

UNITAID

STRATEGY 2013-2016



© World Health Organization

(Acting as the host Organization for the Secretariat of UNITAID) The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

The Photographs used in this report are from UNITAID own stock.

UNITAID

STRATEGY 2013-2016



TABLE OF CONTENT

1	Acronyms	6
2	Executive Summary	9
3	Introduction	21
	3.1 Background	22
	3.2 Context of the new Strategy	22
	3.3 Five-Year Evaluation	23
4	Mission, Scope, and Guiding Principles	25
	4.1 UNITAID's Mission	26
	4.2 Scope	27
	4.3 Guiding Principles	27
	4.4 UNITAID in the Value Chain	28
	4.5 Time-limited Funding	30
5	Strategic Approach	31
	5.1 UNITAID Market Effects Framework for Public Health	32
	5.2 UNITAID Process to Identify, Develop, and Implement Interventions	33
	5.3 Innovative Leverage Opportunity: Innovative Grants Mechanism	37
6	Strategic Objectives	39
	6.1 Strategic Objective 1: Increase access to simple, point-of-care diagnostics for HIV/AIDS, TB, and malaria	44
	6.1.1 HIV/AIDS diagnostics	44
	6.1.2 Tuberculosis diagnostics	47
	6.1.3 Malaria diagnostics	49
	6.2 Strategic Objective 2: Increase access to affordable, adapted paediatric medicines to treat HIV/AIDS, tuberculosis, and malaria	52
	6.2.1 Paediatric HIV/AIDS medicines	52
	6.2.2 Paediatric tuberculosis medicines	55
	6.2.3 Paediatric malaria medicines	57
	6.3 Strategic Objective 3: Increase access to emerging medicines and/or regimens as well as new formulations, dosage forms, or strengths of existing medicines that will improve treatment of HIV/AIDS and coinfections such as viral hepatitis	60
	6.3.1 HIV/AIDS medicines	60
	6.3.2 HIV co-infections medicines	63
	6.4 Strategic Objective 4: Increase access to artemisinin-based combination therapies (ACTs) and emerging medicines, that, in combination with appropriate diagnostic testing, will improve the treatment of malaria	66
	6.4.1 Malaria medicines	66

6.5	Strategic Objective 5: Secure supply of second-line tuberculosis medicines, and increase access to emerging medicines and regimens that will improve treatment of both drug-sensitive and multi drug-resistant TB	69
6.6	Strategic Objective 6: Increase access to products for the prevention of HIV, TB, and malaria	72
	6.6.1 Preventives HIV/AIDS	72
	6.6.2 Preventives malaria	75
	6.6.3 Preventives tuberculosis	78
7	Core Action Areas	79
7.1	Core action area 1: Market intelligence gathering and analysis	80
7.2	Core action area 2: Portfolio and grant management	81
7.3	Core action area 3: Resource mobilization and fundraising	82
7.4	Core action area 4: Strong relationships with global partners, countries, and civil society	83
7.5	Core action area 5: Secretariat management and Governance	85
	7.5.1 Strengthen organizational management at UNITAID to ensure timely and effective delivery of intended results.	85
	7.5.2 Cohesive and effective governance practices	87
8	Planning and Management for Success	89
8.1	Measurement of success	90
8.2	Implementation of the Strategy	92
	8.2.1 UNITAID funding projection	92
	8.2.2 Articulation of implementation plan	92
8.3	Measuring Strategy implementation	92
9	Annexes	93
9.1	Annex 1: UNITAID Transition and Sustainability Framework	94
9.2	Annex 2: UNITAID Proposal Evaluation and Selection Criteria	97
9.3	Annex 3: UNITAID funding projection detail	99

1 ACRONYMS

A2S2	Assured Artemisinin Supply System
ACT	Artemisinin-based combination therapy
AIDS	Acquired Immune Deficiency Syndrome
AMFm	Affordable Medicines Facility for Malaria
ANDI	The African Network for Drugs and Diagnostics Innovation
ANRS	Agence Nationale de Recherche sur la SIDA et les Hepatites Virales
ART	Antiretroviral therapy/treatment
ARV	Antiretroviral drug
API	Active Pharmaceutical Ingredient
CDC	Centers for Disease Control and Prevention (United States America)
CHAI	Clinton Health Access Initiative (formerly Clinton Foundation HIV/AIDS Initiative)
DBS	Dried blood spot
DAA_s	Direct-acting antivirals
DFID	Department for International Development (United Kingdom)
DNDi	Drugs for Neglected Diseases Initiative
DOT	Directly Observed Therapy
DS TB	Drug sensitive tuberculosis
EID	Early Infant Diagnosis
EMA	European Medicines Agency
EML	Essential Medicines List
ESTHER	Ensemble pour une Solidarité Thérapeutique Hospitalière En Réseau
EB	Executive Board (UNITAID)
FAC	Finance and Accountability Committee (FAC)
FDA	Food and Drugs Administration (United States)
FDC	Fixed -dose -combination
FEI	France Expertise International
FIND	Foundation for Innovative New Diagnostics
GDF	Global Drug Facility (Stop TB Partnership)
Global Fund (GF)	Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund)
GLC	Green Light Committee
GLI	Global Laboratory Initiative
GMP	Good Manufacturing Practice
GWG	Governance Working Group (UNITAID)

HAART	Highly Active Antiretroviral Therapy
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IP	Intellectual property
IPT	Intermittent Preventive Treatment (for prevention of malaria in pregnant women and their infants)
IRS	Indoor residual spraying (of insecticides)
KPI	Key performance indicators
LIC	Low income country (World Bank classification)
LLIN	Long-lasting insecticide treated bed net
LMIC	Lower middle income country (World Bank classification)
LOI	Letter of intent
LSHTM	London School of Hygiene and Tropical Medicine
M&E	Monitoring and Evaluation
MDGs	Millennium Development Goals
MDR TB	Multi drug-resistant tuberculosis
MOU	Memorandum of understanding
MMV	Medicines for Malaria Venture
MPP	Medicines Patent Pool
MSF	Médecins Sans Frontières/ Doctors without Borders
MSM	Men who have sex with men
MTCT	Mother to Child Transmission (of HIV)
NCD	Non-communicable disease
NGO	Non-governmental organisation
OI	Opportunistic infection
OPP	Open Polyvalent Platforms
PATH	Program for Appropriate Technology in Health
PCR	Polymerase Chain Reaction
PDP	Product Development Partnership
PEPFAR	US President's Emergency Plan for AIDS Relief
PFSCM	Partnership for Supply Chain Management
PITC	Provider Initiated Testing and Counselling
PLHIV	People living with HIV
PLWHA	People living with HIV/AIDS

PMTCT	Prevention of Mother to Child Transmission of HIV
POC	Point-of-Care
POCT	Point-of-Care Testing
PQ	Pre-qualification
PQP	Pre-qualification program
PRC	Proposal Review Committee of the UNITAID Executive Board
PrEP	Pre-exposure prophylaxis
PSC	Policy and Strategy Committee of the UNITAID Executive Board
PSI	Population Services International
QA	Quality Assurance
QC	Quality Control
R&D	Research and Development
RBM	Roll Back Malaria
RDT	Rapid diagnostic test
RFP	Request for Proposal
RUTF	Ready to Use Therapeutic Food
SCMS	Supply Chain Management System
SRA	Stringent Regulatory Authority
STB	Stop TB Partnership
TB	Tuberculosis
TDR	Special Programme for Research and Training in Tropical Diseases
TPP	Target Product Profile
TRIPS	World Trade Organization Agreement on Trade Related Aspects of Intellectual Property Rights
UMIC	Upper middle income country (World Bank classification)
UNICEF	United Nations Children's Fund
VCP	Vector control and prevention
VCT	Voluntary counselling and testing
VL	Viral load
VPP	Voluntary Pooled Procurement
WHO	World Health Organization
WTO	World Trade Organization
XDR TB	Extensively drug-resistant tuberculosis

EXECUTIVE SUMMARY



2 EXECUTIVE SUMMARY

With this new Strategy 2013-2016, UNITAID enters what could be called the third stage of its development.

The Strategy refines the proven business model of UNITAID

From 2006 to 2009, UNITAID operated mainly as a large scale, procurement group, with the goal of correcting major shortcomings in the markets for drugs and preventive products for HIV, tuberculosis (TB) and malaria. Several major successful initiatives were implemented during this period, notably in the area of paediatric antiretroviral drugs (ARVs), second line ARV drugs for adult HIV infection, long-lasting insecticide-treated bed nets (LLINs) and access to drugs for multi-drug resistant tuberculosis (MDR-TB). During 2006-2009, the Executive Board decided that UNITAID should address market shortcomings through a wide range of actions, rather than only by procuring products. Market transformations lead to long-term improvements that better serve populations of developing countries by encouraging new producers to enter the market, stimulating competition, increasing transparency, improving the quality of medicines and diagnostics, and sustaining these changes. Market-based interventions became the unique feature of UNITAID during the first stage of its development.

During its second strategic phase, from 2010 to 2012, UNITAID built its capacity to describe and analyse the markets for drugs and diagnostic tests for the three diseases, so that it could identify opportunities for market-based intervention at an early stage, focus its efforts, and ensure that UNITAID operations are cost effective. A new proposal review process was set in place, leading to better targeting of projects and improved market impact. A stronger emphasis was placed on innovation and support for the market entry of promising new products. Thanks to this evolving approach, UNITAID entered the field of diagnostic tests for the three diseases, notably at the point-of-care (POC). It also played a major role in increasing access to artemisinin-based combination therapies for malaria, and to drugs for the treatment of MDR TB and paediatric ARVs. The establishment of a market dynamics unit has led to stronger cooperation with other actors in the public health scene and established its reputation as a provider of market intelligence.

In 2012, an independent Five-Year evaluation of UNITAID was conducted, which endorsed the business model of the organization; commended its achievements; and made recommendations for future activities. These recommendations have been incorporated in the 2013-2016 Strategy.

UNITAID is now equipped to analyse market opportunities; define the mechanisms of market interventions; and support selected activities that can have the most significant effect in terms of improving access to key healthcare products for vulnerable populations. Mechanisms for inviting and evaluating proposals have been refined; procedures to finalize grant agreements have been accelerated and streamlined. Market analyses now allow UNITAID to set precise objectives and announce specific goals for its market transformation activities. The current Strategy places great emphasis on innovation, strategic partnerships, performance measurement and value added. The Strategy outlines priorities to improve management of UNITAID operations and the mobilization of resources. The goal is to make UNITAID a reference point for market intelligence, and optimize its ability to implement market-based approaches to improve public health.

Transition from one stage to another has taken place smoothly and seamlessly. Many of the strategic priorities identified for the coming years are already being addressed through grants that were approved in 2012 and this third phase represents an evolution of the successful business model of UNITAID.

The Strategy is based on a clear mission and strict principles

UNITAID's mission has remained constant over the years. It increases access to treatment for HIV/AIDS, TB and malaria for people in developing countries by leveraging price reductions of quality drugs and diagnostics, which currently are unaffordable for most developing countries, and to accelerate the pace at which they are made available.

UNITAID will remain focussed on product markets for the diagnosis and treatment of HIV, TB and malaria, as well as prevention commodities, co-morbidities and co-infections significant to these three diseases. The aim of its interventions is to substantially improve public health outcomes in developing countries. Interventions financed by UNITAID will combine the best market and public health outcomes, and adhere to its guiding principles: innovation, value for money, equity, sustainability, flexibility and transparency. In addition, it will increase and leverage its partnerships, and continue to take a strong 'pro-public-health' approach to intellectual property.

Diverse and result-oriented implementers perform UNITAID's market interventions: they receive time-limited grants to catalyse changes in markets and maximize the public health effects of these projects. The evolution of UNITAID's business model will include the possibility of supporting late stages of product development wherever these activities will have a major impact. UNITAID will also establish a mechanism to provide one-off innovative grants to support the incubation of upstream innovative ideas and initiatives.

The Strategy outlines sound objectives for markets and public health

The purpose of UNITAID is to contribute to the achievement of global long-term goals for HIV, tuberculosis and malaria through its interventions in product markets. These goals have determined the Strategic Objectives described in this Strategy for the coming four years and are shared by the international community at large. The Strategic Objectives have also been guided by the market landscapes, which UNITAID regularly publishes and updates twice a year, and which identify opportunities for market interventions. The Objectives have been divided into three categories: active (UNITAID already supports interventions that will continue throughout the period of the Strategy), potential (clearly identified by the landscapes but not yet considered for funding) and exploratory (identified by experts and stakeholders but not yet vetted through landscape analysis).

STRATEGIC OBJECTIVE 1:

Increase access to simple, POC diagnostics for HIV/AIDS, TB and malaria.

The expected market impact in HIV is to reach 80% coverage for CD4 tests and 50% coverage for viral load and early infant diagnosis; introduce several competing TB diagnostic tests into the market to improve affordable access at the point of care; reach 60% availability of malaria rapid diagnostic tests of assured quality in the private sector and 80% in the public sector of malaria endemic countries. (Estimated impact in countries where UNITAID supports interventions on diagnostics.)

UNITAID'S STRATEGIC OBJECTIVES

1

Simple, point-of care (POC) diagnostics

2

Affordable, adapted paediatric medicines

3

Treatment of HIV/AIDS and co-infections

To achieve this objective, UNITAID already finances interventions to accelerate access to innovative HIV POC diagnostics and to implement their use in sub-Saharan Africa. UNITAID also supports open polyvalent platforms for HIV viral load testing, price reduction and scale-up of the GeneXpert test for TB, and creation of a private sector market for rapid diagnostic tests (RDTs) for malaria, including improved quality monitoring and control of these RDTs. In addition, cross-cutting mechanisms are being implemented via UNITAID funding to improve quality assurance and to harmonize evaluation protocols for diagnostic tests for the three diseases.

Additional interventions will be considered during the 2013-2016 period to expedite market entry of game-changing tests, and to support tests that address specific issues, such as resistance to antiretrovirals in HIV, extrapulmonary TB diagnosis, rapid diagnosis of malaria for asymptomatic pregnant women and for patients infected with *P. vivax*, as well as tests adapted for children. Interventions that can harmonize policies and the regulation of diagnostic products, secure demand for them and reduce their price will also be considered.

STRATEGIC OBJECTIVE 2:

Increase access to affordable, paediatric medicines to treat HIV/AIDS, TB and malaria.

The expected impact is to decrease the price of HIV medicines by at least 20% and to introduce better products; to ensure that coverage of paediatric TB therapy reaches 80%; and prequalified rectal artesunate becomes available for the emergency treatment of malaria in small children to reduce mortality among this age group.

UNITAID already finances interventions that have transformed the market for paediatric treatment of HIV and TB. Grants supporting the development of paediatric formulations including HIV protease inhibitors, the development of appropriate medicines for TB in children and the development of rectal artesunate are currently being implemented.

4

Treatment of
malaria
(ACT)

5

Treatment of
second-line TB

6

Preventatives
for HIV/AIDS, TB
and malaria

Over the Strategy period, other interventions will be identified to consolidate and satisfy demand for paediatric antiretroviral treatment, accelerate market entry of new paediatric drugs for the three diseases, support price reduction of paediatric products and accelerate their registration for widespread use.

STRATEGIC OBJECTIVE 3:

Increase access to emerging medicines and/or regimens as well as new formulations, dosage forms, or strengths of existing medicines that will improve the treatment of HIV/AIDS and co-infections such as viral hepatitis.

The expected outcome is to increase access to medicines for HIV to significantly reduce the price of second line regimens because a growing proportion of patients will require these products; support first-line regimens that can be implemented at community level with decreased overall costs to the health system; and explore the issue of treatment for co-infections, notably viral hepatitis, a major cause of mortality after TB among people living with HIV.

UNITAID already supports projects that aim to decrease the uncertainties linked with the supply of active pharmaceutical ingredients (API) for ARVs, and increasing access to patented innovative products, in particular through the Medicines Patent Pool.

Over the next four years, other interventions will be designed to secure the market and decrease the price of APIs and second-line drugs, and to support market entry of new products and regimens that include better and more cost effective ARVs. In addition, UNITAID will landscape the market of drugs and diagnostics for hepatitis to gain a better understanding of specific challenges related to HIV/hepatitis C (HCV) co-infection in resource-limited settings.

STRATEGIC OBJECTIVE 4:

Increase access to artemisinin-based combination therapies (ACTs) and emerging medicines, which, in combination with appropriate diagnostic testing, will improve the treatment of malaria.

The expected outcome is to contribute to a significant decrease in malaria mortality, notably among infants and children, and to improve the outcome of severe malaria.

UNITAID has already been highly active in this field by being the main funding organization for the AMFm (Affordable Medicines Facility for malaria) and has provided grants to better understand the forecast of ACT demand, the API situation for malaria drugs and to introduce injectable artesunate into the market, as an alternative to quinine for the treatment of severe malaria.

Over the Strategy period, UNITAID will support the market entry of new antimalarials, potentially including for *P. vivax* infections. UNITAID will also support interventions to combine access to rapid diagnostic tests and malaria drugs within the context of integrated management of fever.

STRATEGY OBJECTIVE 5:

Secure supply of second-line tuberculosis medicines, and increase access to emerging medicines and regimens that will improve treatment of both drug-sensitive and MDR TB.

The expected outcome is to stabilize markets to sustain access to safer, simpler, shorter, and more affordable treatment regimens, with particular emphasis on multidrug-resistant and HIV-associated TB. Targets include reduced treatment duration to approximately 4 months for drug sensitive TB and to 9 months for MDR TB; and substantially reduced cost of quality-assured MDR TB treatment of MDR infections, which would lead to more patients accessing treatment.

UNITAID is already active in this field, with on-going grants aiming at gaining better knowledge of the API market for TB drugs and the acceleration of access to MDR TB drugs, notably to avoid stock-outs.

Over the Strategy period, UNITAID aims to develop interventions to improve market intelligence in relation to demand forecasting for TB drugs and their APIs; to facilitate the market entry of new TB drugs approved by the World Health Organisation (WHO); and to harmonize quality standards for MDR TB drugs.

STRATEGY OBJECTIVE 6:

Increase access to products for the prevention of HIV, TB, and malaria, notably to improve the availability of devices for male circumcision and of microbicides, once they are approved; and to increase access to vector control tools to prevent malaria transmission.

UNITAID has supported the market entry of LLINs. This intervention is now completed. It helped create a market that was subsequently supported by Global Fund grants, enabling good coverage of nets in malaria endemic areas.

Over the Strategy period, UNITAID will consider supporting increased access to male circumcision technology and microbicides, once they are available and have been approved for use. Interventions will be explored to support market availability of better and sturdier nets, including the use of new insecticides or combinations of insecticides to address vector resistance; and to make effective and safe medicines available for malaria prophylaxis among pregnant women, infants and children.

The Strategic Objectives are expected to remain constant over the duration of the Strategy period. However, opportunities for each type of product, possibilities for interventions, selection of potential targets will evolve with time, and will also be monitored in relation to epidemiological and disease burden data. Potential and exploratory interventions will be updated regularly and presented to the Board at least once a year.

Strategic objectives will be reached through proven approaches

To achieve the Strategic Objectives, UNITAID works through market interventions that improve access to products for vulnerable populations. To achieve market impact, UNITAID describes and quantifies the access issue and the public health problem that need to be addressed; identifies the market dynamics that contribute to this access problem; provides grants to implementers to carry out market interventions; measures the market impact of the intervention and estimates the extent to which the intervention has improved public health.

The approach includes four phases:

LANDSCAPE ANALYSES AND VETTING

The UNITAID Secretariat compiles research and analyses to publish and regularly update market landscapes for products that are used in the diagnosis, prevention and treatment of the three diseases. These landscapes are discussed in market fora that involve a broad consultation of stakeholders. These consultations allow UNITAID to identify areas where market-based interventions could have considerable public health and market impact. Strategic and practical considerations allow UNITAID to identify the topics that can become the basis of calls for proposals.

PROPOSAL DEVELOPMENT AND TECHNICAL EVALUATION

Based on a review by the Board of potential interventions, UNITAID will issue directed calls for proposals that best correspond to the Strategic Objectives. One open call will also be issued annually to receive proposals that may not correspond to topics identified in the landscape analyses. Proponents send letters of intent, which are reviewed in detail by the UNITAID Secretariat and evaluated against rigorous selection criteria. A limited number of proponents are invited to develop full proposals.

PROPOSAL SELECTION AND PROJECT INITIATION

Proposals deemed suitable, technically sound and feasible by the Proposal Review Committee are recommended to the Executive Board, which makes funding decisions. Approved proposals enter a time-limited process of planning, review of procurement and financial components, review of sustainability and refinement of implementation procedures by the UNITAID Secretariat, and are then formally initiated.

GRANT MANAGEMENT, MONITORING AND EVALUATION OF PERFORMANCE AND IMPACT ASSESSMENT

The success of UNITAID interventions depends on a clear planning process, close monitoring and a strong relationship between UNITAID and its implementers. UNITAID requires annual and semi-annual project reports, through which it monitors grant performance. All grants are externally evaluated at mid-way through the project and at the end of the project. UNITAID summarises its grant and organizational performance annually using a set of Board-identified Key Performance Indicators.

The successful implementation of the Strategy requires a strong and efficient Secretariat

UNITAID's effectiveness depends on the right set of core action areas, carried out to the highest degree of excellence. For the coming four years, five specific areas will contribute most directly to the fulfilment of UNITAID's mission.

MARKET INTELLIGENCE GATHERING AND ANALYSIS

UNITAID will establish a market intelligence system to provide comprehensive and timely information on product markets; identify opportunities from the analysis of landscapes; expand the capacity to analyse information; and share market information and insights internally and with other actors of the international public health scene.

PORTFOLIO AND GRANT MANAGEMENT

Success in reaching the Strategic Objectives will depend on the capacity to manage the process from the call for proposals to the completion of projects. UNITAID is refining its standard operating procedures for grant management. It will monitor the quality of this process through the level of response to calls for proposals, the quality of letters of intent and proposals, the capacity of the Secretariat to recruit new implementers and to reduce the lead time from Board approval to project implementation to less than 120 days.

RESOURCE MOBILIZATION AND FUNDRAISING

UNITAID will work to improve the regularity and predictability of its resource flow and endeavour to broaden its donor base. Securing long-term funding commitments from its current members will remain the main priority for the Secretariat, but it will also seek to attract new donors and increase its funding level, notably through innovative financing mechanisms, budgetary contributions and the development of co-financing. UNITAID recognises the need to maintain and consolidated the current funding level of at least an average of \$300 million per year.

STRONG RELATIONS WITH GLOBAL PARTNERS, COUNTRIES AND CIVIL SOCIETY

Building and maintaining partnerships will be one of the top priorities of UNITAID in the coming four years.

- UNITAID will, in particular, strengthen its collaboration with the Global Fund to maximize the market impact of our initiatives and secure their sustainability, cooperate on strategic developments in market dynamics and accelerate market entry of new products.
- UNITAID will engage with large international public health organizations, notably the WHO, UNAIDS, the Roll Back Malaria Partnership, the Stop TB Partnership, PEPFAR and other global stakeholders to ensure the alignment of our Strategic Objectives with normative guidelines and to accelerate the impact of our initiatives.
- UNITAID will engage with country authorities to encourage national ownership of new products and market conditions, notably through their incorporation into national policies. Implementers are required to develop agreements with country authorities. Communities and civil society

organizations will be encouraged to observe the public health impact of grants at local level. Together with governments, regulatory authorities, implementers and health professionals, they will participate in regional consultative forums that will guide and inform UNITAID.

- UNITAID will actively consult product development partnerships and private product manufacturers to identify candidate products for UNITAID support, agree on the most effective market entry approaches and share experience and information.
- UNITAID will engage with academia to broaden support and identify collaborations to improve the quality of our market dynamics information.

SECRETARIAT MANAGEMENT AND GOVERNANCE

Hosted by the WHO, the Secretariat will adapt its management mechanisms to the new Strategy, maintaining a lean, nimble and highly skilled staff. It will strengthen the effectiveness of its leadership under the Executive Director through a strong senior management team, who are empowered and accountable. It will streamline its work planning and budgeting process, based on results, with clear responsibilities and risk management procedures. The quality of the human resource management will be enhanced to give staff clear opportunities for professional growth and development.

A quality management system will be implemented across the whole organization and an integrated accountability framework will be built on the existing monitoring, evaluation, benchmarking and review processes. Regular reviews will be conducted to assess the implementation of the management and accountability framework, the satisfaction of stakeholders, the satisfaction of staff and effectiveness of work planning, financial planning and grant management.

The effectiveness and cohesion of governance practices will be enhanced. The mechanisms of independent expertise supporting Board deliberations and ensuring technical excellence of decisions on grants will be revised, notably to mobilize a larger pool of experts. Board composition, membership arrangement and accession, as well as the balance of constituencies, will be addressed to better reflect the commitments of donors to UNITAID and to give a role to new donors who join UNITAID.

The proof of the Strategy will be in its implementation

Funding projections show that the Strategy is feasible, but will require a level of steady funding of at least \$300 million each year. With a greater funding envelope, UNITAID could further increase access to commodities, allowing increased availability of products to those who need them most. Additional funding could be invested in projects further upstream (such as the recently approved project to improve paediatric ARV formulations) or downstream (to enhance the delivery of commodities to beneficiaries). During the implementation of the Strategy, UNITAID will consider options for co-funding to leverage its investments.

Continuous assessment of outputs and outcomes from UNITAID grants enables UNITAID to measure its overall achievement; expand its market intelligence; and filter project data, analytics and learning back into its landscape analyses and evaluation of opportunities for market-based interventions. Frequent assessment and sharing of results support continuous quality improvement and strategic redirection of on-going projects as required. Impact estimates will help UNITAID to better understand its influence on public health through its interventions.

By employing findings from all three levels of assessment (outputs, outcomes, impact), UNITAID will continue to work during the Strategic period to develop and implement an approach to measuring value for money that will guide proposal assessment and resource allocation decisions. As the concept is further elaborated and aligned for UNITAID's unique role in global health, key principles will include equity, efficiency, and effectiveness. UNITAID will continue to engage with other global health stakeholders working to establish methodologies and best practices for measuring and quantifying value for money.

The Secretariat will design an implementation plan with key work streams and responsibilities. It will assess the implications of the Strategy in terms of budget; human resources; Secretariat structure and management; and revise the key performance indicators of UNITAID. A mid-term evaluation of the implementation will be conducted in 2015.

The next four years will be challenging and exciting. At the beginning of this new Strategic period, the Secretariat is empowered to achieve significant market and public health impact aligned to its Strategic Objectives.

The UNITAID Strategy 2013-2016 provides an excellent vision that will guide new investments. It identifies the tools needed to implement the Strategy, of which many are already under development, tried and tested. UNITAID remains creative in its approach, and is ready and able to develop new tools or engage in new partnerships that will ensure its objectives are met. UNITAID's innovative source of income will continue to be well invested, and UNITAID will strive to increase its funding capacity through new and existing donors.

UNITAID looks forward to working with you, our partners, donors, countries and implementers, to make available the best treatments, diagnostic and prevention commodities for those in resource-limited-settings who rely on our combined efforts in the fight against the three diseases.

