Rapid Diagnostic Tests Supplier & Partner Consultative Meeting

11 December 2018
Seattle, Washington – USA

The Global Fund

RDT Supplier and Partner Consultative Meeting Agenda

1. Latest WHO Guidelines on HIV testing services using rapid diagnostic tests
2. Meeting of Diagnostic Manufacturers and Procurers
3. WHO Update on Prequalification of in vitro diagnostics
4. PEPFAR Procurement of Laboratory Diganostics with special reference to HIV RTKs
5. Malaria RDT Task Force Market Health Analysis
6. PMI/GHSC-PSM Rapid Diagnostic Tests Sourcing Strategy 2018-2019
7. UNICEF Procurement Update and Joint UN Tender
8. Global Fund Rapid Diagnostic Strategy

Latest WHO guidelines on HIV testing services using rapid diagnostic tests

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On behalf of

WHO HIV and Global Hepatitis Programme

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HIV Testing Services, WHO

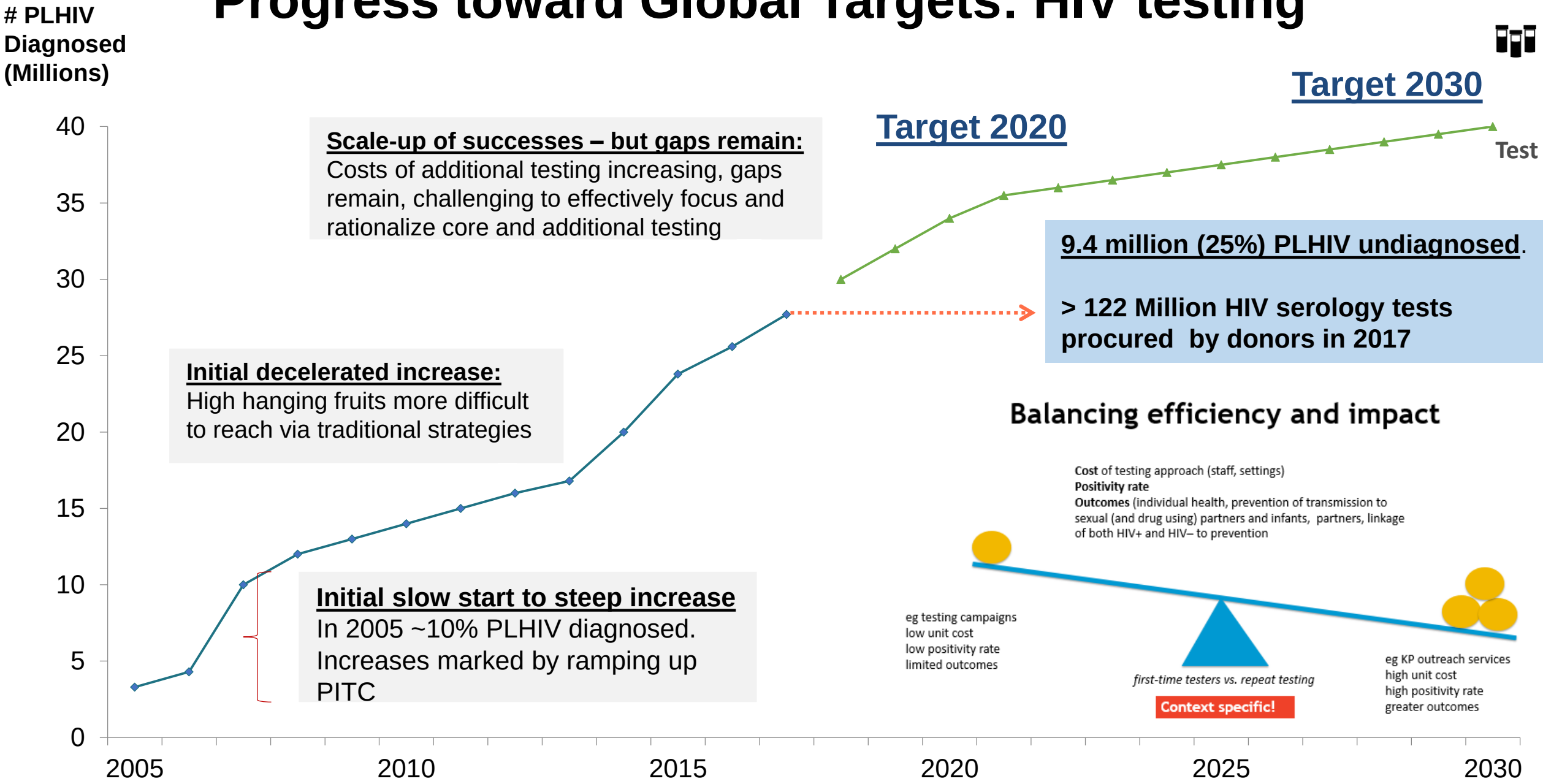
9 Dec 2018

World Health Organization

Outline

- Background
- WHO guidance
- Products approved for use
- Implementation considerations
- Way forward

