD $1035, or less than USD $3 per person per day

[22] Excludes AZT 300mg which was included one year on an exception basis

Figure 11. Price comparison between CHAI and the market for a selected second-line drug



Source: CHAI order tracker and MSF reports

*2013 report records prices from 6/2012-6/2013; MSF reports are annual and are released in July

Relevant project contributions:

Negotiated directly with suppliers to provide cost reduction assistance. Manufacturers willing to engage in cost-plus negotiations shared their products' cost structure as assessed by an independent accounting firm. CHAI offered assistance with cost savings such as helping to secure lower prices on key raw materials, addressing important chemistry challenges, and modeling volume-based cost savings in anticipation of increased demand. Cost reductions were then passed on in the form of lower prices. It was exclusively generic suppliers who agreed to engage in cost-plus negotiations with these terms. For example, five suppliers (Aurobindo, Cipla, Hetero, Matrix and Ranbaxy) participated during the 2010 tender process. According to one manufacturer, the resulting cost savings ranged from 15% to 20% on average for any single product. Particular cost savings were realized for the three TDF formulations, after CHAI engaged in independent research aimed at improving the yields of the final and penultimate stages of Tenofovir synthesis and shared the results of this research with suppliers who had agreed to partner on cost reductions. TDF prices dropped the most – between 63 – 66%.

Pooled demand across 25[23] countries and including the aggregate volume in the tender to ensure suppliers a larger minimum volume in cumulative orders. CHAI employed a rigorous selection process to identify a primary and one to two secondary suppliers. The process also featured guidelines about how to allocate procurement volumes among suppliers; for example, when there was one primary and

[23] The original project agreement was for 27 countries but two countries dropped (Burkina Faso and Thailand) and one did not place any orders. The number of participating countries also went down over time; only 13 countries placed orders in 2011.

one secondary supplier, the primary manufacturer was offered a majority of the volume – up to 70% -- for a given product. The combination of large volume and tender split enhanced the tender competitiveness.

Supported the scale up of ATV/r as a lower-cost alternative to LPV/r. CHAI estimated that ATV/r would be 40-60% cheaper than LPV/r in the long-term. CHAI country teams worked with their government partners to recommend inclusion of ATV/r in national treatment guidelines so that early modification of protocols would enable faster uptake of ATV/r when it was commercialized. CHAI's efforts helped authorities at the country level to overcome some of the lack of clarity in treatment guidelines. ATV/r only came to market in 2011, and although the CHAI-negotiated price for ATV/r was 23% lower than LPV/r in 2011, it is still too early to assess the expected price reductions in the long-term.

Increased volumes for TDF formulations by procuring them for three countries as a 1L treatment. Though varying reasons have been given for why this exception for 1L product procurement was made for Namibia, Uganda, and Zambia, the original project plan proposed that increasing TDF volumes demanded by these three countries would further accelerate price reductions for TDF formulations. There is reasonably strong anecdotal support for this hypothesis. The prices for the three TDF formulations, which can be used for 1L or 2L treatment, decreased the most across the ARVs included in this project. Additionally, TDF procurement for Namibia, Uganda, and Zambia represented between 60-75% of total TDF volumes procured through this project, suggesting that inclusion of the 1L volumes was one contributing factor to the magnitude of the price decrease. However, it is not possible to say this definitively since, as noted above, there were unrelated TDF-specific manufacturing cost reductions undertaken as well.

2L ARV additionality:

A triangulation of evidence collected for this report suggests that CHAI's efforts had a meaningful influence on the overall reductions in prices of 2L drugs. The price decreases observed for 2L products between 2007 and 2012 resulted from a combination of project interventions and external market factors. Some other factors that would influence a manufacturer's pricing decisions include: market power (eg, brand or other influence that would allow them to command a price premium relative to competitors), total production capacity relative to demand (eg, prices would be lower if there was overcapacity), price transparency (eg, pricing would differ in situations where competing prices are not known), and other motivations (eg, desire for social impact or response to specific negotiations).

For 2L ARVs most of these outside factors are less relevant. The greatest challenge in attribution is in separating the effect of the individual project interventions, such as the effect of increased competition and volumes vs. cost negotiations, and acknowledging the existing trends for increased competition that preceded the project. Given that UNITAID volumes were between 50-80% of the second-line market, it is reasonable to think that CHAI's intervention played a very important role in affecting overall prices for 2L drugs.

5.3.3 Outcome 4: Delivery

Market observations:

The supply of second-line ARVs has stabilized among beneficiary countries. The table below shows a decrease in the percentage of emergency orders over time, suggesting a more stable supply. 2012 was an exception since it was a no cost extension of the project to exclusively cover emergencies while countries were transitioning to other sources of funds.

Table 4. Emergency Orders

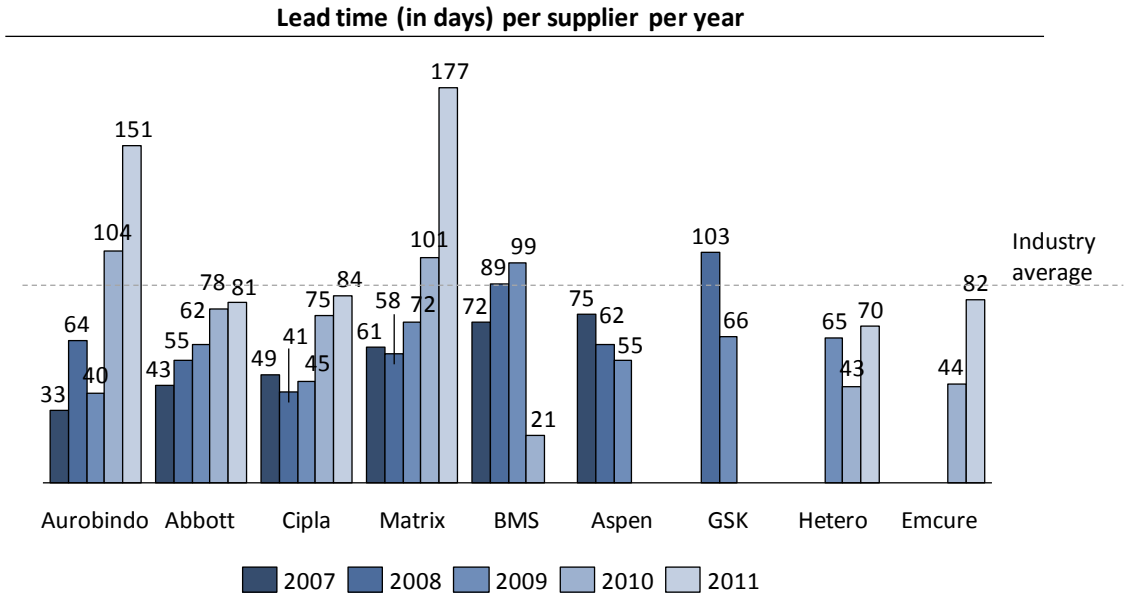
Year	% of total emergency orders in volume
2007	N/A
2008	31%
2009	23%
2010	11%
2011	0%
2012	100%

Project contributions:

Procuring drugs for countries on a quarterly basis and placing emergency orders to prevent stock outs. Country teams sent their quarterly orders to CHAI headquarters, which placed orders with suppliers. Interviews with country teams indicated that quarterly orders allowed for adjustments in the annual forecasts by ensuring that forecasts were based on actual consumption data. In the event of potential stock outs, country teams placed emergency orders.