UNITAID MARKET DYNAMICS DASHBOARD

M = Medicines D = Diagnostics P = Preventives	Product Sub-type	Access	Current Market Shortcomings*						Opportunity for Intervention***		
			Availability	Affordability	Quality	Acceptability/ Adaptability	Delivery	Composite severity of all current market shortcomings** (Apr 2013)	Current (Apr 2013)	Over next 4 years	
HIV/AIDS	M	Adult first-line	54%	X	X	--	X	X		Med-High	High
		Adult second-line	~30%	X	XX	--	X	XX		Med	High
		Paediatric	28%	XX	XX	--	XX	XX		High†	High
		Viral hepatitis C co-infection	TBD	X	XX	X	XX	XX		Low	Med
	D	CD4	<60%	X	XX	XX	X	X		Med-High†	Med
		Viral load (VL)	<30%	XX	XX	XX	XX	XX		High†	High
		Early infant diagnosis (EID)	<30%	XX	XX	XX	XX	XX		High†	High
	P	Male circumcision devices	10% of target	X	XX	X	--	XX		Med	Med
		Female condoms	<1%	--	XX	--	XX	XX		Low	Low
		Microbicides	0%	XX	--	--	XX	--		Low	Low
Pre-exposure prophylaxis (PrEP)		<1%	--	--	--	XX	XX		Low	Low	
Tuberculosis	M	Adult first-line	66%	--	--	XX	XX	XX		Low	Med
		Adult second-line	19%	XX	XX	XX	XX	XX		Med†	High
		Paediatric	<50%	XX	X	XX	XX	XX		High†	High
	D	Near-POC or POC	40% TB Dx 19% MDR-TB Dx <5% DST	X	XX	X	XX	X		Med†	High
Malaria	M	Adult	<20% public <10% private	X	XX	XX	X	XX		Med†	High
		Paediatric	<20% public <10% private	X	XX	XX	XX	XX		Med†	High
	D	Rapid diagnostic tests (RDTs)	77% public Minimal private	X	X	XX	X	XX		High†	High
	P	LLINs	21%	XX	X	X	X	XX		Low	Med
		Indoor residual spraying (IRS)	~5%	X	XX	X	X	X		Low	Low

* Market shortcomings are described as minimal/not present (--), moderate (x), or severe (xx).

** The composite severity of all market shortcomings in each sub-niche is assessed as mild , moderate , moderate to severe , or severe .

*** Level of opportunity for UNITAID market intervention, based on practical & strategic considerations defined in UNITAID 2013-2016 Strategy.

† UNITAID has current ongoing projects

The Market Dynamics Dashboard was designed to provide a snapshot of the Secretariat's assessment of current market dynamics and opportunities for intervention across all diseases and product categories. It describes:

- the severity of current market shortcomings for all product types, detailed across UNITAID's five standard shortcomings categories and classified as minimal/not present, moderate, or severe;
- the composite severity of all market shortcomings, assessed as mild, moderate, moderate to severe, or severe; and
- the level of current and future opportunity for UNITAID intervention, based on the practical and strategic considerations defined in the 2013-2016 Strategy (see Strategy section 5.2).

The dashboard distils UNITAID's current assessment of the markets into a single page summary that adds context and rationale for the areas of intervention considered 'ready' (or near-ready) for potential UNITAID support and those that are not (see Section 5.2, Figure 3). This tool will be formatted for presentation on the UNITAID website, and will be updated frequently as market dynamics and opportunities evolve.

INTRODUCTION



3 INTRODUCTION

3.1 Background

UNITAID is an innovative financing mechanism for health that was launched in 2006. It aims to durably increase access to products to treat, diagnose and prevent HIV/AIDS, tuberculosis (TB) and malaria in developing countries. UNITAID does this by raising additional, sustainable financing, and using these funds strategically to support market interventions that address the shortcomings in the global markets for these products. The ultimate aim is to improve the health of people in developing countries. Over the last six years, UNITAID has become a major, and unique, actor in global public health and development.

UNITAID has made a leading contribution to the fight against HIV/AIDS, TB and malaria. It has achieved significant market outcomes¹. For instance, it spurred the development of better-adapted product formulations; lowered the price of several health-related products; increased the number of suppliers in certain markets; raised the number of quality-assured products; improved product lead times and helped avert stock-outs². These market outcomes have, in turn, contributed to major public health improvements³ – in 2011 through UNITAID’s intervention, over 400,000 children received appropriate treatment for HIV/AIDS compared to 30,000 in 2006. Second-line antiretroviral (ARV) treatment costs are currently less than \$500 per patient per year, down from \$1,500 just 3 years ago, mainly due to UNITAID’s interventions. By investing in 20 million high-quality, long-lasting, insecticide-treated nets (LLINs), UNITAID stimulated the market, and now over 700 million people in malaria endemic countries have access to nets. Through UNITAID’s work to increase access to paediatric TB medicines, over 1 million children in 57 countries have received curative and preventive medicines⁴.

3.2 Context of the new Strategy

During the previous Strategy period (2010-2012), UNITAID achieved substantial market and public health improvements. Over the past three years, UNITAID has taken significant steps to enhance its effectiveness, and improve its tools and processes. At the same time, the global health context was evolving rapidly, with major technological breakthroughs; an evolution in the role of other global health actors; and significant pressures in the international funding environment.

For the first time for UNITAID, this Strategy introduces explicit Strategic Objectives that are intended to serve as a clear statement of intent to achieve market and public health effects in key areas; an invitation to partners (including donors, implementers, industry, and country-level actors) to collaborate on specific efforts; and a signal to the market to orient availability, formulation, quality, pricing, and sustainable access to health products for HIV/AIDS and its co-infections, TB, and malaria in developing countries.

1 UNITAID HIV/AIDS factsheet (July 2012); malaria factsheet (September 2012); tuberculosis factsheet (July 2012). <http://www.unitaid.eu/resources/publications/facts>

2 Examples include: Better formulation: paediatric anti-retroviral (ARV) drugs against HIV/AIDS; lowered price: second line ARV drugs (by over 50 percent); increased number of suppliers: multi drug-resistant tuberculosis (MDR TB) drugs (more than tripled); raised number of quality-assured products: artemisinin-based combination therapies (ACTs) against malaria; improved lead times and averted stock-outs: MDR TB drugs.

3 <http://www.unitaid.eu/resources/results>

4 645,000 prophylaxis and 453,000 treatments since the inception of the paediatric TB interventions.

These objectives are derived from global treatment and access goals for the three diseases, UNITAID's mission, and UNITAID's market intelligence and landscape analyses (see Section 6). UNITAID is committed to the need to focus, prioritize and maximize its effectiveness, as well as ensuring that its interventions represent value for money.

3.3 Five-Year Evaluation

In 2012, the UNITAID Executive Board commissioned an independent 'Five-Year Evaluation' to assess UNITAID's performance to date⁵. The goal was to identify the organisation's strengths and to suggest areas for possible improvement. To complement this work, the Secretariat commissioned an independent study of the external landscape, in order to analyse the key trends affecting UNITAID and to evaluate its position in the global health architecture. These reviews confirmed UNITAID's unique and well-established role in this architecture, and emphasized its value add and comparative advantage as an actor focusing specifically on improving health product markets for the benefit of populations in low income countries. They also highlighted the significant market and public health outcomes achieved, and endorsed the soundness of UNITAID's business model, which is to provide grants to international implementers to carry out promising market interventions on UNITAID's behalf.

The Five-Year Evaluation recognized that:

'UNITAID has been doing the right things to contribute to significant positive outcomes in the fight against the three diseases. Over the past five years, UNITAID has established a successful way of doing business. The evaluation finds that over the course of the evaluation period, UNITAID has validated its business model of identifying, selecting and funding market-shaping interventions carried out by implementing partners. [...] It is highly likely that the successful market and health outcomes could only have been achieved by a multilateral agency – indeed, it is hard to imagine that any bilateral agency or private entity could have achieved what UNITAID has achieved in this time frame. Many engaged stakeholders, and a highly dedicated staff, have contributed to this achievement through their devotion to engage in complex problem-solving to get the business model right.'

The Five-Year Evaluation also recognized the improvements that UNITAID has made to its tools and processes. At the same time, the Five-Year Evaluation, taken together with UNITAID's experience and feedback from its stakeholders, pointed to a number of areas where UNITAID can make further progress. UNITAID has considered all 17 of the recommendations put forward by the Five-Year Evaluation in this Strategy document; it has focused on five recommendations.

- The Strategy reaffirms UNITAID's mission and scope, the guiding principles and the areas of intervention along the value chain. (Section 4)
- The Strategy identifies six Strategic Objectives that are derived from UNITAID's mandate under which forward funding priorities for shaping market interventions are identified within high priority public health areas. (Section 6)

⁵ Final report of the Five-Year Evaluation of UNITAID – documents UNITAID/EB17/2012/6.1.1 and 6.1.2.

- The Strategy demonstrates how UNITAID engages key partners around market shaping priorities in order to create new opportunities; this engagement takes a variety of forms to ensure innovation and shared dialogue to the ultimate benefit of UNITAID's projects. (Section 5 and 7)
- The Strategy outlines the tools that UNITAID has developed, and continues to refine, to ensure ultimate project performance, based on market intelligence. UNITAID is strengthening its processes to improve capacity and practices for portfolio management. (Section 7)
- The Strategy commits to further develop tools to measure grant performance, strengthen monitoring and evaluation, and develop a methodology to measure public health outcomes that is adapted to the UNITAID model. (Section 8)

MISSION, SCOPE AND GUIDING PRINCIPLES



4 MISSION, SCOPE, AND GUIDING PRINCIPLES

4.1 UNITAID's Mission

'UNITAID's mission is to contribute to scale-up access to treatment for HIV/AIDS, malaria and tuberculosis (TB) for people in developing countries by leveraging price reductions of quality drugs and diagnostics, which currently are unaffordable for most developing countries, and to accelerate the pace at which they are made available.' (UNITAID Constitution)

Increasing access to quality health products is defined by UNITAID as achieving the following sustainable target market outcomes as a result of the market interventions it supports:

- Affordability of products;
- Assured quality products;
- Availability of sufficient quantities of products where and when they are needed; and
- Introduction of products and formulations adapted to the needs of specific populations.

Ensuring easy access to safe and effective health products to prevent, diagnose and treat HIV/AIDS, TB and malaria is an essential component of the effort to fight these diseases. Access to these products remains a major bottleneck in developing countries, particularly for populations in low income countries.

UNITAID focuses on markets and market-based approaches because access to health products is often inhibited by one or more market shortcomings that can only be corrected with targeted intervention (see Section 5.1). By correcting these shortcomings, UNITAID works to decrease prices, improve quality, and improve acceptability of products, and these positive externalities ensure other countries and purchasers have access to improved, more affordable public health commodities. For example, a 2-to-1 leverage and multiplier effect is achieved if a \$50 million strategic investment in the procurement of improved medicines boosts competition and decreases prices such that non-UNITAID purchasers save \$100 million on the same products for their own programs. Not only do patients benefit immediately from UNITAID's catalytic impact on access, but the investment also allows other donors to purchase better products for less money.

UNITAID is unique among global health organizations in that it focuses exclusively on addressing market shortcomings at the global level as a means to sustainably increase access to health products for people specifically in developing countries. UNITAID's mission, scope and principles – detailed in this section – provide the highest-level information about the organization's focus and how it functions. These are the essential and natural starting points for the Strategy.

4.2 Scope

Disease focus: UNITAID focuses on HIV/AIDS, TB and malaria. UNITAID also considers supporting access to products that address the co-morbidities of these diseases when there is a demonstrable impact of a specific co-morbidity on the severity and rates of mortality associated with one of the three diseases.

Product focus: UNITAID focuses on the markets for diagnosis and treatment products as its highest priority. UNITAID also funds prevention products on a selective basis.

Country income focus: UNITAID dedicates funds that are used to purchase health products with:

- At least 85 percent to low income countries,
- No more than 10 percent to lower-middle income countries, and
- No more than 5 percent to upper-middle income countries.

In addition, UNITAID works closely with middle income countries to maximize improvements in public health and healthcare product markets for people affected by the three diseases. In this way, UNITAID is able to leverage the large market share these countries represent and maximize its impact on public health and market shortcomings.

Value chain: For the target diseases and products, UNITAID may address market shortcomings at various points along the pharmaceutical value chain. (see section 4.4)

4.3 Guiding Principles

The following principles, derived from UNITAID's Constitution, continue to guide its strategic actions, decisions and operations at all levels:

- In line with the 2005 Paris Declaration on Aid Effectiveness, UNITAID is **complementary** to the activities of other global health actors to enhance effectiveness, and supports and pays attention to its impact on national health systems. It is **flexible** and **forward-looking** so as to respond quickly to changing conditions and to address future needs. UNITAID is **transparent** and **efficient** in its governance, agreements and operations.
- UNITAID focuses its activities on achieving **global impact**, benefiting all developing countries in a way that is **sustainable**. Its time-limited investments in improving health product markets aims to achieve significant **leverage** by increasing global access to products, generating positive externalities for global health and achieving a multiplicative return on the funds invested.

Guiding Principles

Complementary

Flexible

Forward-looking

Transparent

Efficient

Global Impact

Sustainable

Innovative

Value for money

Equity

Pro-public health approach
to Intellectual property

Guided by evidence

It stands prepared to support promising **innovative** approaches to improving global health. Its prioritization and project selection process is underpinned by the objective of maximizing **value for money**.

- UNITAID supports **equity** in facing health disparities systematically associated with social and economic disadvantages related to access to health commodities in vulnerable populations, and based on current scientific evidence.
- UNITAID takes a pro-public health approach to **intellectual property**⁶.
- UNITAID is focused on achieving measurable results and is guided by **evidence** in everything that it does.

4.4 UNITAID in the Value Chain

UNITAID holds a unique place in the Global Health architecture: its focused approach, position and resources have allowed it to achieve its mandate. UNITAID operates outside of a country program model, focusing its efforts on market effects that simultaneously increase access to health products of both public and private actors in low and middle income countries.

For the target diseases and products, UNITAID addresses market shortcomings along the pharmaceutical value chain, starting from the formulation stage through to global level delivery⁷. UNITAID, through its funding, is able to remedy markets upstream by **pushing** health products at a late stage of development onto the market. At the other end of the value chain, UNITAID has a **pull** effect, accelerating availability and boosting access.

UNITAID fixes market shortcomings, and ensures that products are delivered to countries in a timely manner.

UNITAID does not support basic science, discovery or early development of products. However, UNITAID may support developers during the final stages of product development in order to accelerate market entry of products that could have significant public health effects. Examples of potential final development interventions include late stage field evaluation and registration.

UNITAID's support is pragmatic and focused on the market. Typically, UNITAID provides a grant to a developer whose product has the potential to be a 'game changer' in the market – enabling superior products to reach the market, or creating competition within a market. It is a selective and sparingly used tool that UNITAID employs to increase access.

UNITAID's ultimate aim is significant improvement in public health through increased access to products in low and middle income countries. As a result, UNITAID requires that developers who receive UNITAID funds commit to making affordable products available to low and middle income countries.

6 Where intellectual property barriers hamper competition, affordability and/or development of appropriate formulations (e.g. fixed-dose combinations), UNITAID will support the use by countries of compulsory licensing or other flexibilities under the framework of the 2001 World Trade Organization Declaration on the Trade-Related Aspects of Intellectual Property Rights Agreement and Public Health ('Doha Declaration'), when applicable.

7 UNITAID does not fund interventions focused directly on strengthening country systems for supply chain management and logistics, unless they have an impact at a global market level. UNITAID will not fund public health interventions that do not have market impact (e.g. standard service delivery projects); nor does it fund market interventions with little or no public health benefit.

UNITAID uses several mechanisms to ensure that these commitments are fulfilled to achieve market transformation. Developers must achieve a specific endpoint(s) for each product, and/or regulatory/prequalification requirements, e.g. global licenses and technology transfer. More comprehensive guidance and policy on the mechanisms that UNITAID will employ is under development and will elaborate UNITAID's guiding principle of a pro-public health approach to intellectual property. This policy will be developed with input from stakeholders such as global development organizations, civil society, NGOs working on access to medicines/medical products, and product development partnerships (PDPs).

FIGURE 1: UNITAID PORTFOLIO ALONG THE VALUE CHAIN (APRIL 2013)

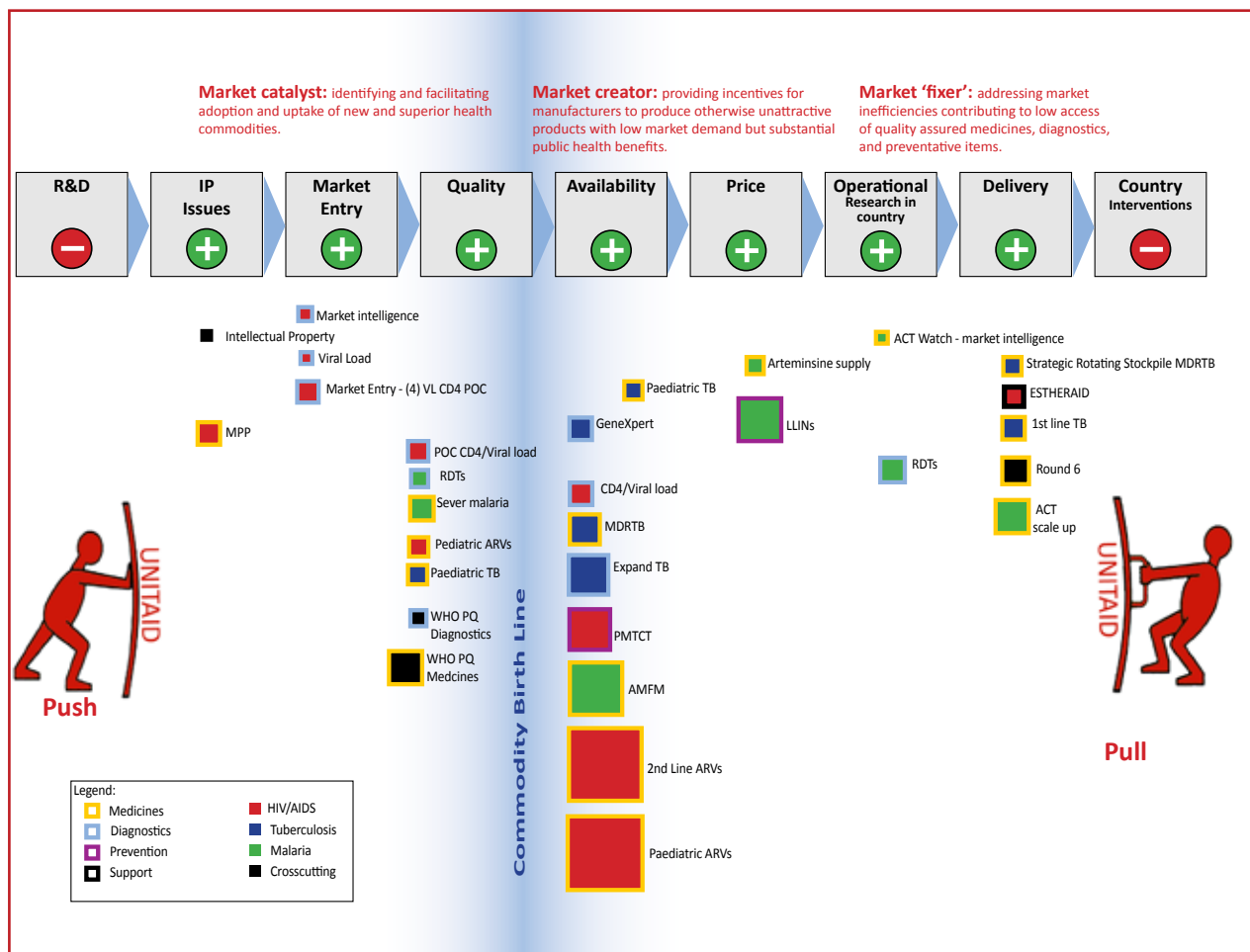


Figure legend: Further details of the UNITAID projects listed in this figure can be found on the UNITAID web site (www.unitaid.eu)

One of the lessons learnt is that upstream interventions usually carry higher risk but require smaller investments for a high potential in the medium term. Conversely, downstream interventions can result in rapid market impact, such as price reductions, and improvements in public health, but they require more substantial funding and their effect may be shorter.

4.5 Time-limited Funding

UNITAID provides short-term (3 to 5 years), catalytic funding to change market conditions and make much needed health products available and affordable in targeted countries. One of UNITAID's goals is long term sustainability: for example product registration, incorporation in national guidelines, affordable prices, and/or distribution networks, and to secure long term funding beyond UNITAID's intervention. Actions are taken in order to maintain the benefits of UNITAID's short-term, catalytic support to a project.

UNITAID defines transition as the continued support by other actors for products that UNITAID initially funded in order to make the necessary market change. Transition is achieved when alternative sources of funding have been secured to prevent treatment interruptions, and to maintain the market dynamic of the health product (see Annex 1).

STRATEGIC APPROACH



5 STRATEGIC APPROACH

5.1 UNITAID Market Effects Framework for Public Health

The UNITAID Market Effects Framework underpins UNITAID’s overall approach to improve public health (Figure 2). The logic in this framework is applied consistently across all key UNITAID activities, including: UNITAID’s landscape analyses; strategic prioritization; proposal development, technical evaluation, and selection; portfolio and project management; monitoring and evaluation; and impact assessment.

FIGURE 2: UNITAID MARKET EFFECTS FRAMEWORK FOR PUBLIC HEALTH



The framework initially evaluates the public health problem and the case for a market intervention; and then describes the pathway from the market intervention to public health effects via five steps:

1. Describe and quantify the public health and access problem: trends in epidemiology and disease burden, and articulation of the number and types of people who lack access to medicines and technologies.

2. Determine the market dynamics that contribute to the access problem: market shortcomings that contribute to reduced access, categorized as follows:

- **Availability:** The optimal medicine or technology to effectively prevent, diagnose or treat a particular disease or condition is not currently available;
- **Affordability:** The medicine or technology is offered at a price that imposes an unreasonable financial burden on governments, donors, individuals, or other payers;

- **Quality:** The medicine or technology is of sub-standard quality or there is a lack of reliable information on the quality of the product. This includes not only the quality of the final, finished product, but also the quality of starting and intermediary materials used to manufacture the final product.
- **Acceptability/adaptability:** The medicine or technology is not available or accessible in a format, formulation, or dose that is appropriate for use in a given population or setting.
- **Delivery:** Supply chain management systems (including product selection, quantification, procurement, storage, and distribution) are unable to equitably provide the right product or technology to the right person, in the right presentation, at the right dose, and at the right time with the least potential for error and at the lowest cost.

Once the market shortcomings have been identified and quantified, the reasons for the market shortcomings can be described. For example, the reasons for unaffordable, high prices may include intellectual property issues that limit competition; inefficient, low demand for products that prevent companies from producing medicines at economies of scale; or costly production of starting materials used to manufacture medicines.

3. Design, solicit and implement market interventions: interventions that aim to improve access to medicine and technologies by addressing market shortcomings (e.g. interventions that lower the price of a medicine allow for more people to be treated with the less-expensive product).

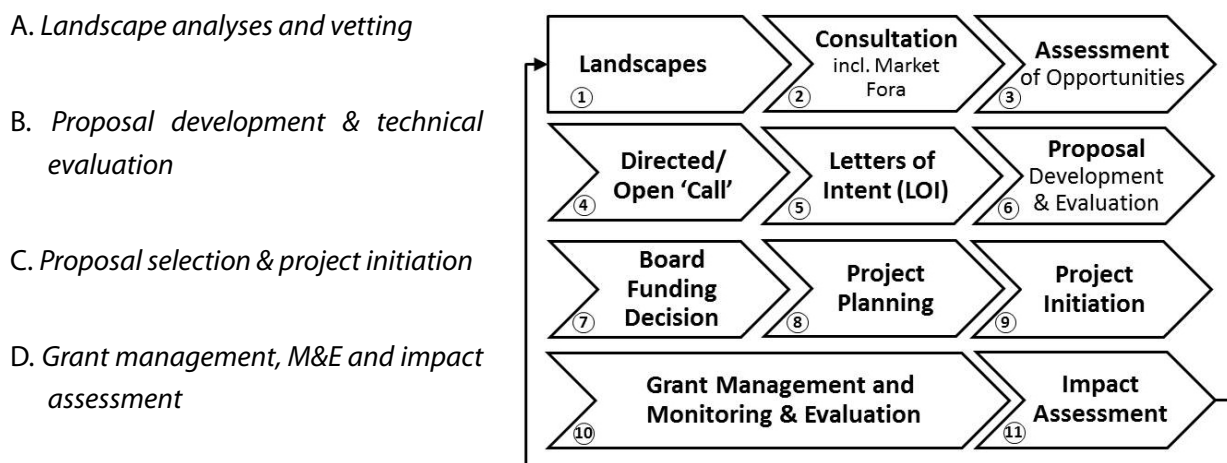
4. Estimate the market effects of the intervention: extent to which the intervention changed the key market shortcomings it was designed to address (e.g. decreased price, increased quality, etc.) and changed the overall structure and functioning of the market in a sustainable manner.

5. Estimate the extent to which the intervention addresses the public health and access problem it was designed to address: the number of people who have access to the medicine or technology as a result of the intervention and, where possible, estimates of changes in disease burden.

5.2 UNITAID Process to Identify, Develop, and Implement Interventions

The UNITAID process to identify, develop, and implement interventions aims to be: *dynamic*, anticipating and rapidly responding to updated treatment guidelines and technological innovation in medicines, diagnostics, and preventive products; *cyclical*, continuously looking at opportunities for UNITAID to develop new interventions; *evidence-based*, with assessment guided by rigorous expert analysis, peer review and decision making based on clear priorities; and *responsive*, incorporating lessons learned from continuous monitoring and evaluation of key performance indicators (KPIs) and impact.

The intervention process is comprised of four major phases:



LANDSCAPE ANALYSES AND VETTING

UNITAID's landscape reports compile research and analyses conducted by the Secretariat and leading external experts to provide the intelligence needed to identify, design, and support interventions with the most potential to optimize public health and market effects. They provide a detailed review of:

- *Diseases*: information on global access goals, the number and distribution of people who have the disease and who lack access to health products, as well as projected directions for future guidelines for treatment, diagnosis, and prevention;
- *Technologies*: information on existing health products already on the market and those that are currently in research and development, including comparisons of their potential, and relative strengths and weaknesses; and
- *Markets*: information on past, current and future market dynamics trends; market shortcomings and their reasons; and the on-going roles and efforts of other global health stakeholders.

UNITAID has made considerable progress in its landscape analyses since first identifying the need for this mechanism to prioritize UNITAID's investments and optimize its impact. Its first round of landscape analyses, in 2011, focused on diagnostics, providing insight into access issues and opportunities for UNITAID intervention. This led to an Executive Board directed call on diagnostics, and the eventual selection and funding of approximately \$200 million in innovative diagnostic interventions. Additional landscapes on medicines for the three diseases have since been developed and UNITAID is in the process of conducting its first round of preventives landscapes.