Progress toward Global Targets: HIV testing



Source: WHO 2005; CHAI 2015; WHO, UNICEF, PEPFAR, GFTAM 2018

WHO Recommended HIV Testing Services

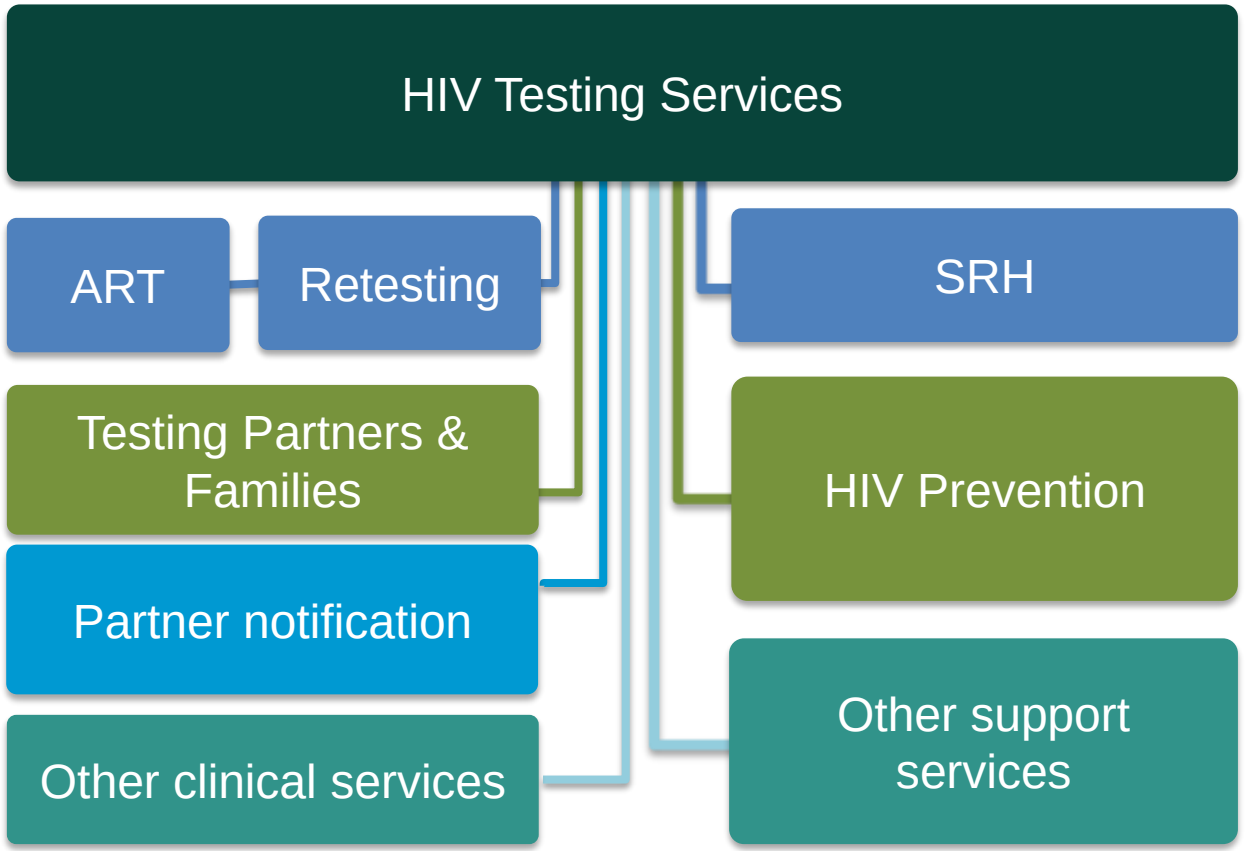
Important gateway to treatment and prevention for individuals, couples, and partners and families

Facility-based: Offering HIV testing in a facility, e.g. VCT, in-patient and out-patient clinics, ANC, TB, STI.

Community-based: Offering HIV testing in natural setting of the community, e.g. outreach, CBOs, workplace, clubs, bars. (including test for triage)

Assisted partner notification: Assisting individuals with HIV by contacting their sexual and/or drug injecting partners and offering them HIV testing services.