CHAI also included a past performance criterion in the tender process to incentivize suppliers to meet the lead time estimated in their proposals. However, the table below shows that lead times did not improve over time and in many instances they were greater than the 12-week industry average. There are many potential reasons for this. On the manufacturers' side, the main causes were delays in production, issues in quality and proper packaging, and lack of production capacity; on the countries' side, the causes were local training requirements and lack of proper legal agreements. In some occasions, the long lead time was due to countries' preferences for having the drugs delivered later. Annual reports do not provide data on stock-outs, but given that the share of emergency orders decreased even as the lead times increased, it does not appear that the longer lead times affected the overall supply stability.

Figure 12. Lead times by supplier, 2007 - 2011



Source: CHAI annual reports

5.3.4 Outcome 5: Sustainability

By 2012, all participating countries had successfully transitioned to new sources of funding. The original objective was to transition to longer-term sources of funding – i.e., PEPFAR and the Global Fund – by the end of 2009.

This transition proved to be challenging, which is quite understandable given the ongoing effects of the global financial crisis. The second extension for the project was a direct result of some countries not having transitioned by the end of the first extension in 2011. The reasons for delayed transition were twofold: (i) lack of a proper transition strategy at the outset of the project, and (ii) global funding constraints and uncertain disbursement timelines. CHAI worked to mitigate these risks with the following actions:

- Increased their engagement with partners at the global level to identify opportunities to accelerate transition
- Allocated resources across CHAI's country teams, regional teams, and global teams, with the Drug Access and UNITAID Program Teams all providing technical leadership in their respective areas of expertise
- Launched a targeted transition response team to help countries address the procurement, marketplace, and funding challenges, particularly in countries with a limited CHAI presence

As a result of these mitigating factors, all 25 countries successfully transitioned to other donors with 6 countries also contributing their own funds. The Global Fund is supporting 22 countries and PEPFAR 11 countries.

UNITAID Second-Line ARV Project: Transition Source (as of November 2012)

COUNTRY	Transition Source
Benin	GF Round (R) 5
Botswana	PEPFAR / Government of Botswana
Burundi	GF R 8 Phase 2
Cambodia	GF R 7 Phase 2/R9
Cameroon	GF R10 / Government of Cameroon
Chad	GF R8 Phase
Cote d'Ivoire	PEPFAR
DR Congo	GF R8 P2
Ethiopia	GF R2 Rolling Continuation Channel (RCC)
Ghana	GF/ PEPFAR
Haiti	GF R1 RCC / PEPFAR
India	GF R4 RCC
Kenya	GF R10 / PEPFAR
Malawi	GF R1 (RCC)
Mali	GF R8
Mozambique	GF R9 / PEPFAR
Namibia	PEPFAR / Government of Namibia
Nigeria	GF R9 / PEPFAR
Rwanda	GF R6/R7/GF National Strategy Application/ PEPFAR
Senegal	GF R9 / Government of Senegal
Tanzania	GF R8 / PEPFAR
Togo	GF R8 Phase 1 & Phase2
Uganda	GF R7 / PEPFAR / Government of Uganda
Zambia	GF R10
Zimbabwe	GF R8 P2 / Government of Zimbabwe

5.3.5 Public health impact

The ultimate goal of this market intervention is to ensure that patients failing first-line ARV treatment can access the second-line drugs they need. Increasing the availability and affordability of second-line treatments means that more people can be treated with less money and better products. The achievements of the project include: (i) an increased access to drugs for patients in low volume countries where UNITAID was the only donor for HIV/AIDS commodities; and, (ii) an increase in the availability and, ultimately, the uptake of ATV/r, which allows for simple delivery and storage as well as improved patient adherence.

In this section we discuss (i) the impact to patient uptake, (ii) attribution of the UNITAID and CHAI interventions to improvements in patient uptake, and (iii) opportunities to improve attribution in the future.

We recognize that patient uptake of second-line drugs is an imperfect measure of health impact. Its utility as a metric of success is tempered by the fact that to increase uptake, more patients must fail the more affordable first-line treatments, which is certainly not the goal. Similarly, lower than predicted patient uptake is not necessarily indicative of lack of second-line treatment access but could just mean that fewer first-line patients are developing resistance to first-line treatment.

For the 2L ARV project, there is limited quality data available on patient uptake, due largely to the fact that in-country activities were not part of the original project scope. The data presented here were collected by CHAI country teams but were not necessarily consistent between countries. In fact, CHAI noted that for some countries the numbers are based on the volumes ordered rather than any measurements taken in-country.

Table 5. Estimate of patients treated with products procured through 2L ARV

Year	Patients receiving 2nd line treatment	Patients receiving 1st line treatment	Total patients treated	Total patients forecasted
2007	**25,517**	**36,156**	**61,673**	**N/A**
2008	**46,107**	**87,216**	**133,323**	**N/A**
2009	**67,490**	**49,834**	**117,324**	**124,000**
2010	**71,342**	**39,850**	**111,192**	**224,962**
2011	**65,690**	**51,451**	**117,141**	**131,546**
2012	**N/A**	**N/A**	**N/A**	**N/A**

Due to both the range of factors affecting patient uptake and the scope of project activities, it is not possible to directly attribute patient uptake to 2L ARV intervention. The project scope did not extend to in-country support activities, such as the collection and analysis of site-level data. What reporting there was relied on often-weak in-country logistics information systems. Beyond the data capture, there was a host of complicating factors from outside the project that could influence patient uptake's deviations from forecast. For example, there could simply be fewer patients failing first-line treatment, countries may lack the diagnostic capacity to identify patients needing second-line treatment, or treatments could be delayed or even mis-delivered between the country's point of entry and the receiving treatment facilities.