UNITAID's landscape analyses are developed with substantial outreach to and input from key players, including donors, international organizations, and leading experts in the field. Once drafted, landscape reports undergo a second round of input via external peer review provided by individual experts, as well as relevant working groups and committees of global health organizations.

To facilitate consultation and feedback on the key findings uncovered in the landscapes analyses, UNITAID convened its first Market Forum in 2012. This was an opportunity to present and discuss UNITAID's malaria landscapes, and to attract new partners with the capacity to implement interventions on UNITAID's behalf. No other venue exists to assemble stakeholders from the scientific, programmatic,

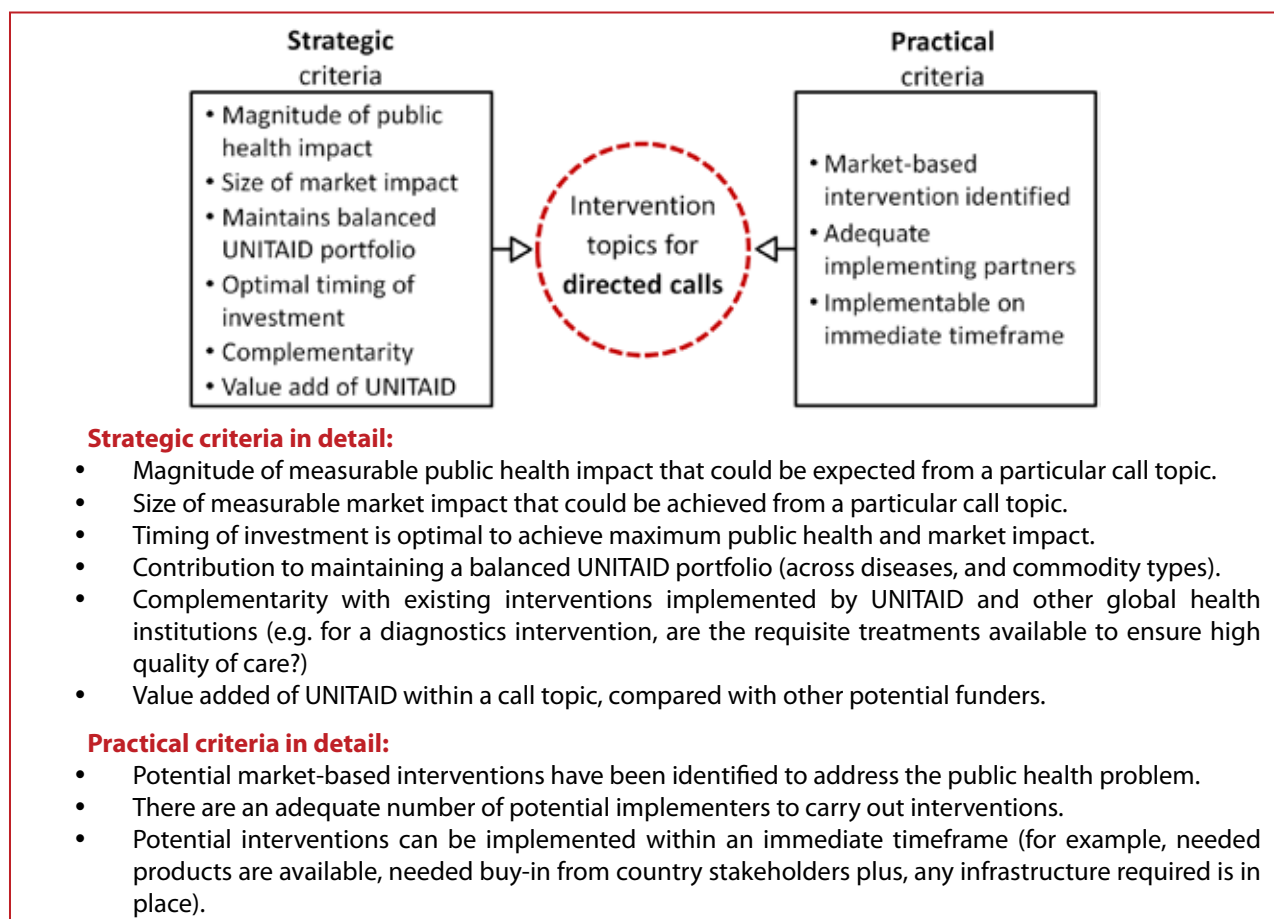
and donor communities to discuss market approaches across interrelated and interdependent health product categories (i.e., preventives, diagnostics, and treatments). UNITAID will hold similar fora annually for each of the three diseases to share lessons learned, examine trends in market dynamics, engage partners, and continuously improve the discipline. In addition, UNITAID will continue to hold Consultative Fora every two years to maximize the number of stakeholders who provide input into UNITAID's strategies and operations.

Potential interventions (Section 6) emerging from UNITAID's landscape analyses and expert consultation are assessed to identify commodity types and cross-cutting areas where market-based interventions could have significant public health and market effects.

The process for assessing potential interventions to generate recommendations for directed calls involves a number of both practical and strategic considerations (Figure 3). Practical considerations can often be mitigated proactively; addressing these limitations is a significant activity for UNITAID. For example, UNITAID works to develop initial concepts for market-based interventions and, through dialogue with stakeholders, seeks to attract and develop new implementers for activities.

Potential interventions that emerge from the assessment process and are considered capable of achieving significant public health and market effects are recommended for Board consideration as subjects of directed calls for proposal letters of intent (LOIs).

FIGURE 3: ASSESSMENT CRITERIA FOR DIRECTED CALLS



PROPOSAL DEVELOPMENT AND EVALUATION

The Executive Board determines UNITAID's investment priorities. It discusses potential interventions identified in the UNITAID landscape analyses that meet the assessment criteria. Up to 2 annual 'directed calls' for proposal LOIs are launched by the Executive Board in areas best suited to meet UNITAID's Strategic Objectives. Directed calls focus on increasing access to specific commodities; previous examples include POC diagnostics and paediatric ARVs. While UNITAID must determine that market-based interventions for a specific commodity type are practically and strategically feasible before a call is made, it is the responsibility of proponents to conceptualise the intervention they propose to implement. 'Open calls' for proposal LOIs are also launched annually to solicit new ideas for interventions. They must be compatible with a Strategic Objective and/or do not fit the themes of directed calls or any intervention identified in UNITAID landscape analyses. Application materials and guidance for proponents are made available on the UNITAID website⁸. LOIs and proposals received through open calls undergo the same rigorous evaluation as those received through directed calls. The majority of UNITAID funds are allocated to the 'directed call' route, with a minority of funds spent via the 'open call' route⁹.

Letters of intent allow UNITAID to review concepts for new interventions at a level of detail sufficient to make a judgment in principle on a potential intervention's suitability for UNITAID support. Successful proponents are invited to submit full proposals and receive guidance and support in this task from the UNITAID Secretariat. Once submitted, full proposals undergo a robust technical evaluation by an independent expert committee – UNITAID's Proposal Review Committee (PRC) – which reviews proposals against a standard set of selection criteria, including sustainable public health and market effects, value for money, innovation, leverage, added value, equity, and ability to transition.

PROPOSAL SELECTION AND PROJECT INITIATION

UNITAID applies a standard process to evaluate and select proposals for UNITAID funding (See Annex 2). Proposals deemed suitable, technically sound, and feasible by the PRC are recommended to the Executive Board, which makes final funding decisions, taking into account available resources and each proposal's contribution to a balanced UNITAID project portfolio. Approved proposals enter a Secretariat-led project planning phase, which first addresses any requests for amendments or clarification required by the Board, and subsequently processes approved proposals into grant agreements and operationalized projects with a clear plan for transition of funding, when needed, to sustain the results of the project once UNITAID funding has ended. Projects are then formally initiated, with UNITAID providing time-limited funding for implementation and supporting implementation over the duration of the grant (see Section 8).

GRANT MANAGEMENT, MONITORING & EVALUATION, AND IMPACT ASSESSMENT

The success of UNITAID interventions depends on a clear planning process, close monitoring, and a strong relationship between UNITAID and its implementers. UNITAID has adopted a collaborative approach, which includes regularly scheduled interactions with implementers, as well as ensuring that UNITAID has the appropriate resources and skilled staff to provide support to implementers at every facet of the project. Project management at UNITAID is underpinned by a robust quality management system to ensure consistent, high performance and continuous improvement at every stage of the project.

⁸ UNITAID calls and associated materials and guidance are posted at: <http://unitaid.org/rfps>

⁹ As agreed by the Executive Board at its 14th meeting June 2011.

UNITAID monitors grant implementation through annual and semi-annual programmatic and financial reports. This information is summarized in UNITAID's annual KPI report: it is used to improve Secretariat management and is presented to the Executive Board.

UNITAID requires mid-term and end-of-project evaluations for all of its funded projects. These assessments provide lessons that can be taken forward for new or existing projects that may face similar challenges.

UNITAID measures its success based on the impact of its project funding choices on the market for medicines, diagnostics and related products of public health importance to treat HIV/AIDS, TB and malaria. UNITAID monitors how the markets respond via KPIs developed specifically for this purpose. (See Sections 7 core area 2 for more detail).

5.3 Innovative Leverage Opportunity: Innovative Grants Mechanism

UNITAID interventions are designed as relatively large-scale grants with a global effect on markets. However, UNITAID also needs to be open to supporting innovations that are small scale and in development, but may have significant future market applications. To develop such innovations, UNITAID will set up a new mechanism to finance innovative grants, given only once to organizations to incubate innovative ideas and mechanisms, as well as to develop potential new implementers for UNITAID. These partners may be civil society groups, NGOs, academics or others. UNITAID expects that innovative grants will help incubate ideas that, if appropriately developed and scaled up, could have the potential to affect markets at the global scale.

The innovative grants mechanism will be further detailed in 2013 and an approach for innovative grants will be presented to the Board for its approval. The innovative grants mechanism will aim to streamline processes around proposal and project development. It will, however, retain an external expert review process and ultimate Board decision making.

Specific mechanisms will be developed by the Secretariat in 2013 regarding the call for, and evaluation of proposals for these innovative grants, and these will be evaluated in 2016.



STRATEGIC OBJECTIVES



6 STRATEGIC OBJECTIVES

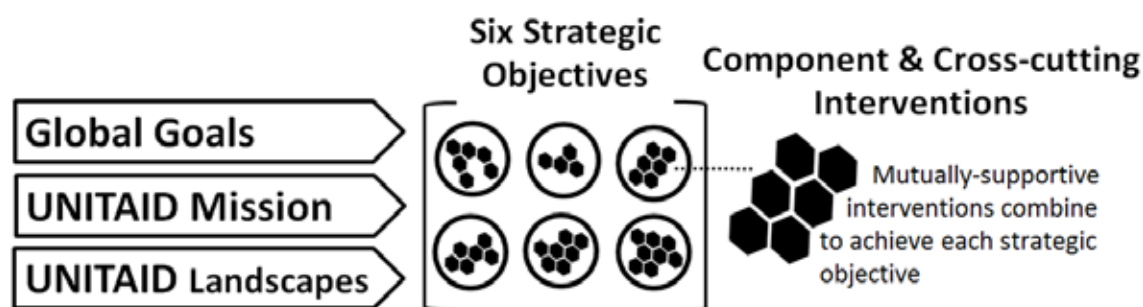
This Strategy introduces, for the first time for UNITAID, explicit Strategic Objectives. UNITAID's Strategic Objectives are intended to serve as:

- A clear statement of intent to achieve market and public health effects in key areas;
- An invitation to partners (including donors, implementers, industry, and country-level actors) to collaborate on specific efforts; and
- A signal to the market to orient availability, formulation, quality, pricing, and sustainable access to health products for HIV/AIDS and its co-infections, TB, and malaria in developing countries.

UNITAID's Strategic Objectives describe how UNITAID intends to contribute to the long-term goals of the global health community for HIV/AIDS, TB, and malaria by increasing access to the key treatment, diagnostic, and preventive products to prevent new infections and provide effective treatment set out for each disease in the global plans of UNAIDS, the Stop TB and Roll-Back Malaria Partnerships, in collaboration with the World Health Organization. The corresponding 2015 global targets¹⁰ for treatment and infection reduction across the three diseases are:

- Reaching 15 million people with antiretroviral medicines, reducing new HIV infections by 50 percent compared with 2010, eliminating new HIV infections among children and substantially reducing AIDS-related maternal deaths¹¹;
- Reducing prevalence and deaths due to TB by 50 percent compared with the 1990 baseline^{12,13}; and
- Reducing malaria deaths to near zero and all cases of malaria by 75 percent¹⁴.

FIGURE 4: DETERMINANTS OF UNITAID STRATEGIC OBJECTIVES AND COMPONENT INTERVENTIONS



10 New common goals for global development that follow from the 2015 Millennium Development Goals are expected to be agreed during this strategic period. Although resulting revised global health targets will likely not require revision of its six core Strategic Objectives, UNITAID may refine its Strategic Objectives and funding portfolio in order to ensure complementarity with any new global targets for treatment and infection reduction.

11 *United Nations General Assembly 2011 Political Declaration on HIV/AIDS*, UNAIDS, available from: http://www.unaids.org/en/media/unaids/contentassets/documents/document/2011/06/20110610_UN_A-RES-65-277_en.pdf

12 *Global Tuberculosis Control 2011*, World Health Organization, available from: http://www.who.int/tb/publications/global_report/en/

13 The tuberculosis targets listed are those in effect as of January 2013. A revision of targets is planned to occur in 2013

14 *World Malaria Report 2011*, World Health Organization, available from: http://www.who.int/malaria/world_malaria_report_2011/en/

COMPONENT INTERVENTIONS

Each of UNITAID's six Strategic Objectives is comprised of a number of *component interventions* required to achieve the Strategic Objective. The component interventions are categorized according to the level of evidence UNITAID currently has to consider supporting the interventions and whether or not UNITAID has already launched interventions to support the Strategic Objective:

- **Active** interventions are on-going UNITAID projects or projects recently approved by the Board that were identified through UNITAID's landscape analyses and vetting processes.
- **Potential** interventions are options identified through UNITAID's landscape analyses and vetting processes, but have not yet been considered for funding (products of interest may not have reached the market or may not yet be recommended in treatment guidelines, required capacity may not yet exist among potential implementers, etc.).
- **Exploratory** interventions are those that have been recommended to UNITAID by technical experts, partners, and stakeholders as part of a consultative process, but have not yet undergone a thorough landscape analysis and vetting process to determine their suitability for UNITAID investment. 'Exploratory interventions' that remain candidates after being analysed and vetted will be classified as 'potential interventions'.

UNITAID landscape analyses are the key input that informs the detailed description of each Strategic Objective that follows. As of February 2013, some landscapes are only available provisionally or are in the early stages of development, particularly those related to preventive commodities and medicines. As these landscapes are completed, articulation of the market shortcomings and exploratory opportunities identified in these Strategic Objectives may change. The Executive Board prioritizes interventions for UNITAID directed calls only after UNITAID's landscape analyses have been conducted and the potential interventions have been identified according to UNITAID's project development process (see Section 5.2).

UNITAID's six Strategic Objectives are:

- **Strategic Objective 1:** Increase access to simple, POC diagnostics for HIV/AIDS, TB, and malaria
- **Strategic Objective 2:** Increase access to affordable, paediatric medicines to treat HIV/AIDS, tuberculosis, and malaria
- **Strategic Objective 3:** Increase access to emerging medicines and/or regimens, as well as new formulations, dosage forms, or strengths of existing medicines that will improve the treatment of HIV/AIDS and coinfections such as viral hepatitis
- **Strategic Objective 4:** Increase access to artemisinin-based combination therapies (ACTs) and emerging medicines, that, in combination with appropriate diagnostic testing, will improve the treatment of malaria
- **Strategic Objective 5:** Secure supply of second-line TB medicines, and increase access to emerging medicines and regimens that will improve treatment of both drug-sensitive and multi drug-resistant TB
- **Strategic Objective 6:** Increase access to products for the prevention of HIV, TB, and malaria

These Strategic Objectives are likely to remain constant during the 2013-2016 Strategic period; however, potential and exploratory interventions are expected to change and be identified through UNITAID market intelligence. Additional promising interventions will also emerge and be considered

during the Strategic period. Interventions are categorized as potential or exploratory, based on UNITAID's project development process and the level of evidence available at the start of the 2013-2016 Strategic period; these categories do not indicate any prioritization by the UNITAID Executive Board.

The Strategic Objectives are focused and specific to enable the maximum impact of UNITAID interventions. For example, the scope of Strategic Objective 1 includes simple diagnostics to be used at the POC. The focus on simple, POC products will allow UNITAID to advance new technologies to improve access for the most vulnerable groups in resource-limited settings, while maintaining the option to invest in other technologies that may play an important role in improving access in specific settings (e.g. more complex techniques or those that are used at the level of central or reference laboratories).

CROSS-CUTTING INTERVENTIONS

In addition to the disease- and product-specific component interventions presented for each Strategic Objective below, UNITAID will continue to support cross-cutting interventions that effectively and comprehensively address shortcomings that exist across multiple diseases or product types¹⁵. Two areas of UNITAID intervention – (i) quality standard of products and (ii) intellectual property rights (IPR) – historically have lent themselves to a cross-cutting approach. They have underpinned UNITAID's work to increase access to medicines, diagnostics, and preventive commodities (Box 1). UNITAID will continue to welcome proposals for interventions that would address market shortcomings across diseases and product types in similar, comprehensive ways.

While quality assurance and IPR are a focus for many UNITAID market-based interventions (for example, quality assurance activities are key to UNITAID's project to accelerate access to innovative POCHIV diagnostics), some cross-cutting interventions are wholly dedicated to addressing market shortcomings in these areas (for example, the UNITAID-supported Sustainable Global and National Quality Control for Malaria Rapid Diagnostic Tests project).

¹⁵ Including interventions for products with utility for multiple diseases (e.g. diagnostic platforms that can diagnose multiple infections simultaneously).

BOX 1: CURRENT CROSS-CUTTING INTERVENTIONS: QUALITY STANDARD OF PRODUCTS AND INTELLECTUAL PROPERTY RIGHTS

Quality standard of products is an important consideration across the development, evaluation, manufacturing, supply chain management, and monitoring of global health commodities. It has been a primary focus of UNITAID's market-shaping interventions since the organization's inception.

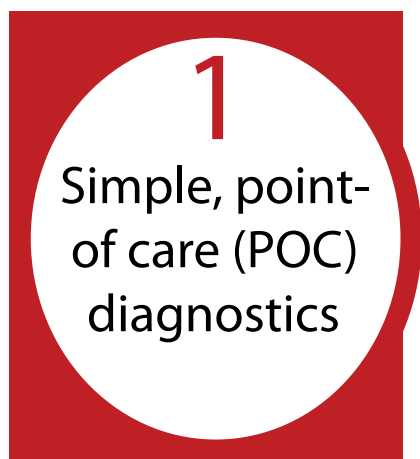
UNITAID is the largest donor to the Prequalification of Medicines Programme (PQP), a United Nations Programme managed by WHO. Every year, hundreds of millions of US dollars' worth of medicines are purchased by or through international financing or procurement mechanisms – such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, UNITAID and UNICEF – for distribution in resource-limited countries. WHO PQP helps ensure that these medicines meet acceptable standards of quality, safety and efficacy and increases the competition for quality products. Through PQP, UNITAID also helps to increase capacity in production of quality medicines; facilitate the development of sustainable regional and national regulatory capacity; and accelerate testing of the quality of medicines. Other advantages of PQP are opportunities for manufacturers to achieve faster product registration; to reduce the costs of registration; and/or to remove regulatory barriers to product availability. During the Strategy period, UNITAID will continue to work closely with WHO to identify further opportunities to increase quality of priority medicines and diagnostics, as well as promote a more balanced and sustainable funding model for this critical work.

Intellectual property (IP) is an important factor in shaping markets, even before a product reaches the market. UNITAID seeks to develop, promote, and implement an innovative, pro-public health approach to IP. Intellectual property is expected to play an increasingly important role in key areas, such as HIV medicines and diagnostics, and MDR TB medicines, which are emerging from the pipeline. These new products are likely to be granted 20-year patents, including in low and middle income countries that previously did not grant product patents for pharmaceuticals. Therefore, new approaches to address IP barriers and ensure affordable, equitable access in resource-limited settings will be required.

UNITAID's first and most significant project on IP to date was the creation of the Medicines Patent Pool, an innovative project that aims to facilitate generic competition through the creation of a 'one-stop shop' for voluntary licenses for ARVs. It has also greatly contributed to transparency by making its licenses public, and by setting up a widely used patent status database on ARVs.

Where intellectual property barriers hamper competition and price reductions, UNITAID will support the use of 'TRIPS flexibilities' when applicable, as per the UNITAID Constitution. UNITAID will assist efforts to identify and address intellectual property barriers in low and middle income countries. In this regard, UNITAID recognizes that middle income countries face specific challenges, and is committed to work with them to identify sustainable solutions.

UNITAID will engage with partners to the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, and seek to actively contribute to its implementation. UNITAID will also seek to collaborate with WIPO Re:Search, and to further leverage the work of the Medicines Patent Pool.



6.1 Strategic Objective 1: Increase access to simple, point-of-care diagnostics for HIV/AIDS, TB, and malaria

6.1.1 HIV/AIDS diagnostics

COMMODITY ACCESS ISSUES

Access to HIV diagnostics lags far behind access to ARV treatment (ART) for HIV. While robust data is unavailable, recent estimates suggest the proportion of existing demand that has been met for CD4, viral load, and early infant diagnostic (EID) testing is only ~60%, ~25%, and ~26%, respectively.

Improving access to CD4 tests that determine when to initiate HIV treatment and viral load tests to determine when to switch from first-line to second-line ART are critical components of HIV care. Proper use of CD4 and viral load tests maximize the benefits of ART, including improved quality of life, and improved transition from first- to second-line regimens, which saves lives, and extends life span. Improving access to EID can have a dramatic effect by saving the lives of HIV-infected infants, many of whom die before they reach two years of age due to insufficient access to EID and ART.¹⁶

Unprecedented innovation is underway to develop simple, easy-to-use, affordable, quality-assured HIV diagnostics to bring these products closer to the POC, and to be optimally integrated into health systems in combination with centralized, laboratory-based diagnostic tools. Three CD4 POC products are already on the market, with four more to be launched over the next two years, including two disposable CD4 tests requiring no instruments. Similarly, more than six viral load and EID POC products will emerge over the next three years, including platforms that allow for multiple types of laboratory tests to be performed on one device.¹⁷

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: Limited availability of CD4 POC; and no availability of viral load and EID POC products.
Reasons: Research and development of POC products is complex, expensive, and time-consuming. Many developers lack finances and other resources to overcome barriers to bring their products to market.

Affordability: Traditional HIV diagnostics performed in sophisticated laboratory settings are unaffordable for resource-limited settings; approximate prices are: CD4 \$25,000-\$90,000/instrument and \$2-\$14/test; viral load \$100,000-225,000/instrument and \$10-\$70/test; and EID \$25,000-\$100,000/instrument and \$10-\$20/test. POC diagnostics tools that have recently entered the market are less expensive (POC CD4 prices \$6,500-\$25,000/instrument and \$6-\$12/test), but are still too expensive to enable equitable access.¹⁸ **Reasons:** Research and development costs for all types of diagnostics are inherently high. Limited competition exists for traditional laboratory products, which also carry substantial costs for service, repair, training, sample transport, etc. Limited competition exists as well for recent POC tools, which are subject to costly requirements for market authorization and use (e.g. multiple clinical trials and registration or validation in each country), and are procured in an uncoordinated manner.

16 WHO *Antiretroviral therapy for HIV infection in infants and children. Recommendations for a public health approach* (2010 revision). WHO *Recommendations on the diagnosis of HIV infection in infants and children*, July 2010

17 UNITAID, *HIV/AIDS Diagnostic Technology Landscape*, 2nd Edition, June 2012 and semi-annual update October 2012.

18 UNITAID, *HIV/AIDS Diagnostic Technology Landscape*, 2nd Edition, June 2012 and semi-annual update October 2012

Quality: Absence of information on quality of newer POC diagnostics. **Reasons:** Few incentives exist for producers to submit applications to stringent regulatory authorities (e.g. United States Food & Drug Administration, European CE-IVD mark, etc.); long timelines for products to achieve WHO Prequalification (PQ); no systematic, standardized alternative(s) to WHO PQ; and lack of post-marketing surveillance to assure quality once new products have been introduced onto the market.

Acceptability/Adaptability: Traditional, laboratory-based products are ill-adapted for low-resource settings because they are complicated to use and maintain, and require sophisticated infrastructure and skilled technicians. Newer POC diagnostics currently on the market allow for more decentralized testing but many are still too complicated for use in remote settings by unskilled workers. **Reasons:** Returns on investment are insufficient to warrant development of high throughput, laboratory-based diagnostics for use in resource-limited settings. Until recently, few incentives existed for large, established diagnostic manufacturers to develop affordable, easy-to-use POC diagnostics designed specifically for low-resource settings.

Delivery: Slow and insufficient uptake of both traditional laboratory-based and newer POC diagnostics. **Reasons:** Complex, non-uniform and costly regulatory frameworks for evaluation and registration of new products at national level, often requiring producers to submit products for evaluation in every country in which they wish to register their product; countries may choose not to adopt new technologies because of previous investments in laboratory infrastructure, and the human resource and costs involved in changing treatment guidelines, training, etc.

COMPONENT INTERVENTIONS

Active Interventions (*On-going and identified in UNITAID's landscape analyses*)

- **Accelerating Access to Innovative POC HIV Diagnostics** – This project, implemented across seven Sub-Saharan African countries will: (i) engage with suppliers to reduce pricing and accelerate market entry of new CD4, viral load, and EID POC diagnostics, (ii) accelerate regulatory approval and initial product adoption, (iii) support normative guidance on POC testing, (iv) procure quality products to accelerate widespread uptake, (v) create an enabling environment for market shaping. (*Implemented by Clinton Health Access Initiative & UNICEF*)
- **Implementation of CD4 and viral load testing in decentralized, remote and resource-limited settings** – This project, implemented across seven Sub-Saharan African countries will: (i) accelerate regulatory approval and initial product adoption, (ii) implement decentralized CD4 and viral load and EID testing, (iii) conduct operational research on feasibility, acceptability, sustainability, and affordability of POC testing and laboratory-based tools to determine optimal implementation approaches across a range of settings, and (iv) provide lessons learned and best practices to WHO for incorporation into Treatment 2.0 guidance. (*Implemented by Médecins Sans Frontières*)
- **Market Entry of HIV POC Diagnostics** – Funding for four POC diagnostics developers (3 CD4; 1 viral load/EID) will support completion of final field validation trials, product registration, and other late-stage commercialization steps to accelerate the launch and availability of critically-needed products and induce market competition.