In hindsight, attribution could have improved by increasing the level of the partner's involvement in the national supply chain, tracking UNITAID drugs from port of entry to end user. The project could also have leveraged the resources and technical capabilities of the Pediatric HIV/AIDS project to improve the national logistics management information systems.

Additional external factors might have influenced the public health impact of this intervention, such as the level of sophistication of national health systems and supply chain; degree of diagnosis capacity in countries or level of commitment from the national authorities to include second-line in the treatment guidelines and secure funding.

Finally, it is important to recognize the project's contributions to the public health outcome separate from patient uptake. The project promoted the uptake of ATV/r manufactured by generic companies. This allowed patients to have access to better formulations. ATV/r is a heat-stable fixed-dose formulation, which provided health professionals with the confidence required to switch patients to second-line treatments and helped patients adhere to their treatment. The project also increased access to drugs for patients in low volume countries where UNITAID was the only donor for HIV/AIDS commodities; these patients would unlikely have had access to treatment otherwise.

5.4 Management

Final review rating: ***Medium-high***

UNITAID and CHAI established an increasingly effective relationship over the length of the project. Project management processes, such as reporting between the two organizations, improved over time; additionally, the partners worked together to adapt to changes in the needs of the market as changes arose. Patient uptake as a target to reflect project performance was the only major point of disagreement.

5.4.1 UNITAID and CHAI developed an effective working relationship after an initial learning curve

The relationship between UNITAID and CHAI matured strongly after initial tensions during the early startup phase. UNITAID was established in 2006 and 2L ARV was its first major intervention; at that time, the CHAI team was fairly small. As two small teams, one only just-established, UNITAID and CHAI at first experienced operational difficulties when team members struggled to coordinate routine tasks such as reporting or other communication. One interviewee noted that early in the project UNITAID was "just so understaffed that they were missing things operationally."

After this initial learning curve, the working relationship strengthened over time. Two main drivers of improvement in coordination were cited during interviews: (i) growing teams over time and assigning individual people to clearly-scoped roles with well-defined responsibilities; and (ii) learning to establish and manage UNITAID's expectations of CHAI and CHAI's expectations of UNITAID. A stakeholder interviewed explained how early staff members had difficulty managing their workloads and being responsive to information requests:"UNITAID and CHAI have struggled in figuring out the proper level of involvement of UNITAID in the project implementation (e.g., choosing procurement agents); but over the length of the project, partners learnt to manage expectations and delineate responsibilities in a more effective and efficient manner."

The strength of CHAI as a partner to UNITAID for this particular project is worth emphasizing. As one UNITAID interviewee described, the criteria for partner selection were knowledge of the dynamics of the HIV market and experience with and knowledge of project design and implementation. This UNITAID stakeholder noted that CHAI "were the only ones to have some idea on how to do this job, and to understand the market dynamics. Very few organizations really understand this work." CHAI's presence across multiple countries, either with country teams or with regional team coverage in countries that lacked a CHAI office, was also particularly called out as critical to the project success. Finally, the fact that CHAI was also implementing the Pediatric HIV/AIDS Treatment project in these countries, as well as programs for other donors, offered opportunities for greater efficiency in country-level management in addition to the notable benefit of continuing to provide transition support even while 2L ARV ramped down.

5.4.2 Partners collaborated in adjusting the project plan to reflect market needs

Both UNITAID and CHAI demonstrated a high degree of flexibility in adapting the project's activities and objectives in order to achieve the intended impact. Evidence of this flexibility was seen in the introduction of mechanisms that were outside the norm for an organization like UNITAID, such as contracting a procurement agent or enacting a project extension to wait for the launch of ATV/r, which was expected in 2008 but came to market in 2011. As one CHAI manager described, "UNITAID was very open to innovation and responsive to us coming to them with new ideas. We came to them with a theory of procurement…that was totally foreign to them and they went with it and embraced it."

5.4.3 Improvement in reporting and M&E frameworks

Alignment of the project stakeholders around a Log Frame and reporting on activity progress were weak in the early years of the project but improved substantially over time. Reporting systems improved significantly between the project's start in 2007 and its conclusion in 2012. 2L ARV's 2008 project agreement introduced a template for its annual and semiannual reports, which helped standardize CHAI's reporting on project progress. From 2008 to 2010, agreements included an M&E plan that described the project actions and milestones. A summary of the actions is included at the beginning of this section. However, this level of reporting did not map activities to market outcomes or the ultimate project objectives.

There did not appear to be any documented log frame prior to 2011 that would have assisted in aligning stakeholders around overall project objectives in market impact, specific market outcomes, and supporting activities. The mid-term evaluation suggested improvements to M&E frameworks, specifically to ensure consistency between outcomes and activities, and in response the 2011 and 2012 agreements introduced clear log frames that were approved by the UNITAID Secretariat. It should be noted that there are differences between the log frames for each year and that in 2012 the project's only activities were to finish securing transition funding for each of the beneficiary countries. The Log Frame included in this evaluation is a consolidation of the activities and outcomes in each of these log frames.

Despite the notable improvement in reporting, through the course of this evaluation we nonetheless found that some key pieces of information needed to track progress over time were unavailable. These included the number of waivers obtained by country, the number of dossier submissions to an SRA encouraged, and the number of national registrations monitored by CHAI.

5.4.4 Lack of clarity on responsibility for patient uptake as an outcome

Throughout the course of the project, CHAI and UNITAID were not well-aligned on whether the project was responsible for either influencing or measuring patient uptake. While managers interviewed from both CHAI and UNITAID acknowledged that patient uptake was not part of CHAI's scope of work, there were several examples cited that explained the confusion and occasional tension around the topic that resulted.

One example is that number of treatments was included as a project indicator. CHAI saw this indicator as contextual: data to collect that is relevant to the project but in no way indicative of success or failure. CHAI's perspective was described in an interview as follows: *"It is important to reiterate that these patient figures are not performance targets, nor metrics for evaluating the program's success. […]It does not make sense to treat lower-than-expected rates of treatment failure as poor performance."* The stakeholder interviewed asserted that this view was presented to UNITAID on multiple occasions.

Even within UNITAID, we heard different perspectives around the need to measure patient uptake. The UNITAID Board was interested in understanding patient uptake, and UNITAID interviewees' perspectives spanned a range. Some UNITAID stakeholders considered these measurements warranted, given the size of the project and the resources allocated to CHAI, while others acknowledged that patient uptake was not part of the scope of the project.