- **Open Polyvalent Platforms (OPPs) for sustainable access to viral load testing in resource-limited settings** – This project will facilitate the development of ‘open polyvalent platforms’ – i.e., diagnostic platforms using reagents originating from multiple suppliers and manufacturers – that are sized for peripheral settings, easy to use, and are rapid and flexible. *(Implemented by France Expertise Internationale)*
- **Global Network to Improve Access and Quality of HIV Monitoring Technologies** – This project will complement the WHO PQ by developing: (i) target product profiles (ii) harmonized evaluation protocols, (iii) a global network of POC technology evaluation sites and (iv) a toolkit to facilitate evaluation and adoption of new technologies. *(Implemented by the London School of Hygiene and Tropical Medicine)*

Potential interventions *(Identified in UNITAID’s landscape analyses; not yet considered for funding)*

- Interventions to expedite market entry and availability of game-changing viral load tests, EID, and multi-platform technologies due to emerge from the pipeline over the next three to four years.
- Interventions to support regional and pancontinental harmonization of diagnostics regulation and quality assurance.
- Interventions to harmonize policies as well as coordinate and rationalize procurement across key stakeholders

Exploratory interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- Interventions to increase access to simplified, affordable POC tests to monitor resistance to ARVs.
- Interventions to increase access to improved rapid HIV diagnostic products for use in decentralized HIV care and treatment programs.
- Interventions to address intellectual property barriers on POC diagnostics, where needed, to ensure access to optimal products.

MEASURING SUCCESS

Expected market effects include development of competitive diagnostics markets that provide high-quality, affordable, well-adapted POC diagnostics to those in need, with on-going investments in further development of game-changing technologies for use in resource-limited settings. UNITAID aims to facilitate availability and access to 2-3 new products in each of the CD4 (including at least one disposable), viral load, and EID POC product categories. Price reductions of at least 50% are expected for viral load and EID tests, with target prices of \$12/test and \$7/test, respectively. Price reductions of 30-50% are expected for CD4 tests, with a target price of \$2-\$3/test.¹⁹

Expected public health effects include increasing CD4 coverage from 60% to 80%, increasing viral load coverage from 25% to 50%, and increasing EID coverage from 26% to 50%.²⁰

¹⁹ Expected impact estimated by CHAI/UNICEF for the UNITAID-funded intervention to accelerate access to innovative point of care HIV Diagnostics.

²⁰ Expected impact estimated by CHAI/UNICEF for the UNITAID-funded intervention to accelerate access to innovative point of care HIV Diagnostics.

6.1.2 Tuberculosis diagnostics

COMMODITY ACCESS ISSUES

Up to 40% of people with active TB do not have access to initial diagnostics, and even fewer have access to drug-susceptibility testing (DST) to guide treatment decisions.²¹ This translates to 2.9 million people with active TB each year who do not receive an initial diagnosis of their disease.²² In addition, fewer than 1 in 20 new TB patients have access to DST.²³ Even among cases of confirmed multi drug-resistant TB cases, only 23% are tested for susceptibility to common second-line TB drugs.²⁴

A novel product, GeneXpert, was endorsed by WHO in 2010 and its availability is being scaled up. This product is a 'game-changer' that can diagnose TB quickly and accurately, and performs some DST. GeneXpert represents the first product from a pipeline of new diagnostic tests. At least four new products, newly available or expected in early 2013, are broadly similar to GeneXpert but could be used closer to the POC in resource-limited settings.²⁵

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: There is no true POC TB diagnostic test: GeneXpert still requires basic laboratory infrastructure. **Reasons:** Unclear potential market and lack of clarity on available market share after GeneXpert scale-up reduce developers' willingness to invest in research. Significant technical challenges in developing a true POC product.

Acceptability/Adaptability: Current diagnostics are not adapted for specific patient groups or decentralized healthcare settings. For example: limited DST ability; no ability to perform multiple different tests (multi-platform functionality); not suited for children (the tests require sputum which is hard to collect from children); not suited for populations with low levels of mycobacteria in sputum (children, HIV co-infected patients, cases of extrapulmonary disease).²⁶ **Reasons:** Technical difficulty in developing technologies to address specimen collection and other challenges presented by specific patient groups.

Affordability: New technologies are expensive: the GeneXpert machine costs ~\$17,500, and each cartridge costs at least \$10 to preferred buyers, or considerably more in the private sector.²⁷ **Reasons:** Monopolistic supplier. High complexity of incorporating multiple reagents into a robust cartridge.

Quality: No information on quality of diagnostics to guide procurement. Common use of inappropriate tests (e.g. serology) that have not been approved for TB in the private sector. **Reasons:** Limited global quality assurance processes for TB diagnostics; current reliance on ad hoc recommendations from WHO committee (Strategic and Technical Advisory Group for Tuberculosis (STAG-TB)). Limited in-country regulation of laboratories.

Delivery: Supply constraints have led to long lead times for delivery of GeneXpert cartridges. **Reasons:** Monopolistic market with a supplier underestimating production capacity. No alternative suppliers for purchasers to use.

21 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

22 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

23 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

24 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

25 UNITAID. *Tuberculosis diagnostics technology landscape: semi-annual update*. Geneva, World Health Organization, 2012

26 UNITAID. *Tuberculosis diagnostics technology landscape*. Geneva, World Health Organization, 2012

27 UNITAID. *Tuberculosis diagnostics technology landscape*. Geneva, World Health Organization, 2012

Barriers to adoption of novel innovative technologies hinder uptake. **Reasons:** Novel product types require extensive training and integration into diagnostic and clinical algorithms.

COMPONENT INTERVENTIONS

Active Interventions (*On-going and identified in UNITAID's landscape analyses*)

- **Scale-up of GeneXpert MTB/RIF** – This project secured a reduced cartridge price and accelerates roll-out of GeneXpert in 20 countries. (*Implemented by Stop TB Department and Stop TB Partnership*)

Potential interventions (*Identified in UNITAID's landscape analyses; not yet considered for funding*)

- **Accelerate market entry for next-generation POC TB diagnostics**, including those with comprehensive DST capability and ability to use specimens other than sputum.

Exploratory interventions (*Identified by stakeholders; full landscape analysis and vetting pending*)

- Support global efforts to develop quality assurance policies and systems for TB diagnostics.
- Facilitate development of open platforms or generic competition; facilitate development of TB diagnostics for use in underserved patient groups, including extrapulmonary TB, children, and people living with HIV.

MEASURING SUCCESS

Expected market effects include the development of competitive diagnostics markets that provide quality-assured, affordable, innovative POC diagnostics adapted for resource-limited settings. Availability and access targets include: new TB diagnostic products from multiple suppliers with the potential for POC use in resource-limited settings – ultimately to include products that can comprehensively diagnose multidrug resistance. Early indications suggest that, for a new cartridge-based test using nucleic acid amplification technology, target prices could range from \$5,000-\$10,000 per instrument and \$4-\$8/test.²⁸

Expected public health effects include increased access to TB diagnosis and appropriate treatment, and, therefore, improved case detection and cure rates. A recent model for Southern Africa found that use of GeneXpert would prevent 132,000 TB cases and 182,000 TB deaths over 10 years, reducing the proportion of the population with active TB by 28%. Costs – driven largely by increased ART for TB-HIV co-infected patients – would be \$959 for every year of healthy life gained.²⁹ Tools will be developed to estimate life-years gained for future diagnostic interventions, both ex-ante and ex-post, to guide implementation of highly cost effective interventions and to quantify market effects.

28 Based on target product profile developed by the Bill & Melinda Gates Foundation, with input from partners (September 2012). For more information, refer to: UNITAID. *Tuberculosis diagnostics technology landscape: semi-annual update*. Geneva, World Health Organization, 2012

29 Menzies NA, Cohen T, Lin H-H, Murray M, Salomon JA (2012) Population Health Impact and Cost-Effectiveness of Tuberculosis Diagnosis with Xpert MTB/RIF: A Dynamic Simulation and Economic Evaluation. *PLoS Med* 9(11): e1001347. doi:10.1371/journal.pmed.1001347

6.1.3 Malaria diagnostics

COMMODITY ACCESS ISSUES

In Africa, which accounts for 80% of the over 200 million malaria cases each year, only 47% of cases seen in the public sector received a malaria diagnostic test in 2011.³⁰ Diagnostics testing in the private sector is minimal: in some high-burden countries, less than 10% of children under five years of age seeking care for fever in the private sector receive a diagnostic test for malaria.³¹ Diagnostic testing can improve the treatment of malaria and febrile illness more broadly; allow better targeting of recommended ACTs; reduce drug expenditures; and, improve surveillance. Current scale-up efforts are primarily driven by increased use of malaria rapid diagnostic tests (RDTs) that are portable and simple to use at the POC. Several technologies are in development that should be superior to existing malaria RDTs, such as rapid tests that use urine samples instead of blood, and efforts to enhance the signal and sensitivity of RDTs with fluorescent dyes and a handheld reader.³² The ability of these technologies to compete with existing RDTs on cost, ease-of-use, and additional value has yet to be determined, and will be critical to their uptake.

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: No tests currently on the market for use in detecting malaria: (i) in asymptomatic pregnant women, (ii) in low malaria transmission areas, or (iii) in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency that causes adverse reactions to the drug used to treat liver stage malaria of *P. vivax* malaria. **Reasons:** Limited funding; unclear regulatory pathway and quality standards; lack of consensus around target product profiles; limited research on desired product characteristics and market size; complexity and cost of evaluating malaria tests.

Affordability: RDT prices in the private sector (median prices of \$0.58 - \$3.22 across 10 African countries³³) are likely unaffordable, especially when coupled with ACT treatment costs. **Reasons:** Add-on costs throughout the private sector distribution chain (e.g. 30-60% mark-ups³⁴) exacerbated by 'cool chain' requirements³⁵; combined costs of RDTs and ACTs likely to exceed ability- and/or willingness-to-pay by consumers.³⁶

Quality: Limited information on the quality of malaria RDTs (e.g. only 30-50% of lots from the public sector are tested); lack of practical methods to test quality along the value chain from manufacturer to point of service; RDTs are available that do not meet minimum quality standards. **Reasons:** Unclear demand for quality control technologies and product specifications; little incentive for manufacturer investments due to market conditions (low barriers to entry, intense price competition); high cost of quality control due to reliance on human-derived malaria samples; lack of national regulatory processes or post-market surveillance programs.

30 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

31 Littrell, M., et al. Monitoring fever treatment behavior and equitable access to effective medicines in the context of initiatives to improve ACT access: baseline results and implications for programming in six African countries. *Malaria Journal*, 2011, 10:327.

32 UNITAID. *Malaria Diagnostics Technology Landscape*. Geneva, World Health Organization, 2011.

33 ACTwatch (<http://www.actwatch.info/results/>), Independent Evaluation of the Affordable Medicines Facility – malaria (AMFm) Phase I, Preliminary Report of July 18, 2012. Available at: <http://www.theglobalfund.org/en/amfm/independentevaluation>. In: UNITAID. *Malaria Diagnostics Market Landscape*. Geneva, World Health Organization, 2012.

34 ACTwatch (<http://www.actwatch.info/results/>) In: UNITAID. *Malaria Diagnostics Market Landscape*. Geneva, World Health Organization, 2012.

35 World Health Organization Global Malaria Programme. *Good practices for selecting and procuring rapid diagnostic tests for malaria*. Geneva, World Health Organization, 2011.

36 Hansen KS et al. (2012). *Willingness-to-pay for a rapid malaria diagnostic test and artemisinin-based combination therapy from private drug shops in Mukono district, Uganda*. Health Policy Plan, published online May 15, 2012 doi:10.1093/heapol/czs048.

Acceptability/Adaptability: Barriers to POC use of RDTs include limited user-friendliness of RDT kits and the need to maintain a ‘cool chain’ during distribution and storage; low compliance with RDT results by providers/patients. **Reasons:** No clear specifications for improving ease of use and interchangeability of RDTs; low margins limit incentives for manufactures to invest in product changes; lack of formal research on RDT heat stability; low awareness of the value of diagnostic testing for malaria; difficulty changing historical practice of presumptive treatment; lack of confidence in RDT results; lack of guidance/treatment options for non-malarial fever.

Delivery: Slow uptake of malaria diagnostics in the public sector and limited market in the private sector. Uncertainty about ability to ensure uninterrupted supply of quality RDTs in the future. **Reasons:** Public sector uptake challenged by supply issues (delays in accessing funds, cumbersome product selection processes, weak quantification methods and distribution systems); and limited education and training. In the future, the supplier base for quality RDTs may decrease due to unpredictable demand, large order sizes and short lead times (4-8 weeks from contract to delivery), and intense price competition (weighted average public sector price for *P. falciparum* RDTs was \$.51 in 2010³⁷). Private sector demand is limited by lack of awareness; lack of affordability; limited incentives for supply chain agents to sell RDTs; and regulations limiting the sale and administration of RDTs.

COMPONENT INTERVENTIONS

Active Interventions (*On-going and identified in UNITAID's landscape analyses*)

- **Creating a private sector market for malaria RDTs** – This project will catalyse the creation of a private sector market for malaria RDTs in five Sub-Saharan African countries by promoting diagnosis among providers and consumers; regulating prices in the distribution chain and managing provider incentives; ensuring RDT quality; making RDTs accessible to private providers through a reliable supply chain; and creating a conducive policy and regulatory environment. (*Implemented by Population Services International, Foundation for Innovative New Diagnostics [FIND], Malaria Consortium & WHO*)
- **Sustainable global and national quality control of malaria RDTs** – This project will support the WHO/FIND Product and Lot Testing programs, which produce and publish data on RDT performance and monitor the quality of batches of RDTs before use, respectively. The long-term sustainability of these programs will also be promoted through the development of quality control testing based on recombinant antigen panels, a move to user-fees to cover the costs of central evaluations, and transitioning lot testing to country programmes. (*Implemented by Foundation for Innovative New Diagnostics [FIND] & WHO*)

Potential interventions (*Identified in UNITAID's landscape analyses; not yet considered for funding*)

- Develop and scale-up new diagnostic tools that address current unmet needs such as pregnant women, low transmission/elimination settings, and populations affected by *P. vivax* infection.
- Support the scale-up of affordable, quality-assured, well-adapted and user-friendly RDTs in the public and private sectors and promote an integrated approach to fever management. For example, support the development of technologies and methods for quality control testing throughout the supply chain; standardization of RDT evaluation protocols; harmonization of RDT testing methods; and development of tests that reduce time to result (currently 15-25 minutes).

37 World Health Organization. *World Malaria Report 2011*. Geneva, World Health Organization, 2011.

Exploratory interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- Ensure a reliable supply of quality-assured RDTs by stabilizing prices and improving predictability of demand.

MEASURING SUCCESS

Expected market effect is particularly focused on generating sustainable and reliable demand for affordable, quality-assured, well-adapted and user-friendly RDTs in both public and private sectors. Specifically, the goal is that 60% of registered private sector outlets in RDT scale-up countries will have quality-assured RDTs available in stock. Acceptability targets include a 60% increase in the number of caregivers that request an RDT for febrile cases, and that 60% of private providers believe that RDTs are a trustworthy diagnostic tool. Efforts directed at quality aim to increase the market share of RDTs that meet WHO procurement criteria from 83% to 90%, and to increase the global RDT public-sector market that has been lot tested from ~30-50% to 80%. Additional improvement could be achieved through investments in the development of technologies that could improve POC testing or address unmet needs for malaria diagnosis.

Expected public health effects include increasing coverage of quality-assured malaria RDTs. Specifically, in RDT scale-up countries, coverage targets are that 30% of children under 5, and 30% of children over five years of age and adults, seeking fever treatment in the private sector receive an RDT; and 30% of children under 5, and 30% of children over five years of age and adults, testing positive for malaria in private sector outlets receive an effective antimalarial treatment. In addition, tools will be developed and used to estimate life-years gained for diagnostic interventions both ex-ante and ex-post towards design and implementation of highly cost effective interventions.

2

Affordable, adapted paediatric medicines

6.2 Strategic Objective 2: Increase access to affordable, adapted paediatric medicines to treat HIV/AIDS, tuberculosis, and malaria

6.2.1 Paediatric HIV/AIDS medicines

COMMODITY ACCESS ISSUES

In 2011, 3.3 million children aged 0-14 years old were living with HIV globally; 330,000 children were newly infected, more than 90% of whom (300,000) lived in sub-Saharan Africa.³⁸ Access to treatment among children

lags far behind that of adults: only 28% of children in need of treatment globally were receiving ART in 2011 (compared to 54% of adults), and 42 countries provide ART to <20% of treatment-eligible children (compared to just 10 countries with adult treatment coverage rates of <20%).³⁹ Despite these shortcomings, tremendous strides have been made in recent years to meet paediatric treatment needs, including increased access to new, child-friendly fixed-dose-combination (FDC) ARVs and progress in clinical trials that have evaluated new paediatric formulations.

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: Few safe and effective medicines are approved for paediatric use (of 26 ARVs approved for adults by the FDA, five are without paediatric indication; only 10 are approved for use in children under two). **Reasons:** Paediatric market is small in comparison with adult market (only 7% of total ARV market⁴⁰) and it virtually does not exist in high income countries. Therefore, there are few commercial incentives for developers of paediatric drugs; and there are long delays between the initiation of adult and paediatric trials. It takes time to adapt and evaluate formulations for paediatrics once an ARV has been approved for adult use.

Affordability: Paediatric HIV treatment is expensive: the recommended first-line therapy in infants,⁴¹ which contains a protease inhibitor, is up to twice the annual cost of the first-line regimen for adults (\$215-296 per paediatric patient annually, compared to adult TDF-based regimen at \$148⁴² per patient annually). **Reasons:** Market fragmentation is due to the requirement for multiple formulation doses for multiple weight bands. Greater cost for protease inhibitors. Greater supply chain costs for liquid formulations.

Acceptability/Adaptability: Key ARVs required to align paediatric and adult treatment are not yet formulated for paediatric use in resource-limited settings; missing formulations among ARVs currently recommended for children include TDF/3TC/EFV scored dispersible tablets, heat-stable LPV/r dispersible formulations, and heat-stable RTV 25mg⁴³ (with this list likely to expand in the near future as guidelines evolve). Current formulations have severe limitations, including high alcohol content in syrups, poor taste, and logistical complexities that are inherent in transporting liquids in resource-limited settings. **Reasons:**

38 UNAIDS. Global Report on the AIDS epidemic. Geneva, UNAIDS, 2012.

39 UNAIDS. Global Report on the AIDS epidemic. Geneva, UNAIDS, 2012.

40 Interagency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers, and their Children. *Report of the Meeting of the Paediatric Working Group, Developing an Optimized list of Paediatric ARV Formulations*. Geneva, Switzerland, May 5, 2011.

41 LPV/r 80/20 mg/ml syrup plus either AZT/3TC 60/30 mg or ABC/3TC 60/30 mg dispersible tablets

42 Lowest price reported into the Price and Quality Reporting Mechanism (PQR) of the Global Fund, through Voluntarily Pooled Procurement (VPP) into 2012 [http://www.theglobalfund.org/en/procurement/pqr/, accessed 21 March 2013]

43 WHO Short-Term Priorities for Antiretroviral Drug Optimization Meeting Report. London, UK. April, 2011.

Few incentives for investment in development of paediatric formulations (due to small patient population relative to adults).

Delivery: Inconsistent and unreliable supply of paediatric ARVs, including stock-outs and long lead times. **Reasons:** fragmented demand across more than 50 formulations and dosages. Overall market size is small, resulting in orders that are often below optimum batch size. As a result, manufacturers delay orders to combine them to reach minimum batch size. Lead times as long as 6-9 months were the norm prior to demand aggregation that was part of the UNITAID/CHAI paediatric ARV project, which has brought lead times down to 3 months. Since the transition of this project, lead times for low-volume products have increased to up to 7 months. Country treatment programs may not have necessary contacts with paediatric ARV manufacturers or the procedures in place for the supply chain management of paediatric ARVs.

Few children are initiated on HIV treatment prior to 18 months of age as recommended. **Reasons:** Poor access to EID (<26%) results in fewer HIV-positive children being diagnosed promptly and initiated on treatment. Fewer children initiated on treatment also reduces the potential market size and can affect attractiveness of the market to developers for engaging in R&D.

COMPONENT INTERVENTIONS

Active Interventions (*On-going and identified in UNITAID's landscape analyses*)

- **Paediatric HIV/AIDS project** – Implemented since 2006 and scheduled to transition from UNITAID in 2013, the paediatric HIV/AIDS project has dramatically improved access to child-friendly FDC ARVs – replacing expensive liquid products that were a burden to health providers, children, and caregivers. The project has pooled procurement across 40 countries and aggregated demand forecasting, giving suppliers increased incentive to manufacture and innovate while significantly improving the functioning of the market for these drugs. (*Implemented by Clinton Health Access Initiative*)
- **Development of child-friendly lopinavir/ritonavir (LPV/r) FDCs and ritonavir (RTV) booster** – This project will develop and seek registration of two new first-line combinations as sprinkles containing LPV/r with two nucleotide reverse transcriptase inhibitors (NRTIs) (one combination with abacavir (ABC)/3TC and the other one with zidovudine (AZT)/3TC). All components of the combination will be developed in the form of tasteless granules that are heat stable and presented in a single package. The project will develop and register a complementary stand-alone granule formulation of ritonavir that can be added to the 4-in-1 LPV/r-containing combination during simultaneous treatment of HIV and TB. (*Implemented by Drugs for Neglected Diseases Initiative*)

Potential interventions (*Identified in UNITAID's landscape analyses; not yet considered for funding*)

- **Establish a system to consolidate and satisfy demand for paediatric ART** – Despite the gains achieved in the UNITAID paediatric HIV/AIDS project described above, the paediatric market is not yet stable and many challenges threaten the reliable and timely supply of paediatric ARVs. The paediatric HIV medicines market continues to be small, fragmented and fragile; interventions ensuring coordination are needed to protect the gains and continue the scale-up momentum created by UNITAID's first paediatric HIV/AIDS project.

Exploratory interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- **Make new paediatric ARV combination formulations available in the shortest time possible** – Paediatric clinical trials typically initiate with great delay following adult trials, due to lack of projected revenue and complexities inherent in evaluating the pharmaceutical safety and efficacy of a new drug in children. There may be scope for UNITAID intervention to create incentives for stakeholders (e.g. prize funds, advanced market commitments) that decrease the delay between adult approval of a given regimen and its adaptation for children.
- **Support scale-up of the WHO's Option B+ in countries** for the prevention of mother-to-child transmission.

MEASURING SUCCESS

The development of combination ARV treatments in sprinkles will have significant public health effects as it will ensure that infants and young children, including those co-infected with TB, have access to WHO-recommended regimens using the best-adapted ARV formulations. With the availability of these products starting in 2015, market effects will include a subsequent reduction from eight to three in the number of paediatric formulations needed for countries to comply with WHO-recommended first-line treatment for infants and young children. A decrease in price of approximately 20% is expected for these new products, as compared to the currently available protease inhibitor-based first-line therapy for infants (which costs \$250 to \$350 per patient per year, depending on the NRTI backbone). In addition, a direct reduction in shipping costs from approximately \$100 per patient per year with liquid PI-based regimens to \$10 with sprinkle formulations is anticipated.⁴⁴

The previous UNITAID paediatric HIV/AIDS project led to a dramatic increase in the number of children on treatment (340,000 children were on treatment in UNITAID-supported countries at the end of 2011 compared to 10,000 children in 2005), enabling: (i) an 80% reduction in prices across paediatric formulations since 2006, (ii) an increase in the number of generics and adapted formulations available, and (iii) coordination and aggregation of orders that helped avoid treatment interruption due to stock-outs, thereby improving health outcomes and slowing disease progression in children.

A new intervention in this area would protect access for children on ART and ensure continued supply for the 65% (26 out of 40) of countries that have fewer than 7,000 children on treatment and for which disaggregated ordering creates significant risk for supply disruptions.

44 Based on market impact targets proposed by DNDi (UNITAID-funded intervention).

6.2.2 Paediatric tuberculosis medicines

COMMODITY ACCESS ISSUES

Tuberculosis is one of the top 10 causes of death in children: WHO estimates that there were 490,000 cases of TB in children under 15 years in 2011.⁴⁵ Actual figures are likely much higher due to challenges in diagnosis; up to 1 million children may need treatment for TB each year.⁴⁶ Access to TB care is poor: only 327,000 of paediatric TB cases were reported to national TB programs in 2011,⁴⁷ and survey data suggest that only half of the cases are treated in some key high-burden countries.⁴⁸ While WHO-prequalified FDCs of the four commonly used first-line medicines exist, none is aligned with the dosages recommended in the 2010 WHO treatment guidelines.⁴⁹ For patients with multi drug-resistant TB (MDR TB) requiring second-line therapy, the current treatment is a combination of injectable and oral drugs with substantial side effects. The TB pipeline includes medicines that could be adapted for children, but this population is typically not prioritized in clinical trials. For example, 2013 sees the launch of the first novel medicines in 40 years aimed at MDR TB,⁵⁰ but paediatric versions of these medicines will arrive substantially later to the market.

MARKET SHORTCOMINGS AND THEIR REASONS

Affordability: Paediatric TB medicines are more expensive than those for adults: a 6-month course of quality-assured, first-line TB drugs costs 40% more (\$22 for adults but \$30 for children),⁵¹ despite containing less active ingredient. **Reasons:** Few suppliers for quality-assured formulations. Small market and fragmented demand increased risk for manufacturers. Higher costs in product development (e.g. formulation, dosing, safety evaluations) and greater complexity in manufacturing.

Quality: Only 1 in 5 children with TB received quality-assured drugs via the Global Drug Facility,⁵² meaning many children are receiving unknown quality drugs in non-standard doses (e.g. split adult FDC). **Reasons:** No appropriately-dosed FDC on the market. A majority of the market is in private sector and the public sector of countries without a stringent regulatory authority.

Acceptability/Adaptability: No appropriately-dosed, quality-assured, paediatric FDC on the market consistent with the 2010 WHO treatment guideline revision. Delays in paediatric trials for novel medicines (≥ 7 year lag between adult and paediatric formulations, despite the requirement for submission of a plan for paediatric development when seeking registration for a novel drug for adults). For second-line drugs, only amikacin and levofloxacin exist in paediatric formulations, but are not widely available. **Reasons:** Small, fragmented quality-assured paediatric market that is unattractive to developers (i.e., low return on investment due to very limited demand). Additional costs of product development. Uncertain regulatory and quality requirements.

45 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

46 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

47 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

48 Detjen, A.K et al. A survey of the adoption of revised dosage recommendations for childhood tuberculosis in countries with different childhood TB burden. *Public Health Action* 2012, 2 (4): 126-132.

49 WHO. *Rapid advice: treatment of tuberculosis in children*. Geneva, World Health Organization, 2010.

50 FDA approves bedaquiline for TB treatment; first new drug in 40 years. Critical Path to TB Drug Regimens, 10 Jan 2013 (<http://cptrinitiative.org/2013/01/10/fda-approves-bedaquiline-for-tb-treatment-first-new-drug-in-40-years/>, accessed 11 Feb 2013).

51 Global Drug Facility Product Catalogue. WHO Stop TB Partnership (<http://www.stoptb.org/gdf/drugsupply/pc2.asp?CLevel=2&CParent=4>, accessed 9 Feb 2013).

52 TB Alliance, unpublished data, 2012 (estimates based on GDF data)

Delivery: Paediatric TB medicines are often subject to supply shortages and stock-outs; prequalified products have long lead times (e.g. the Global Drug Facility reported an average lead time of 146 days in the first half of 2012).⁵³ **Reasons:** Limited number of quality-assured finished product and active ingredient suppliers. Lack of reliable forecasting, and low and variable demand contributes to 'made-to-order' production.