6 Conclusion

In 2007, the market for second-line drugs was underdeveloped and characterized by low access. Although there were external factors signaling that the market for second-line products would be increasing, the project contributed to the acceleration of the creation of an expanded and competitive market. The number of suppliers – and particularly generic manufacturers – increased, better formulations came into the market, and prices decreased to a level more accessible to low-income countries.

The broader effects of this project should also be self-sustaining on the supply side now that suppliers have increased confidence in the level of demand, are producing greater volumes, and have nationally registered their products. The market has crossed a threshold in size and stability where interventions such as demand pooling that guarantee volumes should not be needed any longer.

The 2L ARV project also yielded valuable lessons for UNITAID, which grew and formalized as an organization over the course of the project's lifetime. As UNITAID continues to pursue innovative interventions in nascent and/or volatile markets, findings relevant to how the Second-line HIV/AIDS project was designed and executed can inform the success of future work.

Annex 1 Methodology

This annex provides an overview of the scope of the final review along with the approach taken to pursue the review's objectives. The objectives of this independent evaluation are:

- To assess the performance and impact of the project over its lifetime, and
- To identify opportunities to improve the design or implementation of future projects.

A1.1 Scope

In order to meet the review's objectives, Dalberg was engaged to perform the following activities:

- Review all provided project documentation
- Review available data relevant to the project's work and impact
- Engage key stakeholders in discussion of the project's successes, challenges, and lessons learned
- Rate the project's performance against its objectives and intended impact, and
- Describe lessons learned over the lifetime of the project that could inform future UNITAID projects.

A1.2 Approach

The final review of the 2L ARV project was implemented in three phases:

First phase: Finalization of evaluation framework. The evaluation team:

- Worked closely with the UNITAID Secretariat to finalize the evaluation framework, including: evaluation questions, methodology, and approach, and
- Requested project documents and other relevant materials from the UNITAID Secretariat and the partners.

Second phase: Preliminary assessment and analysis. The evaluation team:

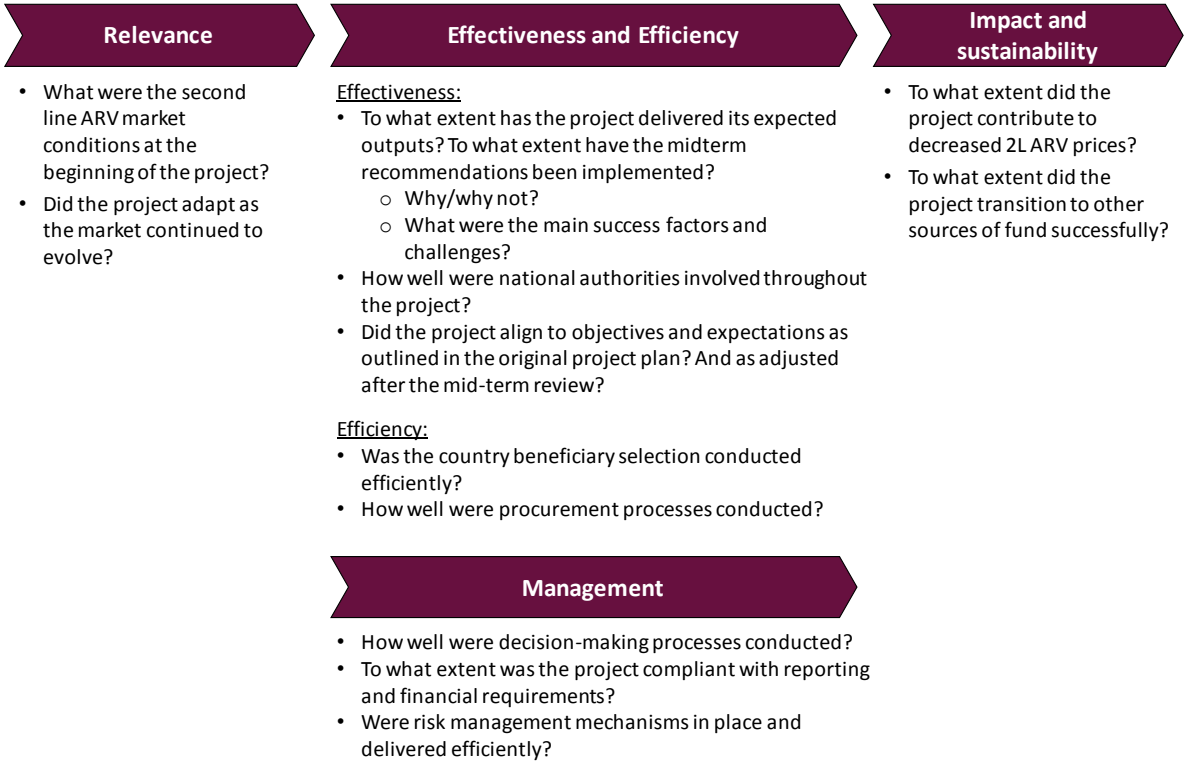
- Interviewed members of the UNITAID Secretariat, CHAI staff who worked on the project, and representatives of ARV manufacturers
- Reviewed provided project documents
- Analyzed relevant available data
- Developed a Theory of Change based on project documents, to evaluate individual activities against their intended outcomes, and
- Conducted a preliminary assessment of project efforts.

Third phase: Final assessment. The evaluation team:

- Refined analyses and summarized and refined findings
- Developed recommendations based on lessons learned
- Drafted the final review for submission to the UNITAID Secretariat and solicited feedback
- Shared the draft review with CHAI for fact-checking, and
- Incorporated all feedback into and submitted a final draft.

During the first phase of the evaluation, the UNITAID Secretariat and the evaluation team agreed on the following evaluation questions:

Figure 1: Methodology for final evaluation



During the second phase of the evaluation, the evaluation team reviewed 49 project related documents (not counting annexes additionally) and interviewed 20 stakeholders. Stakeholders interviewed include nine representatives from the UNITAID Secretariat, eight representatives from the implementing partner CHAI, and three representatives of ARV manufacturers. A complete list of documents reviewed and interviews conducted as part of this review can be found in Annex 2 and Annex 3.

To illustrate the overall logic behind the 2L ARV project's design, as a means to test and learn from 2L ARV, Dalberg created a Theory of Change for the project based on provided documentation, specifically a consolidation of the 2011 and 2012 log frames. The Theory of Change lists the activities and outcomes pursued by the project team, as well as their ultimate intended impact. It served evaluation as a model of how the project intended to create impact.