TB diagnostics are not appropriate for children. 90% of children with TB are smear negative, and specimen collection in children is challenging.^{54, 55} **Reasons:** Smear microscopy is not suited for children because: it requires sputum, which is hard to collect from children; children have low levels of mycobacteria in sputum; and children are prone to extrapulmonary TB.

COMPONENT INTERVENTIONS

Active Interventions *(On-going and identified in UNITAID's landscape analyses)*

- **Development of appropriate TB medicines for children** – This project will map the paediatric market; develop appropriately-dosed, quality-assured, fixed-dose TB medicines for children; and drive policy and regulatory change to scale-up treatment. *(Implemented by TB Alliance)*
- **Paediatric TB medicines scale-up** – This project has provided over a million curative and preventive medicines for children in 57 countries. *(Implemented by the Global Drug Facility)*

Potential interventions *(Identified in UNITAID's landscape analyses; not yet considered for funding)*

- Consolidate demand, negotiate prices, and scale-up quality-assured medicines.
- Scale-up paediatric-focused TB diagnostic products and programs to improve case-finding and subsequent access to appropriate TB medicines for children.

Exploratory interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- Incentivize development and facilitate uptake of novel TB diagnostics appropriate for children; develop mechanisms to accelerate paediatric clinical trials of novel compounds/regimens.

MEASURING SUCCESS

Expected market effects include the development of healthier markets that can sustain access to appropriate and affordable TB medicines for children. Availability and access targets focus first on getting appropriate products to market (at least 3 new formulations⁵⁶), followed by rapid scale-up. Challenges in scale-up notwithstanding, UNITAID's long-term role would be to scale-up from 30% of children currently diagnosed receiving quality assured treatment, to almost all children receiving quality-assured treatment ($\geq 80\%$ access would mean an additional 160,000 children on treatment each year at current rates of diagnosis).⁵⁷ Public health effects will be both direct, in addressing the current conservative estimate of 64,000 children who die of TB each year,⁵⁸ and indirect, through infections averted.

53 UNITAID, unpublished data, 2012 (reported project data)

54 Nguyen Thi Quynh Nhu, et al. Evaluation of Xpert MTB/RIF and MODS assay for the diagnosis of paediatric tuberculosis. *BMC Infectious Diseases* 2013, 13:31. <http://www.biomedcentral.com/1471-2334/13/31>

55 Swaminathan S and Rekha B, Paediatric Tuberculosis: Global Overview and Challenges. *Clin Infect Dis.* (2010) 50 (Supplement 3): S184-S194. http://cid.oxfordjournals.org/content/50/Supplement_3/S184.full

56 Based on market impact targets proposed by TB Alliance (UNITAID-funded intervention).

57 UNITAID assumption on achievable increase in coverage; current coverage and impact in terms of patient numbers based on data from: WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

58 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

6.2.3 Paediatric malaria medicines

COMMODITY ACCESS ISSUES

ACTs are recommended for the first-line treatment of uncomplicated *P. falciparum* malaria in infants and children. In Africa, a region that accounts for 80% of the 219 million total annual malaria cases⁵⁹, fewer than 20% of children who receive an antimalarial in the public sector receive an ACT (median across 12 countries).⁶⁰ In the private sector, this figure drops to less than 10%. While dispersible tablets offer advantages for children in terms of palatability and dosing⁶¹, limited data from the Affordable Medicines Facility - malaria (AMFm)⁶² shows that their availability in registered pharmacies (11-14%) is lower than that of paediatric packs of solid tablets (42-48%).⁶³ Of the estimated 660 000 annual global deaths from malaria, 86% occur in children under 5 years of age.⁶⁴ WHO recommends injectable artesunate for the treatment of severe malaria, as well as rectal artesunate for pre-referral treatment.⁶⁵ However, in 2011 procurement volumes of injectable artesunate were less than 5% of the total needed to treat global annual cases. Further, no rectal artesunate product has been WHO-prequalified or approved by a stringent regulatory authority (SRA). The malaria medicine pipeline includes two paediatric ACT formulations in late stage development.

MARKET SHORTCOMINGS AND THEIR REASONS

For the most commonly used ACTs, adult and paediatric treatments consist largely of the same formulations sold as solid oral tablets in different pack sizes, though two artemether-lumefantrine (AL) dispersible tablets are WHO prequalified and different dosages of artesunate-amodiaquine exist for infants, toddlers and children/adults. The market shortcomings for ACTs as a whole also apply to paediatric pack sizes; these are described under Strategic Objective 4 (Section 6.4). In addition, the following market shortcomings have been identified which are specific to paediatric malaria medicines:

Availability: No rectal artesunate product has been WHO-prequalified or approved by a SRA, despite being recommended by WHO for the pre-referral treatment of severe malaria. **Reasons:** one rectal artesunate product is currently under review by a SRA but has not yet been approved; unknown market size.

Acceptability/Adaptability: Low uptake of child-friendly ACT formulations. **Reasons:** only one prequalified manufacturer of dispersible tablets until December 2012; variable demand for dispersible tablets by different providers and caregivers; multiple non-prequalified paediatric formulations (e.g. suspensions) are available in local markets.⁶⁶

59 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

60 Household surveys, 2010-2011, 12 African countries (Angola, Burkina Faso, Burundi, Liberia, Madagascar, Malawi, Nigeria, Rwanda, Senegal, Uganda, United Republic of Tanzania, Zimbabwe). In: World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

61 Adbulla and Sagara. Dispersible formulation of artemether/lumefantrine: specifically developed for infants and young children. *Malar J*. 2009 Oct 12;8 Suppl 1:S7.

62 In the Affordable Medicines Facility for malaria (AMFm), subsidized or co-paid ACTs are provided through the public and private sectors. In March 2011, the co-payment structure was revised to favour child packs, which increased share of child packs from 32% to 69% of approved orders between March 2011 and August 2012.

63 Health Action International. Retail prices of ACTs co-paid by the AMFm and other antimalarial medicines: Ghana, Kenya, Madagascar, Nigeria, Tanzania and Uganda. Report of price tracking surveys. September-October 2012. Available from: <http://www.theglobalfund.org/en/amfm/pricetracking/>.

64 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

65 WHO Guidelines for the treatment of malaria, 2nd edition - Rev. 1. April 2011.

66 Juma EA, Obonyo CO, Akhwale WS, Ogutu BR. A randomized, open-label, comparative efficacy trial of artemether-lumefantrine suspension versus artemether-lumefantrine tablets for treatment of uncomplicated Plasmodium falciparum malaria in children in western Kenya. *Malar J*. 2008;7:262.

Delivery: Low uptake of injectable artesunate for severe malaria. **Reasons:** Inadequate advocacy, education and training, leading to poor acceptance by patients and providers; high treatment prices (3 times more than injectable quinine) due to low volumes and lack of competition; buyer concerns over single prequalified supplier; commercial interests around injectable quinine which is often procured from local manufacturers.

COMPONENT INTERVENTIONS

Active Interventions (*On-going and identified in UNITAID's landscape analyses*)

UNITAID has several interventions aimed at improving access to ACTs, including paediatric packs/formulations. These are described under Strategic Objective 4 (Section 6.4). In addition, the following interventions actively target improved access to malaria treatment in children:

- **The Affordable Medicines Facility – malaria (AMFm)** is a funding mechanism designed to increase access to ACTs, thereby reducing malaria-related deaths and delaying widespread resistance to artemisinin. The project includes price reductions through negotiations with manufacturers; a buyer subsidy through a 'co-payment' for ACTs at the top of the global supply chain; and supporting interventions to promote appropriate use of ACTs. In March 2011, the co-payment structure was revised to favour paediatric packs of AL (85% of all co-paid ACTs). By July 2011, the proportion of paediatric packs of AL had increased from 32% to 49% of approved orders. The implementation of demand-shaping levers further increased the relative proportion of child packs, which reached 69% during the period January to August 2012.
- **Improving severe malaria outcomes** – This project, implemented across six Sub-Saharan African countries, will expand access to quality-assured injectable artesunate by increasing public sector acceptance and use; encouraging market entry of a second supplier; securing lower prices through negotiation and increased competition. The project will also evaluate market demand for pre-referral treatment of severe malaria (rectal artesunate) and support the market entry of a WHO-prequalified product. (*Implemented by Medicines for Malaria Venture, Clinton Health Access Initiative & Malaria Consortium*)

Exploratory interventions (*Identified by stakeholders; full landscape analysis and vetting pending*)

In addition to potential and exploratory interventions to improve access to ACTs more broadly (see Strategic Objective 4 [Section 6.4]), which will inherently include paediatric treatments, the following exploratory intervention has been identified that specifically targets paediatric malaria medicines:

- **Ensure appropriate use of child-friendly ACT formulations, and minimize resistance**, e.g. through novel strategies to increase the use of RDTs and ACTs in the private sector, and improved monitoring of estimated needs and consumption volumes.

MEASURING SUCCESS

Expected improvements include markets that provide high-quality, affordable, well-adapted ACTs to children in both public and private sectors. As per RDT scale-up efforts, targets for improved malaria case management could include 30% of children testing positive for malaria in the private sector outlets receive an effective antimalarial treatment.⁶⁷ AMFm has been evaluated against the following market effects benchmarks: 20% increase in the availability of quality-assured ACTs at outlets; less than 3-fold price difference between quality-assured ACTs and the most popular antimalarial that is not a quality-assured ACTs; price of quality-assured ACTs is less than three times the price of the most popular antimalarial that is not a quality assured ACT and is less than that of artemisinin monotherapy tablets; 10% increase in the market share of quality-assured ACTs; and decrease in market share of oral artemisinin monotherapy. Public health effect has been measured as a 5% increase in the percentage of febrile children who receive an ACT. For injectable artesunate, market effects will be measured against the following targets: up to tenfold increase in the use from less than 2 million vials in 2011 to 20-25 million vials in 2016; price reductions of 30-35% compared to \$1.48 in 2012; and market entry of at least one additional supplier. Estimated public health effect is an estimated 110,000 to 140,000 additional lives saved between 2013-2016 through the use of injectable artesunate in place of quinine. The estimated effect of introducing a WHO-prequalified, pre-referral treatment for severe malaria is currently difficult to quantify but may be substantial given the magnitude of the underlying health problem. Market research is planned that will assist in understanding current and future potential demand.

67 Based on targets developed for the project *Creating a Private Sector Market for Quality-Assured RDTs in Malaria Endemic Countries*.



6.3 Strategic Objective 3: Increase access to emerging medicines and/or regimens as well as new formulations, dosage forms, or strengths of existing medicines that will improve treatment of HIV/AIDS and coinfections such as viral hepatitis

6.3.1 HIV/AIDS medicines

COMMODITY ACCESS ISSUES

Thirty-four million people are infected with HIV, although up to half of them are not aware of their status. Access to life-saving ART has increased dramatically in recent years; however, significant unmet need remains, despite rapid scale-up of better-adapted and affordable treatment. In 2011, 8 million people, or 54% of those in need of treatment according to current WHO guidelines⁶⁸, were receiving ART in low and middle income countries. An additional 7 million people must be enrolled in treatment by 2015 to meet global targets, which, moreover, are based on conservative eligibility criteria.⁶⁹ In 2011, only 30% of pregnant women and 28% of all eligible children were receiving ART (see Strategic Objective 2).⁷⁰

There have been recent approvals for new combination ART regimens, and there are promising novel drug candidates in the pipeline. However, most short- to medium-term opportunities to improve access depend on optimizing existing ARVs to reduce production costs and decrease toxicity. Mechanisms for these short-term opportunities include dose reduction, reformulation, and improved process chemistry. For new drugs to make a difference in resource-limited settings, they must be safe, effective, robust, affordable, and suitable for multiple patient groups (e.g. pregnant women, children) and co-infected patients (TB, viral hepatitis). One product in late-stage development (the integrase inhibitor, dolutegravir, which has been submitted for regulatory review with approval expected in 2013) has been identified as having particularly high, nearer-term potential for resource-limited settings. Products further back in the pipeline could also have significant advantages for resource-limited settings such as tenofovir pro-drugs, including the Phase III tenofovir alafenamide fumarate. Other promising new approaches include new uses for existing ARVs such as ritonavir boosted darunavir, and the use of newly-approved medicines such as a new FDC containing elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate, as well as other co-formulations under development. However, the role of newly developed FDCs, in particular in resource-limited settings, will likely be limited in the short term due to intellectual property (IP) barriers⁷¹. In addition, some of the co-formulations may not be ideal for resource-limited settings due to higher manufacturing costs over current first-line ARVs. Ultimately, this may result in a disconnect, where standard regimens used in high-income countries cannot be used in resource-limited settings.

68 Initiation of ART (in WHO clinical stages 1 or 2) for adults and adolescents (excluding certain groups) is recommended at a CD4 count of ≤ 350 cells/mm³ (Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach, WHO 2010)

69 2012 UNAIDS Global Report.

70 2012 UNAIDS Global Report.

71 UNITAID will continue to support the Medicines Patent Pool's work to address these barriers, as described under 'Component Interventions', below.

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: There is an absence of treatments that standardize regimens across all groups, and that are easy to take (including long-acting formulations), well tolerated, durable, formulated for use in resource-limited settings, and can be administered by health providers with minimal training. **Reasons:** Low level of dedicated research & development (R&D) investments in HIV therapy for populations/co-infected patients that are prevalent in resource-limited settings. Low profitability of the market in generalized epidemics means pharmaceutical companies focus on more profitable markets such as developed country ARV markets.

Affordability: High prices of existing products⁷². Tenofovir- and zidovudine-based first-line regimens in FDCs are up to three times as expensive as the previous WHO recommended stavudine-based regimens, with some countries slow to switch to the superior products (for example, tenofovir/lamivudine/efavirenz \$158 per person per year; zidovudine/lamivudine/nevirapine \$103 per person per year, and stavudine/lamivudine/nevirapine \$54 per person per year).⁷³ Second-line regimens are more than twice as expensive as first-line regimens (e.g. atazanavir/ritonavir plus zidovudine/lamivudine at \$359 per person per year compared to TDF based regimen at \$158 per person per year); third-line regimens are at least 15 times more expensive than first-line regimens (e.g. raltegravir, darunavir plus etravirine is \$2,398 per person per year⁷⁴ compared to TDF based regimen, which is \$158 per person per year). **Reasons:** High API and production costs for tenofovir, efavirenz, lopinavir/ritonavir, and third-line medicines. Current lack of economies of scale due to insufficient ascertainment of need for atazanavir/ritonavir and some third-line drugs, with limited access to viral load testing.

High prices for new products and lack of adaptability to resource-limited settings. Recently approved, multi-class combination products, such as elvitegravir/cobicistat/emtricitabine/tenofovir, have been priced at \$28,000 in the US, with no differential pricing available. **Reasons:** New ARVs could be subject to IP constraints that lead to high prices in the absence of generic competition. Additionally, manufacturing complexity for new co-formulations may mean that generic prices are higher than current regimens, irrespective of IP constraints.

Acceptability/Adaptability: No darunavir/ritonavir heat stable FDC available to support greater use. No FDCs for WHO-recommended second-line regimens. **Reasons:** Recommended ARVs for co-formulation were originally produced by different companies; lack of incentive for investment; low volumes make the market less attractive to manufacturers.

Delivery: Low uptake of second-line regimens (only 3.7% of adults on ART were on second-line treatment by December 2011 in low and middle income countries for all regions, except Latin America where 21.4% of adults on ART were on second-line⁷⁵); almost no uptake of third-line regimens in low income countries where 0.1% of adults on ART were on third-line regimens for all regions except Latin America which is at 1.7%.⁷⁶ **Reasons:** In addition to the affordability and acceptability issues discussed above, other factors that might explain poor uptake include unavailability of viral load testing to inform treatment switching, and lack of incentives for manufacturers to register ARVs in low income countries.

Lack of clear and standardized recommendations for third-line regimens.

72 Medecins Sans Frontieres, Untangling the Web of Antiretroviral price reductions, MSF, July 2012.

73 Lowest price 2012 reported by the Voluntarily Pooled Procurement (VPP) to the Global Fund's Price and Quality Reporting Mechanism (PQR) [<http://www.theglobalfund.org/en/procurement/pqr/>, accessed 21 March 2013]

74 Highest 2011-2012 prices reported to the Global Fund's PQR for such regimen are up to \$29,439 in a given country [<http://www.theglobalfund.org/en/procurement/pqr/>, accessed 21 March 2013]

75 2012 WHO ARV Survey (<http://www.who.int/entity/hiv/amds/1-PP7.pdf>)

76 2012 WHO ARV Survey (<http://www.who.int/entity/hiv/amds/1-PP7.pdf>)

COMPONENT INTERVENTIONS

Active Interventions *(On-going and identified in UNITAID's landscape analyses)*

- **Market intelligence for active pharmaceutical ingredients** – This project will clarify market drivers, highlighting potential market-based interventions to alleviate problems rooted in this 'upstream' market, including high prices, quality issues, limited competition, long lead times, and stock-outs. *(Implemented by the William Davidson Institute)*
- **Medicines Patent Pool (MPP)** – This innovative project aims to facilitate generic competition and boost the formulation of adequate FDCs and paediatric forms through the creation of a 'one-stop shop' for voluntary licenses for ARVs. It has set up a widely-used patent status database on ARVs. *(Implemented by the Medicines Patent Pool Foundation)*
- **Preventing patent barriers** – This project focuses on pre-grant oppositions by the Lawyers Collective in India. Pre-grant oppositions are administrative safeguards that can help prevent the granting of low quality patents, thereby helping to prevent undue delay in generic competition. *(Implemented by the Lawyers Collective)*

Potential interventions *(Identified in UNITAID's landscape analyses; not yet considered for funding)*

- **Decrease prices and increase access to second-line treatment** – Following WHO prequalification and FDA approval of atazanavir/ritonavir FDC in late 2011, catalytic interventions could be launched to shift second-line market from lopinavir/ritonavir to atazanavir/ritonavir, recognizing certain clinical limitations of atazanavir/ritonavir. While potential cost savings have not yet been fully examined, the lower production costs of atazanavir/ritonavir could generate savings to expedite second-line scale-up.
- **Secure API supply for antiretrovirals** – Via the WDI project, described above, UNITAID is exploring whether there is potential to create incentives for API suppliers and manufacturers that support expansion of upstream API production where needed.
- **Support market entry and facilitate uptake of new, cost effective ARVs**, new ARV doses, and new regimens, pending successful results from on-going research and WHO recommendation, including support for regimens combining novel and existing products that are targeted at generalized epidemics and resource-limited settings.

Exploratory interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- **Facilitate entry of new products/enable access to improved first-line combination ARV treatments as they become available** – UNITAID may explore opportunities to support the development of information to support scale-up, and improve access to superior treatments.
- **Support scale-up of the WHO's Option B+ in countries** for the prevention of mother-to-child transmission.
- **Support and consolidate market information for use in forecasting** to reduce market risk for suppliers and reduce prices or lead times.

MEASURING SUCCESS

Expected market effects include development of competitive treatment markets that provide quality-assured, affordable, well-adapted products to those in need, with potential investment to induce

uptake of game-changing technologies for use in resource-limited settings. These would include (i) second-line ART for those who fail first-line treatment and (ii) first-line ART adapted for use in community-based HIV programs, which if brought to scale may have the potential to revolutionize HIV prevention, treatment, and care.

Opportunities for cost savings exist from dose reduction for products such as efavirenz – which could total as much as \$150 million over the short term – until potentially superior products, such as dolutegravir, enter the market. In second-line treatment, potential cost savings of around \$50 million over the next three years may be realized from switching from lopinavir/ritonavir to atazanavir/ritonavir.⁷⁷ There may be additional gains in quality of care around darunavir, where interventions that dramatically increase volume could bring prices closer to those of lopinavir/ritonavir.

Public health effects will focus on introducing and scaling up more affordable, durable, safer, and easier to use regimens. In addition, supporting expanded access to second and third-line regimens would increase survival and improve quality of life for patients failing first-line regimens.

6.3.2 HIV co-infections medicines

COMMODITY ACCESS ISSUES

There is a paucity of global epidemiological and commodity access data describing HIV-related co-infections including opportunistic infections (OIs). WHO has developed an initial priority list of HIV co-infections to inform guideline development;⁷⁸ however a full review of their respective current prevalence and importance in the ART era has yet to be undertaken. It is assumed that, in the medium term, the relative frequency of many OIs (e.g. cryptococcal meningitis, cytomegalovirus diseases, other bacterial infections) will continue to decrease in low and middle income countries with the expansion of ART. For now, however, the leading cause of death for PLWHA continues to be TB.

There are particular challenges surrounding currently used treatment commodities for a number of co-infections, primarily linked with health systems challenges (e.g. laboratory and cold chain capacity) in resource-limited settings; in addition, in some cases (e.g. cryptococcal meningitis, and especially cytomegalovirus diseases), interventions to expand the use of safer and more effective treatments are challenged by the declining burden of disease resulting from expanded access to ART.

Co-infection, with either TB or hepatitis B (HBV), is significant in terms of disease burden. UNITAID has contributed to increased access to adequate TB medicines and diagnostics and, as an indirect result of its HIV medicines interventions, contributed to increased access to ARVs with activity against HBV (i.e. tenofovir, lamivudine and emtricitabine).

Although epidemiological data are extremely limited, it is estimated that there is a high burden of co-infection with HIV and the hepatitis C virus (HCV) (estimated 4-5 million PLWHA). HCV co-infection is associated with increased rates of both liver-related and AIDS-related death in people living with HIV.⁷⁹ ⁸⁰ Small epidemiological studies have shown varying prevalence of HIV/HCV co-infection by country and

77 CHAI unpublished estimates.

78 WHO Priority OIs' List, 16th International Conference on AIDS and STDs, 2011

79 Operskalski EA, Kovacs A: HIV/HCV Co-infection: pathogenesis, clinical complication, treatment and new therapeutic technologies. *Curr HIV/AIDS Rep* 2011, 8:12-22.

80 Von Shoen-Angerer T, Cohn J, Swan T, Piot P: UNITAID can address HCV/HIV co-infection. *Lancet* 2013,381:628.

setting, from <1% in Kenya to >20% in settings in Niger.⁸¹ Global access data for HCV treatment are also sparse. A recent systematic review of treatment outcomes for HCV in HIV-infected individuals highlights the fact that treatment is often unavailable in resource-limited settings: only three reports of treatment outcomes were from middle income countries; none were from low income countries, and none were from Africa.⁸² While UNITAID is in early stages of investigating the markets for HIV co-infections, there is widespread agreement that the pipeline for new HCV treatments includes promising potential oral medicines, with direct-acting antivirals (DAAs) expected to be on the market in 2015 and four large pharmaceutical companies in a position to develop their own FDCs. One added benefit of these new medicines is that they require no testing for HCV genotype prior to treatment. If these drugs emerge successfully from the pipeline, the products could revolutionize treatment for HCV, including for those living with HCV/HIV co-infection. However, without appropriate market intervention, it can be expected that they will be unaffordable and inaccessible in resource-limited settings.

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: Only two versions of pegylated interferon (PegIFN) exist that are approved by stringent regulatory authorities. No novel HCV oral medicines are currently available that can be used without combining PegIFN and ribavirin. **Reasons:** Complex regulatory pathway for IFN biosimilars with uncertain outcome; lack of clarity about size of ultimate market for HCV treatments. HCV has become a focus of research by pharmaceutical companies, resulting in a pipeline of novel products – however, this is a relatively recent trend and no products are yet approved.

Affordability: Current PegIFN-based treatment regimens are unaffordable for resource-limited settings (prices for PegIFN in low and middle income countries vary from \$8,000-28,000 USD for a full course of 48 weeks, with the exception of \$2,624 USD in Egypt). **Reasons:** Additional landscaping is needed, but reasons likely include lack of competition due to the fact that there are no biosimilar products on the market that are WHO prequalified or are approved by a stringent regulatory authority. This, in turn, may be due to patents as well as the lack of a clear regulatory approval pathway for biosimilars.

Quality: Absence of information on quality of alternative biosimilar PegIFN products. **Reasons:** No registration of alternative products by a stringent regulatory authority; no WHO guidelines or operational WHO prequalification mechanism for biosimilars.

Acceptability/Adaptability: PegIFN is an injectable product that can have significant side effects and varying efficacy (45-80% depending on HCV genotype, 25-60% for HIV co-infected populations). **Reasons:** Patients must be monitored to assess efficacy of treatment (access to relevant diagnostic tests may pose challenges in resource-limited settings); side effects may result in discontinuation; current HCV treatment complicates HIV treatment due to drug-drug interactions, creating additional, specific challenges for people with HCV/HIV co-infection.

Delivery: There is very limited uptake of the standard treatment of PegIFN and ribavirin in resource-limited settings. **Reasons:** Prohibitively high prices for even moderate scale-up of standard treatment; side effects.

81 Modi A. & Feld J. *Viral hepatitis and HIV in Africa*. AIDS Reviews, 2007 9:25-39.

82 Davies A., et al. *Treatment Outcomes of Treatment-Naïve Hepatitis C Patients Co-Infected with HIV: A Systematic Review and Meta-Analysis of Observational Cohorts*. 2013, PLoS ONE 8(2): e55373.

COMPONENT INTERVENTIONS

Exploratory interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- **Make affordable treatment regimen available for HIV/HCV co-infections** – There appear to be potential opportunities for UNITAID to intervene in the market in order to improve or accelerate access to HCV treatment for those with HCV/HIV co-infection. In view of the importance of HCV as a co-morbidity, this could significantly impact on treatment outcomes. UNITAID will further explore this market, as well as the markets for treatments for HBV and other HIV co-infections, to more accurately determine whether there is scope for potential interventions.
- **Consolidate demand and negotiate prices for key HCV diagnostics**, including initial diagnostic tests and viral load technologies.

MEASURING SUCCESS

Expected market effects include development of competitive treatment markets that provide high-quality, affordable, well-adapted products to those in need, with potential investment to induce uptake of new oral therapies for HCV and improve access to medicines needed to treat other HIV co-infections. Expected public health effects will be determined by the scope and focus of the potential and exploratory interventions that are operationalized.

As stated in the UNITAID Constitution, the fight against HIV/AIDS, TB and malaria is the organization's main priority (section 4.2 Scope). Any intervention(s) in the market for medicines for HIV co-infections would only be considered if detailed landscape analyses demonstrated a positive impact of intervening in this market. All potential interventions would have to be compatible with UNITAID's Strategic Objectives and should not divert resources away from UNITAID's main priority.