During the second and third phases of the evaluation, the evaluation team developed and refined findings. A summary of findings evaluation is found in Section 4. These findings have been grouped in the following categories:

- **Relevance.** Assessment of whether or not the objectives of the 2L ARV project, if achieved, would contribute to the goals of UNITAID.
- **Effectiveness & Efficiency.** Evaluation of project outputs completed against those envisioned in the project agreements including an assessment of which outputs have been completed on-time and within stipulated budgets.
- **Impact & sustainability.** Review of the progress towards the main objectives of the project as well as a summary of any unintended impact (either positive or negative) generated by the project's activities. Assessment of the efforts made toward ensuring that the impact of the project will remain after UNITAID funding is withdrawn.
- **Management.** Assessment of the management and coordination within the 2L ARV project and the extent to which they have been conducive to effective project implementation.

For each category, a rating in the range of low to high is provided by the evaluation team. This rating is based on interpretation of key findings and demonstrated progress towards agreed project objectives.

In assessing the impact of the project, the evaluation team made use of Dalberg Global Development Advisors' market shaping framework, which defines the stages of market shaping: desired outcomes, market health symptoms, drivers, barriers and interventions. This framework shed insight on the vicious cycle active in the 2L ARV market before UNITAID's intervention, as well as provided a toolkit with which to approach the task of disentangling the effects of the 2L ARV intervention from the effects of other forces acting on the market.

Lessons learned from the 2L ARV project and recommendations for the design of future initiatives are presented in Section 3. This includes lessons and recommendations that are relevant to funding market interventions, to designing market interventions, to measuring long-term system-wide impact, and implementing market interventions.

Annex 2 List of documents reviewed

Project documentation

	Title	Primary Author	Date
1.	2007 Project Agreement and 6 annexes	UNITAID	Feb-07
2.	2007 CHAI annual report and 10 annexes	CHAI	Mar-07
3.	Interim report for the period May 8, 2007 - June 29, 2007	CHAI	May-07
4.	2008 Project Agreement and 13 annexes	UNITAID	Dec-07
5.	Quarterly activity report for the period November 1, 2007 - January 31, 2008	CHAI	Feb-08
6.	Quarterly activity report for the period July 1, 2007 - October 31, 2007	CHAI	Feb-08
7.	2008 CHAI annual report and 12 annexes	CHAI	Mar-08
8.	Interim report for the period February 1, 2008 - April 30, 2008	CHAI	May-08
9.	Amendment to Project Proposal For UNITAID Second-Line HIV/AIDS Program 2009	CHAI	Nov-08
10.	2009 Project Agreement and 16 annexes	UNITAID	Jan-09
11.	Proposal for Project Extension for UNITAID Second-Line HIV/AIDS Program 2010-2011	CHAI	Feb-09
12.	2009 CHAI annual report and 12 annexes	CHAI	Mar-09

13.	CHAI Project Plan for Second-Line Project- 2009	UNITAID	May-09
14.	2010 Project Agreement and 16 annexes	UNITAID	Jan-10
15.	2010 CHAI annual report and 8 annexes	CHAI	Mar-10
16.	UNITAID Update on Operations	UNITAID	Jun-10
17.	Request for proposal: supply of UNITAID-financed pediatric and/or adult second-line ARVs for March 2011 - February 2012	CHAI	Oct-10
18.	UNITAID Update on Operations	UNITAID	Nov-10
19.	Guidelines for revising price proposals for UNITAID-financed Pediatric and Adult Second-Line ARVs applicable to suppliers opting for Cost Plus basis of Negotiations	CHAI	Nov-10
20.	2011 Project Agreement and 17 annexes	UNITAID	Jan-11
21.	Report of the Recommendations of the Adjudication Panel Regarding Primary Supplier Selection for UNITAID-financed Pediatric and Second-Line ARV Treatment Programs	CHAI	Jan-11
22.	Quarterly update for the UNITAID-CHAI Second Line HIV/AIDS Project	CHAI	Feb-11
23.	2011 CHAI annual report and 5 annexes	CHAI	May-11
24.	2011 Order tracker	CHAI	May-11
25.	Quarterly update for the UNITAID-CHAI Second Line HIV/AIDS	CHAI	Jun-11

	Project		
26.	UNITAID Update on Operations	UNITAID	Jul-11
27.	Quarterly update for the UNITAID-CHAI Second Line HIV/AIDS Project	CHAI	Aug-11
28.	Quarterly update for the UNITAID-CHAI Second Line HIV/AIDS Project	CHAI	Nov-11
29.	UNITAID Update on Operations	UNITAID	Dec-11
30.	2011 Semiannual report logframe	CHAI	Dec-11
31.	2012 Project Agreement and 16 annexes	UNITAID	Jan-12
32.	Second-line project mid-term review	Swiss Tropical and Public Health Institute	Feb-12
33.	2012 CHAI annual report and 5 annexes	CHAI	Mar-12
34.	Procurement and financial review of UNITAID's paediatric and 2nd line HIV/Aids projects	PricewaterhouseCoopers	Mar-12
35.	2012 Order tracker	CHAI	Mar-12
36.	UNITAID Update on Operations	UNITAID	Jun-12
37.	CHAI comments on the Mid-Project review performed by STPH	CHAI	Jun-12
38.	Quarterly update for the UNITAID-CHAI Second Line HIV/AIDS Project	CHAI	Nov-12

39.	UNITAID Update on Operations	UNITAID	Dec-12
40.	2012 Annual M&E report	CHAI	Mar-13
41.	UNITAID Update on Operations	UNITAID	Jun-13

External documents

	Title	Primary Author	Date
1.	Prioritizing Second-Line Antiretroviral Drugs for Adults and Adolescents: a Public Health Approach	WHO	May-07
2.	2007 Untangling the web of antiretroviral price reductions	Medecins sans Frontieres	Jul-07
3.	2008 Untangling the web of antiretroviral price reductions	Medecins sans Frontieres	Jul-08
4.	2009 Untangling the web of antiretroviral price reductions	Medecins sans Frontieres	Jan-10
5.	2010 Untangling the web of antiretroviral price reductions	Medecins sans Frontieres	Jul-10
6.	2011 Untangling the web of antiretroviral price reductions	Medecins sans Frontieres	Jul-11
7.	2012 Untangling the web of antiretroviral price reductions	Medecins sans Frontieres	Jul-12
8.	HIV, tuberculosis and malaria medicines landscape	UNITAID	Jan-13
9.	2013 Untangling the web of antiretroviral price reductions	Medecins sans Frontieres	Jul-13
10.	ARV market report	CHAI	Dec-13

Annex 3 Summary of interviews conducted

	Name	Organization	Title / Position	Project role
1.	Philippe Duneton	UNITAID	Deputy Executive Director	UNITAID secretariat
2.	Raquel Child	UNITAID	Director, Market Dynamics and Operations *(formerly)*	Project secretariat
3.	Kate Strong	UNITAID	Monitoring & Evaluation Officer	Project secretariat
4.	Jane Galvão	UNITAID	Technical Officer, HIV/AIDS	Project secretariat
5.	Gauri Khanna	UNITAID	Technical Officer, Monitoring & Evaluation	Project secretariat
6.	Paulo Meireles	UNITAID	Portfolio Manager, HIV/AIDS *(formerly)*	Project secretariat
7.	Brenda Waning	UNITAID	Coordinator, Market Dynamics	UNITAID secretariat
8.	Irina Avchyan	UNITAID	Finance Officer	Project secretariat
9.	Lorenzo Witherspoon	UNITAID	Supply Officer	Project secretariat
10.	David Ripin	CHAI	Executive Vice President, Access Programs	Implementing partner
11.	Umesh Warty	CHAI	Director of UNITAID Projects	Implementing partner
12.	Amy Meyers	CHAI	Director of UNITAID Projects *(formerly)*	Implementing partner
13.	Sylvia Rowe	CHAI	Senior Advisor	Implementing partner
14.	Julie Feder	CHAI	Chief Financial Officer	Implementing partner
15.	Naoko Doi	CHAI	Associate, 2L Project *(formerly)*	Implementing partner
16.	Jackson Hungu	CHAI	Deputy Country Director, Kenya	Implementing partner
17.	Assefa Gashaw	CHAI	Analyst, Supply Chain, Ethiopia (formerly)	Implementing partner
18.	Annika Lane	Abbvie	General Manager, Virology	ARV manufacturer
19.	Umesh K	Aurobindo	Associate Vice President	ARV manufacturer
20.	Arvind Kanda	Mylan	Vice President	ARV manufacturer

Annex 4 Number of packs ('000) delivered per country under the project

Countries	2007	2008	2009	2010	2011	2012	Total
Benin	-	5.60	3.83	9.60	1.50	11.61	**32.14**
Botswana	49.41	120.65	43.99	224.26	-	-	**438.31**
Burundi	10.83	8.20	33.81	49.64	39.70	-	**142.18**
Cambodia	15.02	28.31	68.79	50.36	-	-	**162.48**
Cameroon	38.32	24.23	43.36	156.73	205.01	112.74	**580.38**
Chad	15.47	4.97	8.52	40.77	-	-	**69.73**
Cote d'Ivoire	11.83	-	30.00	-	-	-	**41.83**
D R Congo	3.56	15.41	22.16	70.11	72.63	20.22	**204.10**
Ethiopia	18.06	42.90	58.02	17.51	-	-	**136.48**
Ghana	-	3.81	-	-	-	-	**3.81**
Haiti	3.00	4.00	19.45	27.29	34.56	12.35	**100.64**
India	2.16	27.15	16.90	57.45	293.53	60.00	**457.20**
Kenya	34.30	222.92	846.36	392.01	-	-	**1,495.60**
Malawi	17.65	14.04	6.86	-	-	-	**38.55**
Mali	2.15	26.76	39.40	21.51	19.50	-	**109.32**
Mozambique	34.49	17.60	42.14	85.19	99.21	12.74	**291.36**
Namibia	8.52	57.35	7.92	2.60	-	-	**76.38**
Nigeria	29.38	97.38	283.22	296.32	369.68	-	**1,075.98**
Rwanda	6.75	43.93	30.23	-	-	-	**80.90**
Senegal	15.68	16.16	1.30	49.72	-	-	**82.85**
Tanzania	5.73	43.50	87.37	-	-	-	**136.61**
Togo	22.70	3.00	15.31	86.51	7.57	18.00	**153.08**
Uganda	216.46	399.92	571.71	831.05	679.46	42.72	**2,741.33**
Zambia	136.32	744.64	664.62	591.11	155.27	-	**2,291.96**
Zimbabwe	6.81	35.65	39.13	122.94	29.05	26.11	**259.68**
Total	**704.57**	**2,008.08**	**2,984.38**	**3,182.67**	**2,006.67**	**316.49**	**11,202.85**

Source: CHAI order tracker

Annex 5 Number of packs ('000) delivered per formulation under the project

Formulations	2007	2008	2009	2010	2011	2012	Total
ABC 300mg	54.78	78.66	334.17	406.61	140.33	66.33	**1,080.88**
ATV 300mg	-	-	-	53.70	170.84	-	**224.54**
ATV/R 300/100mg	-	-	-	-	65.00	38.03	**103.03**
ddI 250mg	32.69	50.30	72.90	112.29	29.08	9.46	**306.72**
ddI 400mg	33.33	54.27	68.89	76.47	16.26	16.39	**265.62**
LPV/R 200/50mg	189.77	356.45	739.57	1,158.66	592.51	96.61	**3,133.57**
Ritonavir 100mg tab (hs)	-	-	-	29.47	102.30	-	**131.77**
TDF/ FTC 300/200mg	279.71	976.09	591.93	518.90	83.33	3.51	**2,453.46**
TDF/ 3TC 300/300mg	27.06	297.62	807.93	771.23	788.81	85.43	**2,778.08**
TDF 300mg	87.22	194.69	352.10	55.34	18.22	0.72	**708.29**
AZT 300mg	-	-	16.90	-	-	-	**16.90**
Total	**704.57**	**2,008.08**	**2,984.38**	**3,182.67**	**2,006.67**	**316.49**	**11,202.85**

Source: CHAI order tracker

Annex 6 Clinton Health Access Initiative — Antiretroviral (ARV) Ceiling Price List, 2012