6.4 Strategic Objective 4: Increase access to artemisinin-based combination therapies (ACTs) and emerging medicines, that, in combination with appropriate diagnostic testing, will improve the treatment of malaria

6.4.1 Malaria medicines

COMMODITY ACCESS ISSUES

Substantial efforts have been made to scale-up access to ACTs since they were recommended as the first-line treatment of uncomplicated *P. falciparum* malaria by WHO in 2006.⁸³ The number of ACTs delivered by manufacturers has increased from 76 million in 2006 to 278 million in 2011, due largely to increased investments from international donors. However, despite considerable progress in recent years, widespread access to ACTs remains an issue. In Africa, a region that accounts for 80% of the 219 million total annual malaria cases⁸⁴, it is estimated that the number of ACTs distributed in 2011 represented only 55% of *P. falciparum* malaria cases seen in public facilities.⁸⁵ In the private sector where an estimated 40% of people with malaria seek care⁸⁶, availability of ACTs is low, particularly outside the Affordable Medicines Facility – malaria (e.g. <10% in Benin and <30% in DRC⁸⁷). The malaria medicine pipeline includes several products in late stage development that show high potential for public health and market effects, including a drug for treating the liver stage of *P. vivax* infection that could substantially reduce treatment duration and improve compliance, and a fully synthetic peroxide for use in the treatment of uncomplicated malaria which could be active in a single dose.

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: No alternative to primaquine for treating the liver stage of *P. vivax*; no single-dose ACTs to reduce current three-day dosing requirements. **Reasons:** Research is on-going but products are not yet available; lack of incentives for manufacturers to invest in R&D due to uncertainties around future demand, market size and return on investment; 8-aminoquinolines are the only class of drugs known to have anti-hypnozoite activity and all suffer from safety issues, especially in glucose-6-phosphate dehydrogenase (G6PD) deficient patients; two candidates for a single-dose cure for uncomplicated *P. falciparum* malaria are under development but earliest availability is 2018.

Affordability: High ACT retail prices (in AMFm countries, baseline unsubsidized prices in private retail outlets ranged from \$2.47 in Niger to \$5.99 in Zanzibar⁸⁸). **Reasons:** High manufacturing costs including expensive and variable raw material prices (artemisinin prices have ranged from \$170-1100/kg); semi-synthetic artemisinin could help to stabilize the supply and price of artemisinin but it is not yet available (regulatory dossier under review); suboptimal price competition; future integration of AMFm into Global Fund grant mechanisms suggests little scope for expansion of private sector subsidies.

83 Guidelines for the treatment of malaria. Geneva: World Health Organization; 2006.

84 Roll Back Malaria, Key Malaria facts, <http://www.rbm.who.int/keyfacts.html>

85 NMCP Reports. IN: World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

86 World Health Organization. *World Malaria Report 2010*. Geneva, World Health Organization, 2010.

87 ACT Watch Group (Population Services International, London School of Hygiene and Tropical Medicine). Outlet Survey results 2009 and 2010. In: World Health Organization. *World Malaria Report 2010*. Geneva, World Health Organization, 2010.

88 ICF International, London School of Hygiene and Tropical Medicine. Independent Evaluation of the Affordable Medicines Facility - malaria (AMFm) Phase 1. Multi-Country Baseline Report. March 22, 2012. Available from: <http://www.theglobalfund.org/en/amfm>.

Quality: Low market share of WHO-prequalified ACTs (e.g. <20% in Benin, <10% in DRC⁸⁹) with high quality control failure rates among non-prequalified ACTs (60% failure rate vs. <4% for prequalified ACTs⁹⁰) and non-artemisinin treatments (e.g. 28% failure rate for SP⁹¹). **Reasons:** Tight production capacity with low incentive for expansion due to uncertain future demand; regulatory loopholes allow significant market penetration by sub-standard or non-proven therapies; existence of counterfeit drugs that form the basis for a profitable business, which benefits from insufficient local quality control.

Acceptability/Adaptability: While ACTs are more widespread than in 2002-2006, their usage is still below that of non-recommended therapies. **Reasons:** Complex dosing regimen of ACTs.

Delivery: Public sector stock-outs of prequalified ACTs; low private sector availability of ACTs particularly outside the AMFm (e.g. <10% in Benin and <30% in DRC⁹²); unpredictable future demand. **Reasons:** Public sector supply is challenged by tight ACT production capacity due to reliance on agricultural raw ingredient with long production cycle; delays in funding disbursements; and sub-optimal in-country planning and supply management. Low private sector demand for ACTs is largely due to high ACT prices compared to non-artemisinin treatments (e.g. ACTs are 6 times more expensive than sulfadoxine pyrimethamine [SP] in Benin⁹³). Unpredictability of future demand is due to uncertainties around future funding and impact of prevention and control efforts.

COMPONENT INTERVENTIONS

Active Interventions (*On-going and identified in UNITAID's landscape analyses*)

- **The Affordable Medicines Facility – malaria (AMFm)** is a funding mechanism designed to increase access to ACTs, thereby reducing malaria-related deaths and delaying widespread resistance to artemisinin. The project includes price reductions through negotiations with manufacturers; a buyer subsidy through a 'co-payment' for ACTs at the top of the global supply chain; and supporting interventions to promote appropriate use of ACTs. This project was piloted in 8 countries and it will be integrated into core Global Fund grant management and financial processes in 2014.
- **UNITAID supports the production of quarterly global ACT demand forecasts** that predict the quantity of pre-qualified ACTs and artemisinin that will be procured. In light of future unpredictability of supply and demand situations, UNITAID will continue to maintain a forecasting service to ensure information is collected and communicated to all supply chain agents. (*Currently implemented by Boston Consulting Group, Clinton Health Access Initiative & Fundacion Zaragoza Logistics Center*)
- **Assured artemisinin supply service** – This project aimed to support an appropriate supply of *Artemisia* and artemisinin to meet the needs for ACTs, specifically through a revolving pre-finance facility to artemisinin extractors and the collection and sharing of market intelligence on artemisinin supply. (*Implemented by i+ solutions, Artepai, FSC Development Services Ltd, Triodos Sustainable Trade Fund*)

89 Poyer S. Role of the private sector in the delivery of antimalarials and diagnostic testing. Presentation at the 61st Annual Meeting of the American Society for Tropical Medicine and Hygiene. November 2012.

90 World Health Organization. *Survey of the quality of selected antimalarial medicines circulating in six countries of Sub-Saharan Africa*. Geneva, WHO 2011.

91 World Health Organization. *Survey of the quality of selected antimalarial medicines circulating in six countries of Sub-Saharan Africa*. Geneva, WHO 2011.

92 ACT Watch Group (Population Services International, London School of Hygiene and Tropical Medicine). *Outlet Survey results 2009 and 2010*. In: World Health Organization. *World Malaria Report 2010*. Geneva, World Health Organization, 2010.

93 ACT Watch. *The private commercial sector distribution chain for antimalarial drugs in Benin*. November 2009.

- **Market intelligence for active pharmaceutical ingredients** – This project will clarify market drivers, highlighting potential market-based interventions to alleviate problems rooted in this ‘upstream’ market: high prices, long lead times, and stock-outs. *(Implemented by the William Davidson Institute)*

Potential interventions *(Identified in UNITAID’s landscape analyses; not yet considered for funding)*

- **Support market entry and facilitate uptake of new, cost effective ACTs** and emerging medicines that, together with access to diagnostic testing, will improve treatment of malaria.
- **Support the development of a more structured and reliable artemisinin supply chain** to stabilize artemisinin prices and supply.
- **Ensure appropriate use of ACTs and minimize resistance**, e.g. through novel strategies to increase the use of RDTs and ACTs in the private sector, and improved monitoring of estimated needs and consumption volumes.

Exploratory interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- Support the sale of ACTs at an affordable retail price that does not require a subsidy.
- Improve treatment for malaria caused by non-*P. falciparum* infections through better access to appropriate diagnostics testing and treatment.

MEASURING SUCCESS

Expected improvements include medicines markets that provide high-quality, affordable, well-adapted ACTs to those in need in both public and private sectors, and market readiness for the next generation of malaria medicines. As per RDT scale-up efforts, targets for improved malaria case management could include 30% of people testing positive for malaria in the private sector outlets receive an effective antimalarial treatment. Public health effect has been measured as a 5% increase in the percentage of febrile children who receive an ACT. Additional improvements could be achieved by supporting the introduction of new products that offer the potential to improve malaria case management.



6.5 Strategic Objective 5: Secure supply of second-line tuberculosis medicines, and increase access to emerging medicines and regimens that will improve treatment of both drug-sensitive and multi drug-resistant TB

COMMODITY ACCESS ISSUES

In 2011, 2.5 million people with active TB – 30% of all new cases – were not treated according to WHO recommendations.^{94,95} Access for TB patients infected with drug-resistant strains is even lower – 19% of multidrug-resistant TB (MDR TB) cases received appropriate treatment.⁹⁶ Many TB drugs are of unknown quality, particularly in the private sector. Current regimens are long, and are complicated, costly, and toxic for MDR TB – negatively impacting patient adherence and, ultimately, outcomes. In 2011, fewer than half of patients with confirmed MDR TB successfully completed treatment.⁹⁷ Treatment interruptions may also contribute to this low adherence; supply disruptions are common for MDR TB medicines. Advances in the pipeline hold promise: the first novel TB medicines in over 40 years are to launch in 2013,⁹⁸ and shortened regimens and new drugs are in development.^{99,100}

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: Existing first-line regimens for drug-sensitive TB (DS TB) are long. MDR TB regimens are complex, expensive, long (20-24 months, including 8 months of injections), and have severe side effects.¹⁰¹ **Reasons:** Existing DS TB drugs are inexpensive, but MDR TB medicines target a small population (diminished further by under diagnosis), so the MDR TB market is far less attractive for investment in development compared to DS TB. Drug resistance evolves, making new drug development high-risk. The typical approach to TB drug development, one medicine at a time, means development of entirely novel regimens is long and challenging.¹⁰²

Affordability: Quality-assured MDRTB drugs are expensive (\$4,000-\$6,000+ per treatment course.)^{103,104} **Reasons:** Increased manufacturing costs driven by low total volumes, quality assurance requirements, lack of market transparency, market fragmentation from variable tender requirements by purchaser and complex production.¹⁰⁵ Limited competition: few suppliers exist for finished products and active ingredients; effective near-monopolies. Price increases due to manufacturer exit (e.g. Eli Lilly, capreomycin) and product shortages (e.g. kanamycin).¹⁰⁶ Moxifloxacin, an MDR TB medicine, remains under patent in certain countries.¹⁰⁷

94 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

95 WHO. *Guidelines for the programmatic management of drug-resistant tuberculosis*, 2011 update. Geneva, World Health Organization, 2011.

96 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

97 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

98 FDA approves bedaquiline for TB treatment; first new drug in 40 years. Critical Path to TB Drug Regimens, 10 Jan 2013 (<http://cptrinitiative.org/2013/01/10/fda-approves-bedaquiline-for-tb-treatment-first-new-drug-in-40-years/>, accessed 11 Feb 2013).

99 The evaluation of a Standardised Treatment Regimen of Anti-tuberculosis drugs for patients with Multi-drug resistant tuberculosis (STREAM). Presentation at RESIST-TB Meeting, Union Lung conference, Kuala Lumpur, 15 Nov 2012. (http://www.resisttb.org/uploads/STREAM_RESIST_TB_KL.pdf, accessed 9 Feb 2013).

100 Kuaban C. 12-month standardised MDR TB regimen: experience in Cameroon. Presentation at Union Lung conference, Kuala Lumpur, 16 Nov 2012. (http://uwclh.conference2web.com/content/1806/details?from_view=all&view_address=page%3D14, accessed 9 Feb 2013).

101 UNITAID. *Tuberculosis medicines technology landscape*. Geneva, World Health Organization, 2012.

102 Critical Path to TB Drug Regimens (CPTR) 3rd Annual Workshop, Arlington VA, 2-4 Oct 2012 (<http://cptrinitiative.org/2012/12/17/cptr-fall-2012-3rd-annual-workshop/>, accessed 9 Feb 2013).

103 Global Drug Facility Product Catalogue. WHO Stop TB Partnership (<http://www.stoptb.org/gdf/drugsupply/pc2.asp?CLevel=2&CParent=4>, accessed 9 Feb 2013).

104 MSF. *DR-TB drugs under the microscope*. Geneva, 2012.

105 Mostaghim S. *The Market for Second Line TB Drugs*. Geneva, 17 Oct 2012.

106 Summary: *DR-TB drugs under the microscope* 2011, MSF, 2011.

107 Summary: *DR-TB drugs under the microscope* 2011, MSF, 2011.

Quality: Quality-assured medicines make up only 13% of the total market.¹⁰⁸ TB medicines bought by the private sector or National TB Programs are often of variable or unknown quality. For example, a recent study showed 10% of first-line, private-sector TB drugs were of substandard quality.¹⁰⁹ **Reasons:** A small quality-assured market limits incentives for producers to invest in stringent regulatory approval. Procurement by the private sector or National TB Programs may prioritize lowest price or domestic production over quality assurance.

Acceptability/Adaptability: Current TB regimens are long (6 months for DS-TB, 20-24 months for MDR TB), increasing treatment costs and decreasing adherence. **Reasons:** There are limited incentives for developers to invest in clinical trials, including those required to develop short regimens; DS-TB treatment is high-volume but low-margin; MDR TB treatment is expensive but low-volume.

Delivery: Low uptake of MDR TB drugs: <20% of multidrug-resistant cases receive appropriate treatment.¹¹⁰ **Reasons:** Low availability of drug-susceptibility testing means few MDR TB cases are detected or treated appropriately. MDR TB treatment is long, burdensome, expensive, and prone to supply interruptions – reducing adherence and willingness to initiate treatment. National treatment programs focus on first-line treatment and, as a result, often provide limited diagnosis or treatment for MDR TB.

TB medicines are prone to supply shortages and stock-outs; prequalified products have long lead times (e.g. Global Drug Facility lead time of 146 days for first half of 2012).¹¹¹ **Reasons:** Limited number of suppliers, especially of active pharmaceutical ingredients. Complex in-country supply chains. Lack of reliable forecasting and low, variable demand contributing to ‘made-to-order’ production.

Inappropriate DS TB and MDR TB medicine selection and use in the private sector. **Reasons:** Inappropriate prescribing by private-sector physicians. Lack of enforced quality standards.

COMPONENT INTERVENTIONS

Active Interventions (*On-going and identified in UNITAID’s landscape analyses*)

- **Multidrug-resistant TB scale-up and acceleration of access** – This project aims to accelerate scale-up, prevent treatment interruptions, and reduce delivery lead time. (*Implemented by the Global Drug Facility of the Stop TB Partnership*)
- **Quality assurance support** – Prequalification of Medicines facilitates quality assurance of TB drugs where resources are limited or medicines regulation is lacking. (*Implemented by WHO*)
- **Market intelligence for active pharmaceutical ingredients** – This project will clarify market drivers, highlighting potential market-based interventions to alleviate problems rooted in this ‘upstream’ market: high prices, long lead times, and stock-outs. (*Implemented by the William Davidson Institute*)

108 Summary: *DR-TB drugs under the microscope 2011*, MSF, 2011. (http://www.doctorswithoutborders.org/publications/reports/2011/Report_Summary_DR-TB_Drugs_Under_the_Microscope.pdf, accessed 8-Feb-2013)

109 Bate R, et al. Substandard and falsified anti-tuberculosis drugs: a preliminary field analysis. *Int J Tuberc Lung Dis*. 2013 Jan 14.

110 WHO. *Global tuberculosis report 2012*. Geneva, World Health Organization, 2012.

111 UNITAID, unpublished data, 2012 (reported project data)

Potential interventions (Identified in UNITAID's landscape analyses; not yet considered for funding)

- **Improve demand forecasts** for TB drugs, enabling producers to invest in quality and supply capacity.
- **Consolidate demand for quality-assured TB drugs** by harmonizing quality standards and driving demand for quality-assured TB drugs, preventing the use of substandard products and counterfeits.
- **Pending a WHO recommendation for use, support market entry and facilitate appropriate access to new medicines** that will improve treatment of MDR TB and encourage further innovation.

Exploratory interventions (Identified by stakeholders; full landscape analysis and vetting pending)

- Stabilize the market and reduce prices for quality-assured second-line drugs (finished products and active ingredients), via support for robust procurement processes among high-volume, non-donor purchasers, (e.g. private sector, governments); new supply chain entities or product 'banks' to cushion demand volatility; incentives for expanded capacity of quality production.
- Simplify second-line recommendations to rationalize regimen options and to incentivize development of more user-friendly regimens.
- Intervene through manufacturing innovations or process chemistry to ensure reliable access to active ingredients, at reduced cost, for key DS TB and MDR TB medicines.

MEASURING SUCCESS

Expected market effects include stabilization of markets to sustain access to safer, simpler, shorter and more affordable treatment regimens, with particular emphasis on MDR and HIV-associated TB. Early indications suggest that targets for shortened regimens may be <4 months for DS TB (vs. 6 months currently)¹¹² and ≤9 months for MDR TB (vs. 20-24 months currently).¹¹³ Assuming that the price differential between WHO-PQ and non WHO-PQ medicines can reasonably be halved through market based interventions, then the low-end price for an MDR TB treatment course could decrease from \$4,000 per person to \$2,250 – a price reduction over 40%.¹¹⁴ To enable price reductions through an adequate number of suppliers for MDR TB medicines, quality assurance may be needed for 30+ new formulations of MDR TB medicines, based on the range of medicines and number of prequalified formulations currently in use.¹¹⁵ This target may be reduced by consolidation of second-line treatment recommendations, or a reduced requirement for number of formulations per medicine.

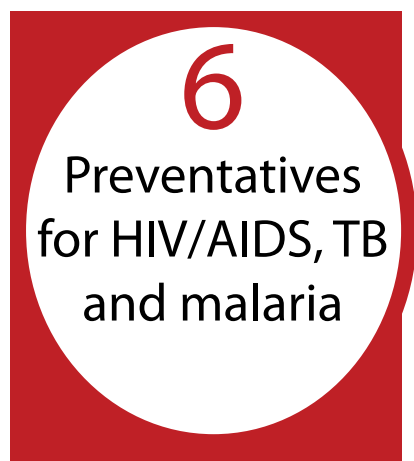
Expected public health effects include increased access to appropriate TB medicines, and therefore improved cure rates. Dramatic reductions in MDR TB medicine prices would substantially increase the number of people receiving treatment by more than two-fold. Tools will be developed to estimate life-years gained for interventions, both ex-ante and ex-post, to guide implementation of highly cost effective interventions.

112 Shortened treatment regimens in development discussed in: UNITAID. *Tuberculosis medicines technology landscape*. Geneva, World Health Organization, 2012. Examples include evaluation of: 8 weeks of high-dose rifampicin; gatifloxacin to replace ethambutol (OFLOTUB); evaluation of moxifloxacin to replace ethambutol or isoniazid (ReMox).

113 Shortened treatment regimens in development discussed in: UNITAID. *Tuberculosis medicines technology landscape*. Geneva, World Health Organization, 2012. Examples include Bangladesh regimen (STREAM).

114 UNITAID assumption, based on cost of WHO-recommended regimen with drugs sourced by Global Drug Facility. Prices from: MSF. *DR-TB drugs under the microscope*. Geneva, 2012.

115 UNITAID assumption, based on prequalification status of current TB drug formulations. Data from: *WHO List of Prequalified Medicinal Products*, WHO, 2012 (<http://apps.who.int/prequal/>, accessed 12-Mar-2013).



6
Preventatives
for HIV/AIDS, TB
and malaria

6.6 Strategic Objective 6: Increase access to products for the prevention of HIV, TB, and malaria

6.6.1 Preventives HIV/AIDS

COMMODITY ACCESS ISSUES

A number of preventive commodities will help to reduce the current 2.5 million new cases of HIV each year. For instance, only 10% of male circumcisions have been undertaken towards achieving the modelled HIV prevention targets. Condom usage varies considerably between high-burden countries: from 13.7% usage at last sexual intercourse in Uganda to 90.2% in Botswana.¹¹⁶ Female condom access, however, is much lower – few donor-funded female condoms were purchased per woman in Sub-Saharan Africa in 2011 (1 per 1000 women).¹¹⁷

In 2007, WHO and UNAIDS issued guidance for voluntary male medical circumcision (VMMC) as an HIV prevention intervention in 13 high-priority countries. Modelling showed an 80% VMMC rate in these countries could reduce HIV incidence by >20% by 2025.¹¹⁸ To reach this rate, there is a need to ‘catch up’ 20.3 million circumcisions between 2010-2015, and an additional maintenance of 8.4 million circumcisions between 2015-2025 as males reach the target age group. Initial scale-up has been slow, and, by late 2012, it was estimated that no more than 10% of the target had been achieved. PEPFAR (US President’s Emergency Plan for AIDS Relief) is targeting 4.7 million circumcisions during 2012 and 2013 through its programs.

The traditional standard of care for VMMC is surgical. In order to facilitate scale-up, several devices to implement VMMC are being tested. This includes PrePex and the Shang Ring. Both devices have completed clinical trials for WHO Prequalification, which is expected in early 2013 (PrePex) or mid/late 2013 (Shang Ring). There are other devices used for adult and adolescent male circumcision, but these are not expected to be prequalified in the near future, if at all.

While female condoms have been on the market since 1993, research has focused on decreasing their unit costs and increasing acceptability. The female condom, FC2, is the current market leader and has been WHO-Prequalified for some time. Another female condom product, Cupid, was WHO-Prequalified in 2012 and a third product under development, the PATH Woman’s condom, is expected to be WHO-Prequalified in early to mid-2013.¹¹⁹

Five phase 2 and 3 studies are underway for microbicides.¹²⁰ Commercial products will likely be developed after 2016 if on-going studies are successful. In July 2012, the US Food and Drug Administration (FDA) approved a tenofovir-based oral pre-exposure prophylaxis (PrEP) for non-infected high-risk individuals.¹²¹ WHO has also issued guidance on oral PrEP for serodiscordant couples, and men who have sex with men (MSM).¹²² Studies of alternative ARVs for oral PrEP are at an early stage.

116 UNAIDS AIDSInfo, Accessed 30 January 2013

117 UNAIDS Global Report 2012. Accessed 30 January 2013

118 Njeuhmeli E et al. (2011). Voluntary medical male circumcision: Modelling the impact and cost of expanding male circumcision for HIV prevention in Eastern and Southern Africa. *PLoS Med* 8:e1001132.

119 Beksinska M, Smit J, Joanis C, Potter W. New female condoms in the pipeline. *RHM* 2012; 188-96

120 <http://data.avac.org/OngoingMicrobicideTrials.aspx>, accessed 31 January, 2013

121 <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm312210.htm>, accessed 31 January, 2013

122 World Health Organization. Guidance on Pre-Exposure Oral Prophylaxis (PrEP) for serodiscordant couples, men and transgender women who have

MARKET SHORTCOMINGS AND THEIR REASONS**Male Circumcision**

Affordability: PrePex does not yet have an established market price; however, the unit price has been quoted to be \$15-20.¹²³ Data of relative costs of device-based programs compared with surgery-based programs currently do not exist because devices are not in widespread use. One published model does not show a cost advantage of devices.¹²⁴ The actual effect of devices on cost, demand, and ease of implementation is yet to be seen. **Reasons:** A monopolistic market is expected in the short term with only one product initially. Market entry by Shang Ring, if/when WHO-Prequalified, may introduce competition, but the devices are not necessarily interchangeable. There is a lack of other potential competitors in plastics manufacturing with global health expertise to rapidly enter the market and compete.

Quality: Unclear regulatory pathway for future new male circumcision devices. **Reasons:** Because of the lack of analogous products and pathways, PrePex and Shang Ring required a novel evaluation pathway to be developed by WHO Prequalification of Diagnostics program. Regulatory and clinical trial requirements for new analogous products are unclear and could delay or prevent market entry and further innovation.

Delivery: Slow scale-up of male circumcision in high-impact countries. **Reasons:** Lack of trained surgeons and health systems structure to support rapid expansion. Demand and acceptability are also major barriers; best practices for optimal demand creation are needed.

Female Condoms

Affordability: High cost of female condoms compared to male condoms. Female condom unit costs are as much as 20 times more expensive than male condoms, with a cost of \$0.57/unit, compared to \$0.03 for a male condom.¹²⁵ **Reasons:** Major driver is the complexity of the manufacturing process. Minor contributions from lack of scale and greater regulatory requirements in some countries.

Delivery: Low uptake of female condoms. **Reasons:** Greater requirement for training programs in condom use, compared to male condoms. As in the case of male condoms, female condom use not high in established couples and those with reproductive desires. Challenges with broad product acceptability.

sex with men at high risk of HIV. July 2012. http://apps.who.int/iris/bitstream/10665/75188/1/9789241503884_eng.pdf. Accessed 31 January 2013.

123 McNeil D. AIDS Prevention Inspires Ways to Make Circumcisions Easier. New York Times; January 30, 2012. http://www.nytimes.com/2012/01/31/health/aids-prevention-inspires-ways-to-simplify-circumcision.html?pagewanted=1&_r=3&ref=science. Accessed 5th February, 2013

124 Obiero W, Young MR, Bailey RC. The PrePex Device Is Unlikely to Achieve Cost-Savings Compared to the Forceps-Guided Method in Male Circumcision Programs in Sub-Saharan Africa. PLoS One. 2013;8(1):e53380.

125 UNFPA AccessRH 2013 catalogue. <http://www.myaccessrh.org/documents/10157/ba5b4329-6d6e-4205-968c-5ca8455a3c9c>. Accessed 5th February, 2012

Microbicides

Availability: No efficacious microbicide currently on the market. Proof of concept for coital use of tenofovir gel established but clinical trial data is not yet complete. No data on use of other ARVs for microbicides, or other dosing or formulations of tenofovir. **Reasons:** Development and study challenges in enrolment/design. Limited funding focus for research until recently. Research challenge of development of a new class of products.

Acceptability/Adaptability: No acceptably formulated microbicide yet on the market. **Reasons:** Challenges in developing efficacious microbicide. Long term adherence with coital or daily dosed microbicide may present challenges, and affect population and individual impact. Regimen with high adherence and acceptability for long term use yet to be determined. Technical challenges in engineering ARV(s) into plastics for intravaginal rings that stay in place, in order to reduce reliance on the woman's ability to use the device appropriately.

Pre Exposure Prophylaxis

Acceptability/Adaptability: Slow uptake of PrEP. **Reasons:** Knowledge about and demand for PrEP low. Unclear if developing country governments will adopt intervention due to comparatively high cost and continuing treatment gap.

Delivery: Low availability of PrEP in developing countries. **Reasons:** Complex health system and programmatic requirements to support roll out. Lack of PrEP alternatives that do not use tenofovir in areas where tenofovir is a key first-line medicine.

COMPONENT INTERVENTIONS

Potential interventions (*Identified in UNITAID's landscape analyses; not yet considered for funding*)

- **Support effective regulatory/quality assurance (QA) processes for male circumcision devices** through inclusion in WHO Prequalification of Diagnostics Program and support for clear regulatory pathways for future competitor products.

Exploratory interventions (*Identified by stakeholders; full landscape analysis and vetting pending*)

- **Promote competition for male circumcision devices to reduce prices** through incentives for additional manufacturers to enter in each product category.
- **Support introduction and scale of microbicide** once an appropriate product has been introduced to the market (2016 onwards).