ADULT PRODUCTS		2012 CEILING PRICE (USD)			SUPPLIER							
Name and strength	Packaging	Per Year	Per pack	Per unit	Aurobindo	Cipla	Emcure	Hetero	MacLeods	Matrix	Ranbaxy	Micro
3TC (150mg)	HDPE bottle 60 tablets	$31	$2.6	$0.04	✓[2]	✓[1]		✓[1,2]	✓[1,2]	✓[1,2]	✓[1]	✓[3]
ABC (300mg)	HDPE bottle 60 tablets	$186	$15.5	$0.26	✓[2]					✓[1,2]		
AZT (300mg)	HDPE bottle 60 tablets	$89	$7.4	$0.12	✓[2]	✓[1,2]		✓[1,2]		✓[1,2]	✓[1]	✓[1]
AZT (300mg) + 3TC (150mg)	HDPE bottle 60 tablets	$105	$8.8	$0.15	✓[2]	✓[1,2]	✓[2]	✓[1,2]	✓[1,2]	✓[1,2]	✓[1]	✓[1]
AZT (300mg) + 3TC (150mg) + NVP (200mg	HDPE bottle 60 tablets	$134	$11.2	$0.19	✓[2]	✓[1,2]		✓[1,2]		✓[1,2]	✓[1]	
ATV (300mg)	HDPE bottle 30 capsules	$265	$22.1	$0.74			✓[2]			✓[1,2]		
d4T (30mg)	HDPE bottle 60 capsules	$24	$2.0	$0.03	✓[2]				✓[1]		✓[1]	
d4T (30mg) + 3TC (150mg)	HDPE bottle 60 tablets	$45	$3.8	$0.06		✓[1,2]		✓[2]	✓[2]		✓[1]	
d4T (30mg) + 3TC (150mg) + NVP (200mg)	HDPE bottle 60 tablets	$79	$6.6	$0.11		✓[1,2]	✓[2]	✓[1,2]	✓[2]		✓[1]	
EFV (600mg)	HDPE bottle 30 tablets	$55	$4.6	$0.15	✓[2]		✓[2]			✓[1,2]	✓[1]	
LPV/r (200/50mg)	HDPE bottle 120 tablets	$378	$31.5	$0.26	✓[2]					✓[1,2]		
NVP (200mg)	HDPE bottle 60 tablets	$36	$3.0	$0.05	✓[2]		✓[2]	✓[1,2]	✓[1,2]	✓[1,2]	✓[1]	
RTV (100mg) heat stable *	HDPE bottle 30 tablets	$90	$7.5	$0.25						✓[1,2]		
TDF (300mg)	HDPE bottle 30 tablets	$58	$4.8	$0.16	✓[2]			✓[2]		✓[1,2]	✓[1]	
TDF + 3TC (300/300mg) *	HDPE bottle 30 tablets	$70	$5.8	$0.19	✓[2]			✓[1,2]		✓[1,2]		
TDF + FTC (300/200mg)	HDPE bottle 30 tablets	$97	$8.1	$0.27	✓[2]			✓[2]		✓[1,2]		
TDF + 3TC + EFV (300/300/600 mg)	HDPE bottle 30 tablets	$159	$13.3	$0.44						✓[1,2]		
TDF + FTC + EFV (300/200/600 mg)	HDPE bottle 30 tablets	$183	$15.3	$0.51						✓[1,2]		
ATV (300mg) /RTV 100mg	HDPE bottle 30 tablets	$276	$23.0	$0.77						✓[1,2]		
ATV (300mg) /RTV 100mg + TDF /3TC (300/300mg)	2 HDPE bottle 30 tablets each of ATV/RTV + TDF/3TC	$346	$28.8	$0.96						✓[1,2]		

The Clinton Health Access Initiative (CHAI) supports national governments to expand high-quality care and treatment to people living with HIV/AIDS. CHAI offers reduced prices for antiretrovirals (ARVs) to members of its Procurement Consortium.

SUPPLIERS & PRODUCTS

CHAI has agreements with eight manufacturers of ARV formulations, active pharmaceutical ingredients and/or pharmaceutical intermediates: Aurobindo Pharma, Cipla Ltd., Emcure Pharmaceuticals, Hetero Drugs, Micro Labs, Matrix Laboratories, Ranbaxy Laboratories and Strides Arcolabs. The ARVs included in CHAI's pricing agreements are: abacavir (ABC), atazanavir (ATV), efavirenz (EFV), emtricitabine (FTC), lamivudine (3TC), lopinavir/ritonavir (LPV/r), nevirapine (NVP), ritonavir (RTV), stavudine (d4T), tenofovir (TDF) and zidovudine (AZT).

TERMS & CONDITIONS

Prices listed below are available to countries participating in the CHAI Procurement Consortium, which currently includes over 70 nations. These prices apply to procurements by national governments that are members of the CHAI Procurement Consortium, or organizations procuring on behalf of member governments, to support public care and treatment programs. Products should be purchased directly from partner suppliers or through procurement agents representing the aforementioned programs. Please contact Carolyn Amole at camole@clintonhealthaccess.org with any questions regarding eligibility to access these prices. For TDF products offered by suppliers under a voluntary license from Gilead, indicated pricing is available only to countries covered under the voluntary license. Please contact Sunil Panicker at spanicker@clintonhealthaccess.org with any questions related to this issue. Access to CHAI prices assumes prompt payment following the shipment of orders. Purchasers issuing requests for price quotes and/or tenders to which CHAI partner suppliers are invited to respond should reference membership in the CHAI Procurement Consortium, but requests and tenders need not be restricted to CHAI partner suppliers.

PRICES

CHAI ceiling prices represent the maximum levels at which indicated suppliers may price their products when selling or communicating price quotes to members of the CHAI Procurement Consortium. CHAI notes that there may be, in several cases, opportunities to obtain lower prices as a result of higher volumes, greater competition, and other market factors. We encourage consortium members to seek and take advantage of such opportunities and to base treatment decisions on observed market prices, with ceiling prices indicating the upper bounds of treatment costs. Prices listed below are FCA Airport from the point of export. Annual treatment costs for pediatric formulations are determined based on the recommended daily dosing for a 10 kg child (unless a formulation is not recommended for a 10kg child, in which case the annual price is calculated based on dosing for an applicable weight band).

QUALITY

CHAI is committed to the sustainable supply of high-quality ARVs, consistent with the specifications of dossiers approved by the World Health Organization (WHO), U.S. Food and Drug Administration (U.S. FDA), or a stringent regulatory authority (SRA) as defined by the International Conference on Harmonization (ICH). In the list below, footnotes specify the applicable quality assurance status for each formulation: (1) Approved by the WHO Prequalification Programme; (2) Approved by the U.S. FDA or other SRA; (3) Submitted to the WHO, U.S. FDA or other SRA for review and recommended for procurement by Expert Review Panel (ERP) of The Global Fund; (4) Submitted to the WHO, U.S. FDA or other SRA for review but not yet recommended by ERP.

Source: Clinton Health Access Initiative, Antiretroviral ceiling price list

Annex 7 Average price (USD) per product pack procured under the project

Formulations	2007	2008	2009	2010	2011	2012
ABC 300mg	30.07	26.61	20.76	16.90	15.09	13.00
ATV 300mg				20.55	21.06	
ATV/R 300/100mg					25.00	22.50
ddI 250mg	18.19	17.55	15.24	14.53	13.00	13.00
ddI 400mg	23.32	23.43	21.94	21.23	20.00	20.00
LPV/R 200/50mg	47.69	46.24	38.90	35.85	32.52	29.34
Ritonavir 100mg tab (hs)				9.24	9.07	
TDF/ FTC 300/200mg	22.83	21.21	16.08	12.06	9.79	7.20
TDF/ 3TC 300/300mg	16.21	14.59	11.13	9.08	8.07	5.33
TDF 300mg	14.61	13.82	12.22	7.12	6.26	4.74
AZT 300mg			8.45			

Source: CHAI order tracker

Annex 8 Summary of the project's achievements from the midterm review by Swiss Tropical and Public Health Institute

Action	Indicator	Target	Achievement	Comments
Identify beneficiary countries for the project in line with UNITAID's eligibility criteria	Percent of total budget allocated to LICs, LMICs, UMICs	At least 85 % disbursed to LICs; <10 % disbursed to LMICs; < 5 % disbursed to UMICs by Q4 of the previous year	Target is met in 2008 and 2009 but not in 2007 and 2010	In 2010, the decrease in LMICs may be the result of the transition. UNITAID has endorsed the list of beneficiary countries and hence was aware that the 2010 country list did not meet eligibility criteria. There is no information in CHAI Annual Reports on whether patients belong to 'vulnerable groups' as defined by UNAIDS
Sign amendments to MoUs containing updated annexes for ARVs to be supplied	Percent of beneficiary countries with signed amendments and updated annexes with ARVs to be supplied	100% of beneficiary countries have signed amendments and updated annexes with ARVs to be supplied in each year by Q4 of the previous year	The target was not met in 2009 and 2010 (less than 70 % of participating countries signed an MoU) but was substantially met in 2007-2008 (96 % of participating countries signed an MoU)	The main reasons quoted by CHAI to justify the absence of signed MoUs are political and administrative challenges
Engage in forecasting with countries for the purposes of estimating purchases of ARVs and the number of people to be treated (to be provided in September of each year)	Forecast of estimated quantity of ARVs, and estimated number of patients to be treated	Forecast of estimated quantity of ARVs and estimated number of patients to be treated to be provided by September	Forecasting and budget were prepared each year but the evaluators lacked information to assess the timelines of CHAI's submission to UNITAID	Quality of the forecasting (for both required budget and patients to be treated per country) is questionable
	Forecast of estimated patients to be treated with ARVs purchased	Annual consolidated targets for patients to be treated with first-line and second-line	Consolidated annual targets were substantially met between 2008 and 2010 (90 % for second-line and 100 % for first-line)	Although consolidated targets were met, the level of achievement of the individual target per country varies significantly
Identify potential suppliers and prices to be paid for	Number of suppliers in each product area where possible	At least 3 suppliers available for 4 of the existing products	For the four existing second-line ARVs (ABC, LPV/r, ddI	

products in each year			250mg and 400mg) there were at least three available suppliers from 2007 onwards Target was met	
	CHAI pays the lowest price for products in each product category	Price reductions in median price (US$) paid for ARVs procured every year achieved	Comparison of the applicable prices from 2007 to 2010 shows a decrease in all treatment prices	CHAI paid the lowest prices compared to MSF and WHO GPRM, however countries under the CHAI consortium appear to have benefited from lower ceiling prices
Enter into contractual arrangement with suppliers for the supply of ARVs based on the outcome of the application selection and price negotiation process for the product	Percent of suppliers that have signed MSAs or other long-term agreements	100% of the annual Master Supply agreements or other long-term agreements concluded by CHAI and suppliers by Q3, as applicable per product type	CHAI signed an MSA/LTA with primary and secondary suppliers or purchased ARVs under Access prices. CHAI did not sign an LTA/MSA with pool suppliers	
Determine the suppliers to be used for each purchase order (Monitoring of supplier performance)	Decrease lead time from purchase order to delivery in country	Average lead time no greater than 12 weeks for each supplier in each product area by Q4 of each year	2007 lead time per supplier was below or around 12 weeks. Based on the information available for the years 2008 and 2010, the evaluators note that lead time per supplier has generally increased, and for some suppliers, exceeded the 12-week target. Between 2007 and 2010, lead time per country was above 12 weeks for the majority of countries	Most delays are attributable to suppliers, and result from technical problems. Other causes of extended lead times are CHAI's re-allocation of shipments to other countries (deemed necessary to avoid a stock out) and, in a few cases, caused by delays in getting documentation (registration, pre shipment testing or waiver)
	Number of suppliers that have had products registered or applied for waivers during 2010, including those still supplying product based upon previous waiver(s)	Increased number of registrations per drug in beneficiary countries	This target is deemed achieved for the 2007-2008 period. However, achievement of this target could not be measured for 2009 and 2010. Moreover, the evaluators did not have	More information is required to assess CHAI's actual contribution to the achievement of this target

			information on the number of cases where CHAI had to request a registration waiver	
Work towards improving the market for UNITAID-funded commodities to support UNITAID's mission of lowering prices and broadening the supplier base	Number of pre-qualified ARV formulations available each year	Complete dossiers submitted to WHO Prequalification Programme (or SRA) for at least 2 ARV formulations (new formulations or products from new manufacturers) by Q4 of each year	This target was achieved in 2008, 2009 and 2010, with an additional 6, 9 and 10 newly approved suppliers by SRA	More information is required to assess CHAI's actual contribution to the achievement of this target
Submission of Order Requisitions by Country Teams to Central Project Managers on a quarterly basis	Percent of orders (per product area) placed through pooled procurement	80 % (in 2008 MoU) or 100 % (in 2009 and 2010 MoU) of all orders placed through the application of pooled procurement each year unless there is a significant impact on the delivery schedule	This target was not fully achieved but in 2008, 2009 and 2010, more than 74 % of orders were pooled	Procurement pooling does not have an effect on drug prices but rather on lead time. Pooling orders allows CHAI to reach the minimum volume/threshold of product above which suppliers agree to start production
Placement of purchase orders for and delivery of products	Percent of value of ARV packs ordered and delivered to each country that match the value of ARV packs budgeted	100% of budgeted products are delivered, allowing for a 15% deviation per country budget allocation	This target has not been achieved. Less than 25 % of countries in 2008 and 2009 have had their commitments matching their budget +/- 15 %. This percentage went up to 40 % in 2010	Weak forecasting, compounded by imponderable factors and CHAI flexibility (gap filling) in the use of UNITAID-funded second-line ARVs, has negatively impacted the budget per country, although the overall budget has not been affected
Facilitate improvements in in-country distribution systems for ARVs	Project support provided where needed to increase the timely delivery of products to ports of entry or a designated central medical store	Relevant processes in place for in-country distribution support by Q4 2010	N/A	Activities not implemented