MEASURING SUCCESS

The approach to measuring market and public health effects will become clearer as UNITAID explores specific opportunities for intervention. Expected market effect varies by product type, but broadly focuses on rapid scale-up to create a competitive market, with multiple suppliers whenever possible. For male circumcision devices, market effects could include creating a market with multiple manufacturers competing on price. This could reduce the expected market price of products considerably as the cost

of production is expected to be considerably less than the initial market prices proposed. Public health effects in a recent study in South Africa included a cost per infection averted for VMMC of \$1,096.

For microbicides, measuring market effect focuses on rapid scale-up of new products once they reach market – ensuring multiple manufacturers can produce the product and creating adequate volumes to attract them to stay in the market. Public health effects will focus on the reduction of incidence of HIV. The magnitude of the effect depends on the final efficacy of the product, and the effect/interaction of microbicides with other prevention efforts.

For female condoms, market effects would be modest as it is expected that there will be three prequalified products from 2013 onwards. It may be focused around harnessing innovations on the cost of production, and securing volumes that meet price breakpoints. However, other players, such as UNFPA, have a dominant role in this space.

For PrEP, market effects are mostly tied to the market for the underlying ARV used. Public health effects would be focused in high risk populations where the intervention will be most cost effective.

6.6.2 Preventives malaria

COMMODITY ACCESS ISSUES

Current coverage of insecticide-treated nets (ITNs) or indoor residual spraying (IRS) remains inadequate to protect the 1.35 billion people worldwide at high risk of malaria who would benefit from these vector control interventions.¹²⁶ In sub-Saharan Africa, where an estimated 780 million people would benefit from vector control, household ownership of at least one ITN was 53% in 2012, while the proportion of the population sleeping under an ITN was only 33%.¹²⁷ While ITN deliveries to malaria-endemic countries in sub-Saharan Africa reached 145 million in 2010, deliveries decreased to 92 million in 2011 and 66 million in 2012.¹²⁸ Nearly all ITNs distributed in Africa are long-lasting insecticide-treated nets (LLINs) that typically last 3 years. Current delivery levels are below those needed to replace LLINs reaching the end of their lifespan, which could result in decreased coverage. Coverage with IRS has also been increasing but remains limited; in 2011, an estimated 153 million people were protected with IRS, representing ~11% of the global population at high risk of malaria and ~5% of the at-risk population overall.¹²⁹ In addition to coverage gaps, mosquito resistance to the insecticides used for vector control has been identified in 64 countries¹³⁰ and has the potential to significantly challenge malaria control efforts. Other vector control interventions include space spraying, wall coverings, and consumer products, such as topical repellents and nuisance-abating coils.

Vector control products under development include incremental improvements to existing technologies, new active ingredients, and new tools. LLINs in Phase III development¹³¹ include products with longer efficacy than existing products, and products with synergists (chemicals that block resistance mechanisms in mosquitos) designed to have increased efficiency against pyrethroid-resistant mosquitos. Long-lasting IRS is also under development that could improve on the convenience and cost effectiveness of this approach.

126 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

127 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

128 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

129 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

130 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

131 These products are currently in the WHOPES evaluation process.

Other types of malaria prevention measures exist, such as larval source management and preventive chemotherapy. For intermittent preventive treatment (IPT) of pregnant women and infants, a potential replacement for SP is a priority for new product development in light of widespread parasite resistance to SP. Seasonal malaria chemoprevention (SMC) is recommended by WHO for children 3-59 months in areas of high seasonal malaria transmission across the Sahel sub region in Africa¹³²; a co-blistered combination of SP and amodiaquine (SP+AQ) for use in children in SMC is currently under review by WHO Prequalification Programme. Efforts are also underway to develop a malaria vaccine, although WHO recommendations on the most advanced candidate, RTS,S/AS01, will not be available until at least 2015.¹³³

MARKET SHORTCOMINGS AND THEIR REASONS

Availability: Lack of effective tools to address insecticide resistance and LLIN durability challenges; no alternative to SP for intermittent preventive treatment in pregnant women and infants; no alternative to SP+AQ for SMC which limits the use of this intervention to a single region in Africa. **Reasons:** Low investment in R&D for vector control (5.1% of total R&D for malaria); high cost and long timeframe to develop new insecticides; low incentives for manufacturers to invest in R&D due to uncertain willingness-to-pay for innovations and the accelerated entry to market of generic, 'me too' equivalent products that realize revenues without making investments in innovation; lengthy WHO Pesticide Evaluation Scheme (WHOPES) process, leading to delays in the availability of new tools; WHOPES quality standards are not sufficient to acknowledge differences between approved products (e.g. longer efficacy, increased durability). For SP replacement, research is on-going but products are not yet available. Anticipation of effective vaccines for malaria before 2020 may have contributed to declining interest in developing more chemoprevention options for infants and children in Africa. As with all malaria medicines, there is limited incentive for manufacturers to invest in R&D due to uncertainties around future demand, market size and return on investment.

Affordability: Uncertainty of donor funding for LLIN replacement campaigns threatens to decrease current coverage levels (129 million LLINs needed/year for Sub-Saharan Africa to replace 2010 deliveries and reach steady state coverage¹³⁴, at a cost of \$619 million/year if delivered through mass campaigns); high cost of IRS campaigns (\$15-30 to spray one house for up to 6 months of coverage, vs. \$9.60 - \$14.40 to deliver 2-3 LLINs [equivalent coverage of one house] through a mass campaign for 3 years of coverage); higher cost of organophosphate and carbamate insecticide classes may act as a barrier to the adoption of insecticide resistance management strategies (e.g. IRS rotations). **Reasons:** Concentrated donor landscape (the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) and the President's Malaria Initiative (PMI) - account for 62% of deliveries) and minimal funding from domestic sources; cancellation of GFATM's Round 11 funding has created a potential funding shortage for LLIN replacement; potential for manufacturers to decrease production capacity in response to unpredictable donor demand, which may lead to increased prices (prices decreased by 39% since 2006¹³⁵). Fragmented LLIN market comprised of products with differing specifications (e.g. shape, size, colour) with undifferentiated benefit. IRS campaigns are complex to deliver, with spray operations accounting for 42-52% of total costs.

132 World Health Organization. WHO Policy Recommendation: *Seasonal Malaria Chemoprevention (SMC) for Plasmodium falciparum malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa*. Geneva, World Health Organization, 2012.

133 World Health Organization. *World Malaria Report 2012*. Geneva, World Health Organization, 2012.

134 John Miliner and the Net Mapping Project of the Alliance for Malaria Prevention.

135 World Health Organization. *World Malaria Report 2011*. Geneva, World Health Organization, 2011. UNICEF Price Transparency Report.

Quality: Some LLINs are not meeting minimum durability standards to last the recommended 3 years; sub-optimal quality of insecticides and/or spray operations can limit the effectiveness of IRS. **Reasons:** Difficulties in predicting LLIN durability due to regional variations; quality may be compromised in an effort to cut costs in a highly price sensitive market that encourages purchasing based on absolute price rather than on cost effectiveness; durability and other measures of quality are not taken into account in purchasing decisions due to lack of guidance/methods and lack of country data on proposed durability metrics. Quality challenges in IRS include the technical complexity of spray operations, including monitoring the quality of spraying, and lack of local structures and capacity for quality assessment.

Acceptability/Adaptability: Limited uptake of products and recommendations for insecticide resistance management; low acceptance of IRS as a vector control tool. **Reasons:** High cost and technical complexity of insecticide resistance management approaches; cost and complexity of IRS spray operations and short duration of protection; IRS necessitates removal of household items and requires occupants to remain outside their dwelling until insecticide is dry (up to 2 hours).

Delivery: Supply insecurity and risk of product shortages; uncertain future demand and ability to maintain/expand coverage; overreliance on mass campaigns (78% of nets distributed in Africa) limits efficiency and sustainability of distribution, is less suitable for on-going maintenance, and may lead to coverage gaps. **Reasons:** Unpredictable future funding; concentrated donor landscape (GFATM and PMI account for 62% of deliveries) and minimal funding from domestic sources; concentrated supply landscape (10 manufacturers have WHOPEs-approved products but only 2 manufacturers account for 70% of GFATM/PMI spending on nets); large tenders limit competition from smaller manufacturers; lack of transparency around overall manufacturing capacity; lack of country/district level delivery monitoring or demand forecasting to quantify replacement needs; reliance on mass campaigns linked to the major scale-up efforts of recent years; donors have historically concentrated efforts on populations at greatest risk.

COMPONENT INTERVENTIONS

Exploratory Interventions *(Identified by stakeholders; full landscape analysis and vetting pending)*

- **Ensure a reliable supply of vector control commodities**, for example by creating demand estimates to facilitate the planning of both donors and manufacturers, or by facilitating long-term purchase agreements between manufacturers and purchasers.
- **Maximize coverage within available resources** by supporting improved procurement efficiency through standardization of LLIN specifications and acceleration of the use of cost effectiveness data for purchasing decisions (support the uptake of standard durability testing methods being established by WHO).
- **Maximize vector control coverage levels by** stabilizing funding for replacement of products and services, either through direct funding or indirectly via financial arrangements such as loans or bonds.
- **Support the uptake of new vector control tools** by catalysing the adoption of innovative technologies and increase incentives for manufacturers to invest in new technologies. In particular, support the market entry of new LLINs that offer advantages over existing products in terms of lifespan or resistance management.

- **Accelerate the adoption of insecticide resistance management strategies**, e.g. by supporting interventions in high risk areas, global surveillance activities, and/or the adoption of new technologies.
- **Make effective and safe medicine combinations available** for malaria prophylaxis among pregnant women, infants and children, including new products for use in IPT in pregnant women and infants, and SMC.

MEASURING SUCCESS

Expected market effects include development of competitive preventives markets that provide quality-assured, affordable, well-adapted products to those in need, with a particular focus on supporting the development and uptake of new technologies that offer advantages in terms of product lifespan or resistance management.

Expected public health effects include, at a minimum, maintaining the gains in vector control coverage achieved in recent years and ensuring the continued effectiveness of tools. Additional improvement could be achieved through efforts to expand coverage to currently underserved populations.

6.6.3 Preventives tuberculosis

Strategies to prevent active TB infection include: immunization; preventive therapy in individuals at high risk for developing active infection; and preventive therapy in those with latent TB infection. WHO guidelines recommend routine immunization for HIV-negative infants in TB-endemic areas, but the only available TB vaccine (BCG) has limited effectiveness. Vaccines in development may offer greater effectiveness, but are not expected to be commercially available until 2020 or later.¹³⁶ WHO also recommends isoniazid preventive therapy to prevent active TB infection in people living with HIV, but access is extremely low, even among people attending HIV care services. Shortened treatment of latent TB infection with rifapentine and isoniazid¹³⁷ has been evaluated, but guidance on implementation is not yet widespread. While the role of market-based approaches to increase access to currently available preventive commodities is unclear, UNITAID is monitoring developments to identify potential opportunities. Meanwhile, UNITAID's role in TB prevention focuses on reducing transmission by increasing access to appropriate TB diagnostics and medicines.

¹³⁶ Kaufmann, S. H. (2011). *Fact and fiction in tuberculosis vaccine research: 10 years later*. *The Lancet Infectious Diseases*, 633-640.

¹³⁷ 12 weeks of once weekly dosing of rifapentine and isoniazid, as an alternative to 9 months of daily dosing of isoniazid. UNITAID. *Tuberculosis medicines technology landscape*. Geneva, World Health Organization, 2012

CORE ACTION AREAS



7 CORE ACTION AREAS

The five core action areas that UNITAID believes contribute most directly to achieving its mission, are: market intelligence gathering and analysis; portfolio and grant management; resource mobilization; relationships with global partners, countries and civil society; and Secretariat management and Governance.

UNITAID's effectiveness depends on focusing on the *right set* of core action areas and then on rolling them out to the *highest possible degree of excellence*. UNITAID is already performing relevant activities within each of the core action areas; however, in a number of activities, there is scope for moving further toward the standard of excellence to which UNITAID aspires.

This section sets out how UNITAID aims to achieve this and, in so doing, addresses the challenges and Five-Year Evaluation recommendations. For each core action area, a brief description is provided of why the area is core to UNITAID, what standard UNITAID ultimately aims to attain in the area, and the results expected.

7.1 Core action area 1: Market intelligence gathering and analysis

Complete, reliable, and up-to-date information on market dynamics trends underpins UNITAID's success in increasing access by improving markets for HIV, TB, and malaria. UNITAID's market intelligence is critical to inform decision making such as priority setting, grant making, project management, and impact assessment from UNITAID's interventions. In addition, it has proven to be of great utility to other global health stakeholders who also play a key role in shaping markets for HIV, TB, and malaria commodities.

UNITAID's market intelligence comes from many sources. These include UNITAID's landscape analyses prepared by the Secretariat and consultants; UNITAID funded forecasts, external reports and academic papers; UNITAID interventions; and transactional level reporting by purchasers such as the Global Fund and PEPFAR, international organizations, global health development agencies and Civil Society engagement. Input from these varied sources provide a perspective on the opportunities for a market-based intervention, the degree of improvement that could be expected from potential projects ex-ante, and how much improvement has been achieved from past projects ex-post. There remain, however, significant data gaps that are priorities for understanding market interventions that UNITAID will actively pursue.

In order to gain maximum utility from the market intelligence UNITAID collects, including facilitating additional analysis of this data, UNITAID is developing a market intelligence system to compile the various sources of data into one system that will facilitate and expand UNITAID's use of this key market intelligence.

Over the period 2013-2016, UNITAID aims to:

- Establish a market intelligence system that provides comprehensive access to timely, high-quality information on product markets;
- Identify on-going insights and opportunities from the regular UNITAID landscape analyses effort;
- Expand capacity within UNITAID to analyse and interpret market data; and
- Put new approaches in place to use and share market information and insights, both internally and with other actors.

7.2 Core action area 2: Portfolio and grant management

UNITAID's ability to make progress towards the six Strategic Objectives depends on the capacity of the Secretariat to manage the processes that follow the launch of a 'call for proposals'. Strong Secretariat skills, as well as well-defined processes that guide the management of portfolios and grants, are required to achieve this progress. These processes, and their recent refinements, are discussed in section 5.2 under core area 5 (Secretariat Management and Governance).

Over the period 2013-2016, UNITAID aims to:

- Refine tools and standard operating procedures to improve the timeliness of initiating new projects.
- Develop new and existing processes for proposal development and assess and document them.
- Update the project management processes, informed by best practice benchmarks and lessons learnt from past project implementation, by the end of 2013.

The overall success of the improvement to UNITAID's project and portfolio management processes will be measured through several indicators of performance that will be included in the KPI report, namely a reduction of lead time from Board approval to Project Implementation¹³⁸ from 180 to 120 days for a standard project.

Improvement across performance areas will be supported by training of Secretariat staff in using tools for project management, including UNITAID's Portfolio Management System. The Monitoring and Evaluation (M&E) team will support the processes using a refined M&E framework and by providing timely feedback to implementers on semi-annual and annual reports. Independent, external mid-term and end-of-project reviews will provide transparent feedback on progress made towards improved grant management by UNITAID and its implementers and also recommendation for additional improvements, where needed.

In addition to strengthening the Secretariat's standard operating procedures for grant management, the Board will be provided with additional tools and support to make sound funding decisions. This work will be linked to the reform of the expert groups. (See core action area 5).

138 Defined here as signature of the grant agreement

7.3 Core action area 3: Resource mobilization and fundraising

To achieve significant and sustained market effects, it is critical that UNITAID has secure, predictable and sustainable long-term funding. UNITAID's robust business model means that it is able to select the best projects to achieve both market and public health improvements. Therefore, its donor funds cannot be earmarked to a specific cause or to a country. Secure and predictable multi-year funding allows UNITAID to cover high-priority activities and provides the financial security necessary to engage strategically and effectively with the implementers and other stakeholders to catalyse significant market interventions that can yield the desired outcomes.

More than 70 percent of UNITAID's funds have been raised through air ticket levies and the rest through traditional budgetary contributions. UNITAID has 29 members of which just two, France and the United Kingdom, provided 81 percent of funding; the donor funding level between 2006-2011 has averaged \$300 million a year.

Based on analysis of donors, cost effectiveness and return on investments, UNITAID will prepare a Fundraising Strategy and Resource Mobilization Plan by December 2013. The Fundraising Strategy will define a plan for 2013-2016 financial support sought for UNITAID. It will assess the current and potential donor base, fundraising systems and processes, as well as the strategies and techniques that UNITAID will utilize in its fundraising.

To work towards achieving a more stable and sustainable resource base, UNITAID will continue advocating for the use of innovative financing mechanisms during 2013-2016, and will increase global awareness of UNITAID's role and 'added value' among stakeholders through an effective communications strategy.

Multi-year commitments from the current UNITAID donors, as well as a broader engagement with new donors and exploration of new types of funding, will ensure sufficient funding to achieve UNITAID's core mission. UNITAID will secure and expand the proportion of its funds raised from sources that provide additional and sustainable financing, towards the aim of maximizing funding predictability.

To achieve a more secure, predictable and sufficient long-term funding base, by 2016, UNITAID aims to:

- i. **Secure long-term funding commitments from UNITAID's current members.** UNITAID will achieve this by:
 - Working with its current donor base to secure multi-year commitments and predictable contributions (United Kingdom, France, Norway, Republic of Korea, Brazil, Chile and six African country contributing members). It will ensure that UNITAID achievements and added value are communicated to key decision makers, and they are aware of the donor countries' commitment to UNITAID and the quality of work that has been achieved for the benefit of global health;
 - Focusing on developing strong relationships with its current members and in particular, with the non-contributing members¹³⁹, towards achieving pledges.

139 Currently there are 12 non-contributing members. African members include South Africa, Cote d'Ivoire, Senegal, Benin, Burkina Faso.

- ii. **Expand donor base and increase revenue from new types of funding to UNITAID.** UNITAID will work with new donors to diversify its donor base and to increase its funding level (see section 8.1). UNITAID will achieve this by:
- Securing new funding from new donors with whom dialogue already exists¹⁴⁰, and by exploring opportunities for securing funding from other new traditional and emerging donors.
 - Reaching out, and advocating, to all countries that are ready to explore innovative financing mechanisms, such as the air ticket levy and the financial transaction tax, through a variety of portals for example, the Leading Group on Innovative Financing.
 - Exploring new types of funding, contributors and partners including private foundations, specialized funds and other contributions, while avoiding any conflict of interests or reputational risks. UNITAID will not consider contributions of health products in-kind.
 - Preparing a guide on how to become a member of UNITAID targeting potential new donors, which outlines the advantages of becoming a 'UNITAID donor'.¹⁴¹
 - Developing co-funding and co-financing opportunities through strategic partnerships seeking collaboration and strategic alliances with the bilateral cooperation agencies and inter-governmental organizations. (see section 7.4.2)

7.4 Core action area 4: Strong relationships with global partners, countries, and civil society

UNITAID interacts with a number of partners, including global health organizations, implementers, country-level entities, countries, civil society, and product developers and manufacturers. Maintaining and strengthening these relationships will be essential to ensure that UNITAID's goals, approaches and activities complement and leverage those of other actors in global health, and to disseminate results and lessons learned. UNITAID will take individual approaches to building and maintaining these relationships, and communicate effectively and appropriately according to the various categories of partners.

Over the period 2013-2016, UNITAID aims to:

i. **Strengthen collaboration with the Global Fund**

The Global Fund is a major partner for UNITAID, and both organizations work in a complementary manner. UNITAID works upstream, at the global level, with innovation and early market changes, predominantly on the supply side with limited funds and time-limited interventions; the Global Fund works at country level, with products integrated in national policies on the demand side, with large amounts of funds over long periods. The paediatric ARV and second-line ARV projects are good examples where the Global Fund has taken on large scale implementation projects that follow on from UNITAID's successful market and public health achievements.

- Through an upstream approach and diversification of interventions in key new areas, UNITAID will improve cost efficiency and quality of care through improved treatment and diagnostic projects that will directly benefit the Global Fund and the populations they serve.

140 For example, Japan, India, Russia, Kuwait

141 Member's package does not define Governance or Board membership issues

- The Global Fund's new funding model demonstrates a proactive approach towards actions that have the potential to leverage market shaping effects and to contribute to the sustainability of UNITAID projects.
 - UNITAID will work with the Global Fund systematically at all levels – Board level, Committee level (Market Dynamics Advisory Group) and with the Secretariat – and at each stage of the development of projects, as well as share market intelligence and demand forecasting.
 - Incorporate regulatory strengthening in countries as part of Global Fund grants to accelerate product entry or uptake.
- ii. **Engage large international public health organizations** to ensure complementarity and explore new opportunities. In order to achieve this, UNITAID will:
- Consult with experts and disease-specific partnerships – including the World Health Organization (WHO), UNAIDS, the Stop TB and Roll-Back Malaria Partnerships, UNICEF, drug discovery partnerships and leading financing organizations – to ensure alignment of UNITAID strategic goals with normative guidelines and established priorities.
 - Formalize its relationship with PEPFAR and strengthen its ties with other actors in the international public health architecture, in particular UN agencies¹⁴², the GAVI Alliance, and bilateral cooperation agencies in the health sector.
 - Ensure that a broader base of implementers will execute UNITAID-funded interventions.
 - Increase its capacity to identify and develop relationships with new potential implementers, including those from developing countries.
 - Improve communications with implementers so that they fully understand UNITAID's market approach, and the potential public health and market effects of UNITAID's funding.
 - Explore increasing the number of co-funding partners to improve the effect of UNITAID's grants including supplementary financing from multilateral development banks and public private partnerships.
- iii. **Engage at country level** to ensure that products are incorporated into local policies. In order to achieve this, UNITAID will:
- Engage at country level and with governments in assisting the MOU agreement between UNITAID's implementer and national authorities; be involved in the regulatory aspects of UNITAID funded commodities; ensure that the supported products are included in the countries' essential medicines lists; and work with the country coordinating mechanisms of the Global Fund toward ensuring sustainability of the intervention.
 - Promote and enhance in-country engagement of stakeholders to gather information on market effects as they translate at country level and to ensure that interventions are benefiting people and match their need. Working with the UNITAID Community Support Team, which is made up of Civil Society representatives, this will involve interactions at multiple levels with civil society organizations, governments, national regulatory authorities and health workers both through country visits and in UNITAID and regional consultation fora.

142 Including UNICEF, UNDP and UNFPA.

- Develop an approach to engaging with middle income countries with a high disease burden (e.g. TB). Improving the markets for specific healthcare products (e.g. TB drugs) in middle income countries will not only benefit vulnerable populations in these countries but also have a favourable influence on the market in low income countries (e.g. lower prices, increased quality, etc.).
- iv. **Consult with product development partnerships and product manufacturers** to support innovation and shape new opportunities. In order to achieve this, UNITAID will:
 - Cooperate more actively with PDPs to systematically identify candidate products that could be supported by UNITAID initiatives and help shape the most effective approach to their market entry,¹⁴³
 - Hold regular consultations with manufacturers of pharmaceutical and diagnostic products, including both innovators and generic manufacturers, to share information and experience on relevant product market issues.
- v. **Engage regularly with academia and the scientific press.** UNITAID will develop relationships with universities, notably in developing countries, and with research institutes¹⁴⁴ to broaden the base of possible collaborators and contractors for market dynamics and market intelligence and share its results.

UNITAID will regularly review its engagement with global partners, civil society and countries and enhance its communication efforts in order to develop engagement opportunities and increased co-funding that will leverage both market and public health improvements. These achievements will be monitored and reported on through the KPI report.

7.5 Core action area 5: Secretariat management and Governance

7.5.1 Strengthen organizational management at UNITAID to ensure timely and effective delivery of intended results.

Following the Five-Year evaluation recommendations and regular audits, UNITAID has put in place a number of organizational management processes that streamline the Secretariat's effectiveness and support good working practices. Following the Board's decisions in this area, UNITAID has adopted a staffing level that allows it to remain lean and nimble, with teams of highly skilled staff that work collaboratively.

The Secretariat of UNITAID is responsible for carrying out and managing day-to-day operations, and for coordinating the implementation of the workplan. The Secretariat manages relationships with partners, and coordinates their activities, in order to ensure both programme and financial monitoring and reporting.

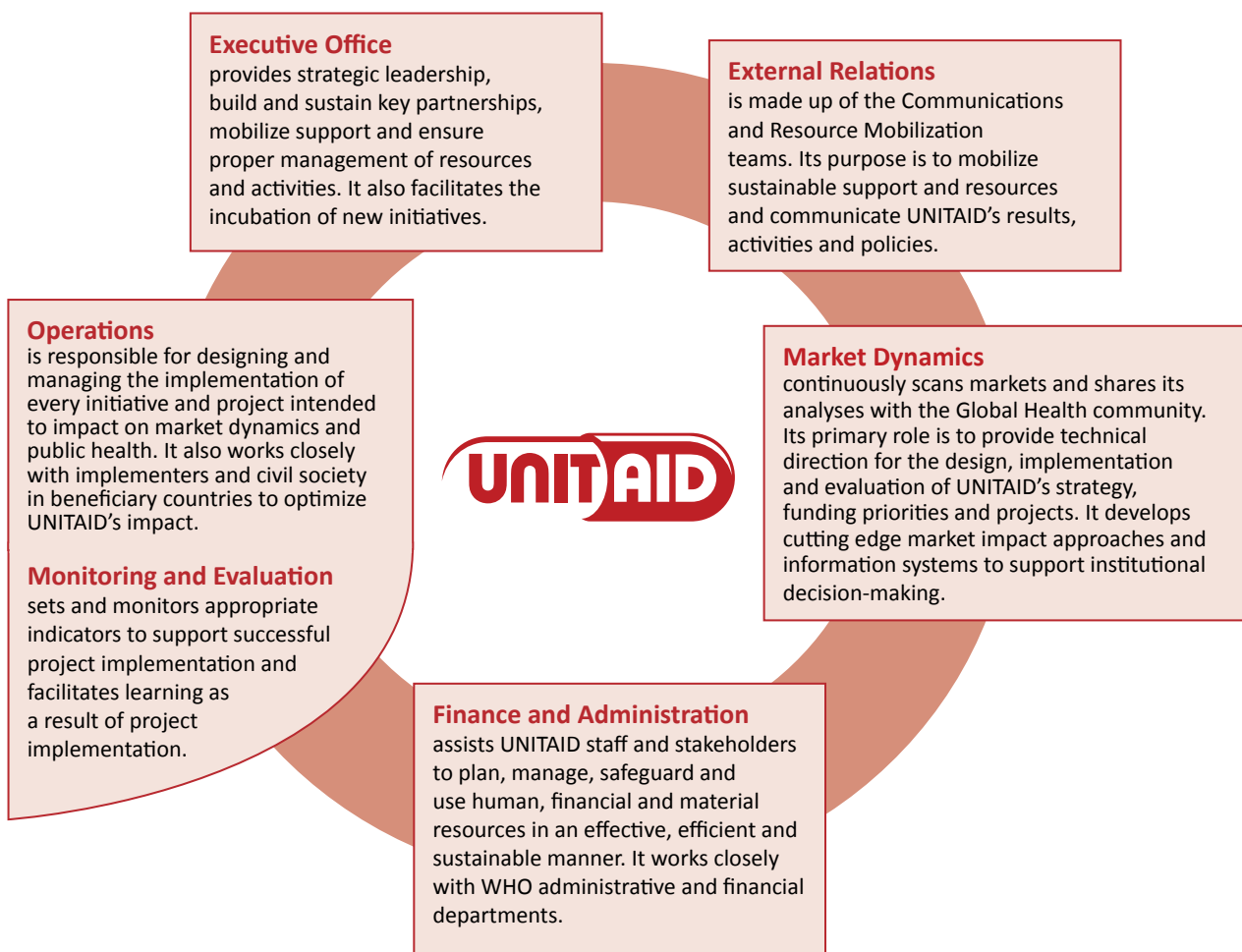
The Secretariat implements the policy set by the Executive Board and provides support to the Consultative Forum. It prepares project reports and budgets for approval by the Board, and reports on the results of the actions undertaken and the use of UNITAID resources.

¹⁴³ Relevant initiatives include the Medicines for Malaria Venture, the Drugs for Neglected Diseases Initiative and the Global Alliance for TB Drug Development.

¹⁴⁴ For example, France's Agence Nationale de Recherche sur le Sida, USA's National Institute of Health

The Secretariat of UNITAID is hosted by the World Health Organization (WHO) in Geneva, Switzerland. The operations of the Secretariat (including recruitment, procurement, financial matters and management of the Trust Fund, UNITAID) are administered in accordance with the Constitution of UNITAID and WHO rules.

FIGURE 5: FUNCTIONAL ORGANIZATION OF UNITAID SECRETARIAT



In order to achieve its mandate and Strategy in a manner that is aligned to its core guiding principles (innovation, flexibility, transparency, results orientation, value for money, efficiency), the Secretariat has the following key attributes:

- **Effective Leadership throughout the Secretariat:** leadership at various levels to ensure that the organization can adapt continuously to its constantly changing environment Leadership from the Executive Director, is complemented by support from Senior Management. Senior Management ensures that staff throughout the organization are aligned to UNITAID's overall objectives and guiding principles. Senior Management promotes and exemplifies organizational values (excellence, collaboration, integrity and responsibility among others). Staff are empowered to make appropriate decisions and are kept strictly accountable. Roles and responsibilities within the Secretariat and between the Board and the Secretariat are clear.

- **Planning practices that enable the achievement of objectives at all levels:** Expected outcomes from the Strategy are cascaded into organizational and individual activity plans that take human and financial resources into consideration. Using a Result Based Management framework, UNITAID managers ensure that deliverables are clearly defined at all levels, monitor their delivery closely, and hold themselves and their teams accountable. Consideration of risks and opportunities is incorporated into all UNITAID planning and decision making activities.
- **A high performing Secretariat with robust and efficient organizational processes:** UNITAID's human resource management practices enable a vibrant organizational culture and provide appropriate support to both team and individual performance. UNITAID implements a strong and adaptable organizational structure in which cross-cutting work processes are facilitated. UNITAID staff have clear opportunities for professional growth and development. Performance management practice sets clear expectations and ensures a sense of individual ownership and responsibility towards UNITAID's success.

To move from its current practices to develop the key attributes required to successfully achieve its Strategic Objectives, UNITAID will undertake the following actions:

- A flexible, yet robust, Results-Based-Management and accountability framework will be designed and implemented. Organizational objectives will be cascaded throughout units and then individuals to ensure timely and quality delivery of agreed deliverables at all levels. Rigorous monitoring and annual rolling plans will be adopted in order to facilitate the adjustments needed by a constantly changing environment. Planning will be informed through a transparent and risk-based approach.
- UNITAID will enhance its current human resources management practices to ensure that the Secretariat is a vibrant work place.
- UNITAID will fully develop and implement a Quality Management System across all areas of the organization. Building on the existing monitoring and evaluation framework, UNITAID will develop and implement an integrated accountability framework that includes transparent organizational reviews, benchmarking and audits.

7.5.2 Cohesive and effective governance practices

UNITAID's Executive Board performs an essential leadership role for overseeing:

- Performance of UNITAID, by taking a proactive, forward-looking view that (a) focuses on strategy, value creation, resource allocation and mobilization and (b) guides UNITAID's decision-making.
- Its accountability, i.e., conforms with regulations, promotion of transparency, assurance that objectives are achieved and decisions are made timely, efficiently, and in an effective way, monitoring and assessment of UNITAID performance. (This role includes internal processes of the Board.)

UNITAID benefits from using external expertise in the form of expert groups to help in informed decision making, based on evidence. External expert advice provides inputs to the Secretariat and the Board in setting priorities and review of the technical merits of proposals. Within the scope of the three diseases, UNITAID has experienced a growth in the diversity of market based interventions it pursues. This

diversity has resulted in an evolution from general proposals, to very specific and nuanced proposals that require very specific expertise on a topic. In response to this change, UNITAID has developed tools such as UNITAID landscape analyses, market fora and proposal assessment tools. Now, UNITAID plans to explore an expert group structure that balances consistency through a core group of experts who are familiar with UNITAID's approach with depth, by drawing on a larger pool of specific expertise as needed. This revised structure will be in place by end of 2013.

UNITAID's Secretariat has a key role in helping to develop cohesive and effective governance practices by continuously promoting innovative ideas and by implementing Executive Board decisions.

In line with the requirements of the new Strategy, it will help the Executive Board build on the recent reforms and propose new reforms of UNITAID's governance structure to:

- **Promote further refinement of the Board decision-making and high level consultation processes.** In particular with regard to the overall proposal review and decision cycles, the Board will take steps to support efforts that will reinforce robust and streamlined projects that are implemented in a timely manner. To this end, it will review the functioning of expert groups.
- **Better reflect the commitments of donors to UNITAID** by exploring the issue of the Board composition, membership arrangements and accession, balance of constituencies, promotion of representation and welcoming new donors to the UNITAID trust fund.
- The effectiveness and efficiency of the Board and the decision making process will be reviewed through periodic self-assessment and external evaluations.

PLANNING AND MANAGEMENT FOR SUCCESS



8 PLANNING AND MANAGEMENT FOR SUCCESS

8.1 Measurement of success

Outputs are the direct, easily enumerable, and immediate market and public health results used to assess early results from individual UNITAID grants. Outputs typically relate directly to the market shortcomings each grant is designed to address; they are necessary, but not sufficient to produce outcomes and impacts.

Examples of market outputs include: number of beneficiary countries adding a priority product(s) to national treatment guidelines or approving priority product(s) for marketing; satisfactory completion of competitive & transparent tender to select product suppliers. Examples of public health outputs include: number of products (e.g. medicines, diagnostic tests) procured or delivered; number of quality assurance dossiers submitted to WHO Prequalification or other SRA.

Implementers report output indicators to UNITAID as part of their performance update (semi-annual and annual) reports, which are evaluated by the UNITAID M&E team and published on the UNITAID website.¹⁴⁵

Outcomes are the intermediate changes in markets and public health resulting from UNITAID grants and initiatives that are measurable within the timeframe of the grant. Outcomes are the most commonly used assessments, applied at the grant, disease portfolio, and overall portfolio levels. Continuous assessment of outputs and outcomes from UNITAID grants enables UNITAID to monitor progress towards goals and objectives. Frequent assessment and sharing of results support continuous quality improvement and strategic redirection of on-going grants as required. Outcomes are necessary, but not sufficient to produce impact measures.

UNITAID uses data obtained through its landscape analyses, consultancies, and externally available sources to complement data provided to UNITAID by implementers to develop a comprehensive understanding of market and public health outcomes (see Core Action Area 1, Section 7.1). Outputs and outcomes inform UNITAID's key performance indicators, which are reported to the UNITAID Board on the 30th June of each year.

Examples of market outcome indicators include: number of medicines newly prequalified, by disease and product type (e.g. paediatric formulations, second-line treatments); rate of adoption and uptake of priority products; change in price per unit; price mark-ups; and change in market share (by manufacturer, purchaser, etc.).

Examples of public health outcome indicators include: change in treatment coverage (%) and estimated number of patients on treatment; change in diagnosis coverage (%) and number of screens/diagnostics performed.

¹⁴⁵ www.unitaid.eu/impact

Where possible, outcomes reflect both direct and indirect contributions from UNITAID. Direct outcomes are derived when interventions include large-scale commodity purchases, while indirect outcomes are estimated from the market effects observed, i.e., improvements in public health outcomes that are not directly related to increased coverage from UNITAID procurement but that could be attributed to changes in prices, quality or other market characteristics spurred by UNITAID intervention.

Impacts are the ultimate, sustainable changes in public health that reflect UNITAID's contribution or attribution to those changes. Impact estimates are typically applied to the assessment of UNITAID grants and are based on their reported outcomes.

There are numerous actors that contribute in a given market, and so, impact estimation must take into account the contribution not only of UNITAID grants, but also those of multiple global health stakeholders who are intervening in the same space. Impact estimates are commonly expressed in terms of life years gained or disability-adjusted life years (DALYs), but analytic methodologies must be developed and applied to assess the impact of market-based approaches on public health. These methods can be applied to estimate impact both ex-post and ex-ante.

Given the complexities and the relatively considerable resources required, UNITAID will focus its efforts in public health impact estimation on those Strategic Objectives where UNITAID investment is substantial and/or where learning would be critical to the success of on-going or future strategies of UNITAID and other organizations adopting market-based approaches to health.

UNITAID's initial work in this area has focused on developing ex-ante public health impact estimation methodologies and impact estimates of potential UNITAID interventions to scale-up access to, and use of, RDTs for malaria, GeneXpert for TB, and POC CD4, viral load, and early infant diagnostic tests for HIV. While this work is on-going, some initial research has been published.^{146, 147} As UNITAID develops its own approaches to modelling public health impact, it will continue to use available impact estimates from published research, and also adapt and optimize models developed by other partners and stakeholders wherever possible in order to benefit from proven and tested methods and to avoid duplication of effort. Key principles across all measurements of success include data and methodology sharing, coordination, harmonization, and standardization with other global health stakeholders.

Finally, employing findings from all three levels of assessment, UNITAID will continue to work during the Strategic period to ensure UNITAID resources are used in a manner that facilitates maximum value for money. UNITAID will continue to engage with other global health stakeholders working to establish global consensus on a common definition and individual organizational applications of value for money in the context of global health interventions. For UNITAID, this will involve further articulation of how existing frameworks, proposal tools, Strategic Objectives, and measurements of success can together be used to describe three key components of value for money: equity, efficiency, and effectiveness.

146 Estill J., et al. Cost-effectiveness of point-of-care viral load monitoring of ART in resource-limited settings: Mathematical modelling study. *AIDS*. 2013;27:000–000.

147 Menzies N., et al. Population Health Impact and Cost-Effectiveness of Tuberculosis Diagnosis with Xpert MTB/RIF: A Dynamic Simulation and Economic Evaluation. *Plos Medicine*. 2012;9(11):e1001347.

8.2 Implementation of the Strategy

8.2.1 UNITAID funding projection

While sustainable and predictable funding is desirable in any organization, the nature of UNITAID's work makes it absolutely fundamental to its effectiveness. The capacity to influence manufacturers and other market agents is dependent on UNITAID's capacity to make investments of sufficient magnitude and duration in a given market. This cannot happen without sustainable and predictable funding and UNITAID seeks to secure this through its resource mobilization plan.

The UNITAID Secretariat will ensure that it will continue to invest at the level that it invested in 2012 to continue building its credibility in the markets that it seeks to influence. An overall steady level of investment sends a clear message to markets and partners alike. An annual revenue of around \$300 million (with the cash flow associated with it) would therefore seem the minimum that UNITAID needs to receive in order to implement the Strategy.

With a greater funding envelope, UNITAID could further increase access to commodities, allowing an increased availability to those who need it most. The extra funding could be invested in projects further downstream in the value chain to enhance delivery of commodities and further support UNITAID's existing investment. For example, the recently approved project with DNDi to develop infant paediatric formulations, which is an upstream project, could see these new quality approved formulations rolled out in greater numbers if further funding was available. UNITAID could also consider other co-funding mechanisms to achieve greater market and public health impact throughout its portfolio of projects.

8.2.2 Articulation of implementation plan

The Secretariat will begin implementation of the Strategy immediately after its approval by UNITAID's Executive Board.

The preparation of the strategic implementation plan will include the following elements:

- An implementation plan, including key workstreams and responsibilities will be presented at the Executive Board meeting (EB18) in June 2013;
- An assessment of the implications of the Strategy in terms of budget, human resources, Secretariat structure and management; and
- The incorporation of Strategy implementation tasks into UNITAID 2013 operational plan.

8.3 Measuring Strategy implementation

UNITAID and its Executive Board will review its KPIs to incorporate the new elements of this Strategy, including its core action areas, the overall performance of the Strategy towards achieving its Strategic Objectives, and measurements to monitor the implementation of the Strategy.

An implementation table will track the actions that have been outlined in this Strategy and will form the basis of the implementation plan and provide the key steps over the strategic period that can be regularly reviewed and reported to the Board. The Policy and Strategy Committee have tasked themselves with following the evolution of the Strategic Objectives with yearly updates on the progress made in achieving them and following the evolution of the pipeline.

ANNEXES



9 ANNEXES

9.1 Annex 1: UNITAID Transition and Sustainability Framework

BACKGROUND

UNITAID funded projects aim to increase availability and access to quality tests and treatments for HIV, TB and malaria at the lowest prices in low and middle income countries that would not otherwise have the means to afford these life-saving interventions. UNITAID provides short-term (3 to 5 years), catalytic funding to change market conditions and make these much needed products available and affordable in the target countries. However, other national governments and global funders benefit from these market changes and are able to do more with the monies that they also allocate to health interventions.

UNITAID refers to the continued support by others for products that it initially funded to make the necessary market change as transition. Transition happens when there is a need for continued supply of these products in countries initially supported by UNITAID for a period after the initial investment.

Sustainability becomes an issue when there is a need to support a market for a product of public health importance for a longer period of time beyond that of the UNITAID intervention. This is because the changes initiated in the market, i.e., quality, availability, access or price reductions, should be sustained over a longer time-period. Action must be taken in order not to lose the benefits of UNITAID's short-term, catalytic support to a project. This paper examines the differences between transition and sustainability and outlines the strategies and tools that UNITAID is putting into place to address these concepts.

TRANSITION

Transition is a project specific activity and is focused on identification of funding sources for interventions that will need to be continued after the UNITAID-funded project ends. Whether or not a project transitions to another source of funding depends entirely on the nature of the changes expected as a result of project implementation. For some projects, transition is not necessary because the project is time-limited. For example, UNITAID's support to UNICEF to supply 20 million Long Lasting Insecticide Treated Bed-nets to 8 high burden malaria countries aimed to provide a specific quantity of nets to the countries to coincide with the distribution of these nets before the season when malarial mosquitoes become active. The timeliness of the project implementation encouraged manufacturers to stay in the market for nets and, as a result, lower prices were achieved. However, the main aim of the project was specific to the placement of 20 million nets at a specific time and in specific places and therefore did not require transition to other funders. Another example is UNITAID's support to CHAI for provision of 2nd line ARVs. This project aimed to increase access to quality 2nd line ARVs by supporting generic manufacturers to supply these medicines at the lowest cost to countries in need. The project generated a market change, in that a greater number of quality assured generic manufacturers were able to supply the required ARVs at much lower prices. This market is secure over the long term because the need for these products is expected to increase over time as more and more people using first-line regimens face treatment failure. Fortunately, the over 60% price reductions for specific ARVs generated by this project can be passed on to national governments and the larger global health funders, including GFATM and PEPFAR. Transition is an integral part of project planning for those projects where there is a need to continue to support an intervention in low income countries.

SUSTAINABILITY

Sustainability refers to the need to maintain key market changes over a longer time-period. Unlike transition, which is focused on funding, sustainability is multi-dimensional, involving sustaining access, availability, quality and a competitive market for products of public health importance. Sustaining a UNITAID-funded project's impact on the market becomes a problem with markets that are not stable over the medium to long term. An example of this problem is the UNITAID supported CHAI paediatric ARV project. The paediatric ARV market was a new market when UNITAID provided its initial support to CHAI for this project. UNITAID's support helped to encourage manufacturers to make FDC products that were specially formulated for children. Quality products became available at lower prices as a result of the availability of funds to buy these products and the support of CHAI to negotiate within the market for better affordability for low income countries. However, unlike the market for 2nd line ARVs, where the need for the product is expected to increase over time, the market for paediatric ARVs is expected to decrease over time as a result of a scale-up of prevention of mother to child transmission of HIV/AIDS programmes and the push to eliminate the disease in children. This means that the paediatric ARV market is an 'artificial market', created by UNITAID's support but in need of longer term support in order for the positive changes in the market to be sustained. In the absence of UNITAID or alternative support, without an effective means to procure these drugs and with the market expected to shrink in the medium to long-term, manufacturers will stop production on key ARVs or increase their prices over the longer term. If the market changes are not sustainable, then governments and other global public health funders cannot benefit from them and transition of the project funding will be more difficult. Consequently, sustainability of project outcomes depends on both the market for the products in question and the intervention that has been implemented to change and stabilize that market. Therefore, planning for sustainability requires market intelligence to identify which dimension needs further support and to inform the types of interventions needed to address specific market conditions.

CHALLENGES

The concepts of transition and sustainability have consequences for the UNITAID project planning cycle. Not all projects will need to transition and sustainability of project outcomes may not be a problem for some projects. To identify which projects are at risk, UNITAID needs to monitor the markets for medicines and tests for HIV, TB and malaria to identify when sustainability of project outcomes may become a problem. Transition will be needed where funding gaps are expected after the time-limited support from UNITAID ends. If sustainability is an issue, we first need to identify what aspect of the intervention needs to be sustained. For example, if catalytic UNITAID funding has encouraged generic manufacturers to produce a beneficial, quality medicine for a small market that is not expected to expand, then financial support for this product may be needed from another source. UNITAID will work with Implementers and other stakeholders to find solutions to the market need.

For transition, UNITAID has developed a Transition tool that monitors and tracks the transition status of projects. The UNITAID Transition tool is structured to identify gaps in funding support to countries benefiting from project support and guides implementers through producing a plan for aligning with stakeholders who are interested in benefiting from the positive market changes that are expected from the project.

SOLUTIONS

Successful transition and sustainable project outcomes can only be achieved if planning for both starts early, even at the project proposal stage. For this to work, UNITAID needs to be clear with all potential implementers about the time-limited nature of its project funding. Implementers need to understand at the very beginning that their project plan will need an exit strategy. Furthermore, implementers should be encouraged to use market intelligence to identify the types of interventions that may be expected to produce a sustainable market. Additional thought should be given to what funding gaps may become apparent at the end of the project. Steps should be taken to identify from the beginning of project planning, the potential sources for continued funding. Implementers can also be encouraged to seek co-funding of projects between UNITAID and other interested stakeholders. Once a project starts, implementers should also be transparent with the project countries that UNITAID funding is time-limited and focused on projects that will shape the market for products of public health importance and that the expected positive market changes are to be passed on to other potential funders. In this way, project countries may be able to leverage UNITAID-funded projects to encourage other funders to support the products in the longer term because they understand that the UNITAID project outcomes are better, cheaper medicines and tests.

CONCLUSIONS

In summary, the need for transition and sustainability of project outcomes will differ from project to project. This is because projects intervene in different markets and expect to generate different outcomes. Not all projects will require transition. Some projects will be time-limited by nature. Some project will generate project outcomes that are sustainable over the long term. This is because of the nature of the markets they target and the interventions that they use. For this reason, identification of the need to transition projects to other funding sources has to be done on a case by case basis. The same is true for long term sustainability of project outcomes. The identification of projects at risk of not having medium to long term sustainability of project outcomes requires monitoring of the specific markets and identification of longer term expected changes in this market. Planning for both risks needs to be done before project implementation and requires transparency about the time-limited nature of UNITAID funding both with implementers and the countries benefiting from UNITAID funded projects.

9.2 Annex 2: UNITAID Proposal Evaluation and Selection Criteria

UNITAID focuses on seven specific categories of assessment in its evaluation and selection of proposals for UNITAID funding. Proposals received through its directed and open calls are first evaluated by the UNITAID Proposal Review Committee (PRC), which reports the results of its evaluation to the UNITAID Executive Board. The Executive Board selects proposals for funding based on the same criteria, and both the Board and the PRC hold transparency and consistency as their primary aims. Proposals' technical merits are assessed across the seven Evaluation Categories summarized below.

- i. **Public health problem and commodity access issue** – *i.e., is there a well-articulated and significant public health problem to be addressed? Has a commodity access issue been appropriately characterized and quantified?*
- ii. **Market shortcomings and their reasons** – *i.e., does the proposal provide clear baseline characteristics of the current, pre-intervention market landscape, indicate current and future market 'game changers', and explain the market shortcomings contributing to the commodity access issue and the reasons for these shortcomings?*
- iii. **Innovative market intervention** – *i.e., is the project well-conceived, well-designed, and feasible?*
- iv. **Sustainable market effects** – *i.e., will the project achieve substantial and sustainable market effects? Does the proposal include credible projections of short-term, long-term, and indirect market outcomes?*
- v. **Public health effects** – *i.e., will the project achieve substantial public health outcomes that lead to long-term public health impact? Does the proposal include credible projections of short-term, long-term, and indirect public health outcomes? Does it target vulnerable groups?*
- vi. **Logical framework, budget, and value for money** – *i.e., does the proposal include a complete and robust logical framework? Are its overall costs and commodity costs appropriate?*
- vii. **Capacity and capability to deliver** – *i.e., does the proponent have the capacity to manage and deliver the project?*

The PRC technical evaluation scores proposals on a set of eight first- and second-tier criteria established by the UNITAID Board that are embedded within the six main Evaluation Categories summarized above. **First tier criteria reflect the specific strategic priorities determined by the Board** and established during UNITAID's first Strategic period (2010-2012). These are: (i) public health effects; (ii) market effects; (iii) value for money; and (iv) innovation. In addition, four **second-tier criteria draw on principles embedded in the UNITAID Constitution**, which are: (i) leverage; (ii) value add; (iii) equity; and (iv) ability to transition (if applicable).

The UNITAID proposal evaluation and selection process also considers proposals' fit with UNITAID's current portfolio mix, as determined by the characteristics of the projects it supports (individually, as well collectively across all funded projects) and the relative proportion of funding focused on particular diseases and product types.

The target portfolio mix is determined by portfolio principles, which are agreed upon by the Board, and re-considered on a periodic basis. Such principles can be in the form of specific quantifiable targets or more general considerations to be monitored on a regular basis. These may include: (i) balance across the three diseases; (ii) types of products; (iii) size and number of investments; (iv) investment per implementing partner; and (v) level of resources available for 'directed' calls, etc.

Portfolio principles may also determine Board decisions about which individual projects to fund among those evaluated as technically sound by the PRC. In so doing, the Board may take into consideration characteristics of the current funding portfolio as well as any changes to that portfolio which may result from new funding decisions.

9.3 Annex 3: UNITAID funding projection detail

While sustainable and predictable funding is desirable in any organization, the nature of UNITAID's work makes it absolutely fundamental to its effectiveness. The capacity to influence manufacturers and other market agents is dependent on UNITAID's capacity to make investments of sufficient magnitude and duration in a given market. That cannot happen without sustainable and predictable funding to UNITAID itself.

Slightly less than 90% of 2011 and 2012 revenue was raised through multi-year contributions. This achievement is not risk-free: The two key multi-year contributions from France and the United Kingdom (61% and 20% of UNITAID's cumulated revenue through 2012 respectively) are coming to an end in 2013. Cyprus and the Bill and Melinda Gates Foundation have made much more modest commitments to UNITAID through 2014 and 2016 respectively. Brazil passed a law in 2011 that provides for annual funding to UNITAID. Multi-year agreements from other donors elapsed in 2011 (Spain, Luxembourg). The overall level of funding of UNITAID has decreased from \$350 million for each of the first two years of operation to \$260-270 million in the last two. The number of donors has stayed fairly stable over the years.

The Finance and Accountability Committee of the Board has adopted an approach to delineate the amount the Board may wish to invest in new projects or cost extensions for current projects that is designed to take advantage of present opportunities while preserving investment capacity for future investment and taking into consideration financial risks associated with funding, foreign exchange, cash flow among others.

The level of funding approved by the Board (\$ 1.8 billion) through the end of 2012 is very slightly below the amount of cumulative revenue of UNITAID and very close to the amount of contributions actually received through 2012. \$260 million of commitments made for 2013-2016 have not been invested yet. \$190 million out of this amount has already been set aside for specific projects including subsequent phases of certain key projects (e.g. AMFm, Prequalification of Medicines). The level of funding approved by the Board each year has varied greatly. Funding decisions in 2008 represented an all time high of close to \$590 million. Investments in 2006, 2007, 2009 and 2012 have all been around \$250 million a year. The amount invested in 2010 and 2011 was less than half of the amount invested in previous years because of timing difficulties encountered with certain key contributions.

While the opportunities for investment have become more complex to identify and pursue and although the capacity of the Secretariat to manage grants is not likely to increase markedly over the period of this new strategic plan given the current budgetary constraints, a yearly investment of around \$ 300 million seems to correspond to an amount the Secretariat can ably handle.

The relative amount invested in cost extensions has decreased over time. In 2012 for instance, only 10% of funding was allocated to on-going projects. This is linked to the fact that more rigorous project design and planning, and a more realistic approach to transition, have been utilised by implementers, under the guidance of the Secretariat. That was naturally only possible because of the knowledge that funding was available to fund those projects in their entirety.

The UNITAID Secretariat will need to keep investing at the level it has invested in 2012 to continue building its credibility on the markets it seeks to influence. An overall steady level of investment sends a clear message to markets and partners alike. A yearly revenue of \$200-\$300 million (with the cash

flow associated with it) would therefore seem the minimum UNITAID needs to receive yearly in order to implement the Strategy.

CURRENT REVENUE (JANUARY 2013):

The two key multi-year contributions from France and the United Kingdom (61% and 20% of UNITAID's cumulated revenue through 2012 or €110 million and \$53 million per year respectively) are coming to an end in 2013. The Bill and Melinda Gates Foundation has committed \$10 million per year until 2016. The Cyprus contribution (€400k per year) will end in 2014.

There is no other information currently available on the amounts the traditional UNITAID donors are willing to commit to UNITAID. Although Brazil has repeatedly stated its commitment to fund UNITAID, it has been in arrears since 2009. Norway and Korea in particular (6% and 2% of cumulated commitments respectively) have not given an indication of their level of contribution for 2013 and beyond.

FUNDING CEILING (JANUARY 2013):

The project funding ceiling or the amount available to fund new projects as of January 1, 2013 is \$153m. This is net of a reserve of \$187 million set up to cater for likely cost extensions of existing projects mainly. All existing donor commitments are considered in full to arrive at the \$153 million figure except for a portion of the 2014 and 2015 commitments from the Bill and Melinda Gates Foundation.





UNITAID SECRETARIAT

WORLD HEALTH ORGANIZATION
AVENUE APPIA 20
CH-1211 GENEVA 27
SWITZERLAND

T +41 22 791 55 03
F +41 22 791 48 90
UNITAID@WHO.INT
WWW.UNITAID.EU

UNITAID IS HOSTED AND ADMINISTERED BY THE WORLD HEALTH ORGANIZATION