HIV self-testing: Offering self-test kit for individual, and/or their partner, enabling them to collect their sample (oral or blood), perform test, and interpret results in private. **All reactive results need confirmation.**



Source: WHO 2015; WHO 2016

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Task sharing – lay provider HIV testing

- Task-sharing HIV testing services with lay providers (**WHO recommended**)
  - High uptake, often preferred & acceptable (esp KP)
  - Accurate
  - Low cost

Lay providers who are trained can, using RDTs, independently conduct safe and effective HIV testing services (strong recommendation)

Should trained lay providers perform HIV testing? A systematic review to inform World Health Organization guidelines

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ABSTRACT

New strategies for HIV testing services (HTS) are needed to achieve UN 90-90-90 targets, including diagnosis of 90% of people living with HIV. Task-sharing HTS to trained lay providers may alleviate health worker shortages and better reach target groups. We conducted a systematic review of studies evaluating HTS by lay providers using rapid diagnostic tests (RDTs). Peer-reviewed articles were included if they compared HTS using RDTs performed by trained lay providers to HTS by health professionals, or to no intervention. We also reviewed data on end-users' values and preferences around lay providers preforming HTS. Searching was conducted through 10 online databases, reviewing reference lists, and contacting experts. Screening and data abstraction were conducted in duplicate using systematic methods. Of 6113 unique citations identified, 5 studies were included in the effectiveness review and 6 in the values and preferences review. One US-based randomized trial found patients' uptake of HTS doubled with lay providers (57% vs. 27%, percent difference: 30, 95% confidence interval: 27-32, $p < 0.001$). In Malawi, a pre/post study showed increases in HTS sites and tests after delegation to lay providers. Studies from Cambodia, Malawi, and South Africa comparing testing quality between lay providers and laboratory staff found little discordance and high sensitivity and specificity (≥98%). Values and preferences studies generally found support for lay providers conducting HTS, particularly in non-hypothetical scenarios. Based on evidence supporting using trained lay providers, a WHO expert panel recommended lay providers be allowed to conduct HTS using HIV RDTs. Uptake of this recommendation could expand HIV testing to more people globally.

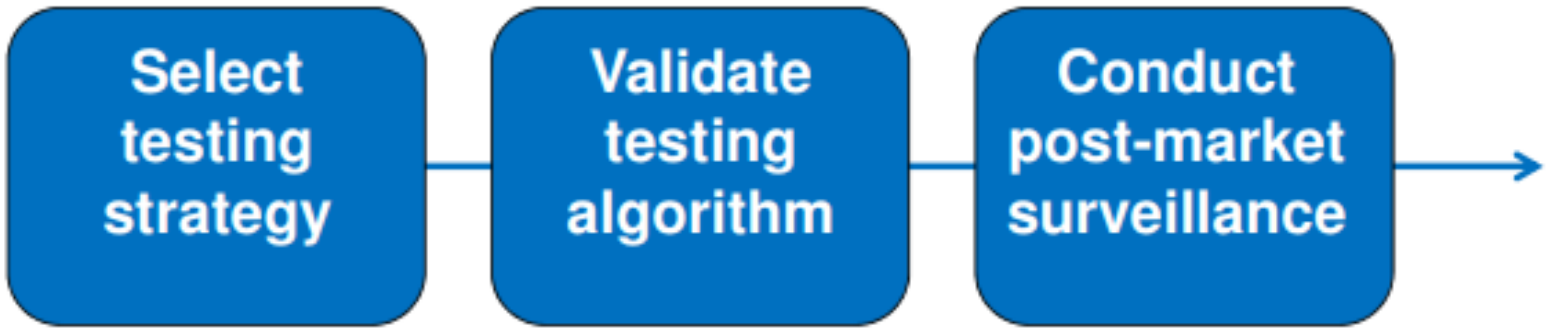
ARTICLE HISTORY
Received 30 September 2016
Accepted 5 April 2017

KEYWORDS
HIV testing; HTS; lay providers; task shifting; task sharing

Considerations for success

- *Select lay providers well-matched to clientele*
- *Training, mentoring and support is key*
- *Quality assurance system is essential*
- *Adequate remuneration and inclusion of trained lay providers in the staff establishments*
- *Policies should allow trained lay providers*
- *Give pre-test information and post-test counselling – including support for linkage*
- *Collect specimens and perform HIV RDTs; including interpreting test results and issue HIV results to clients*
- *Can also integrate HIV self-testing, test for triage and assisted partner notification*

Assuring quality of diagnostics



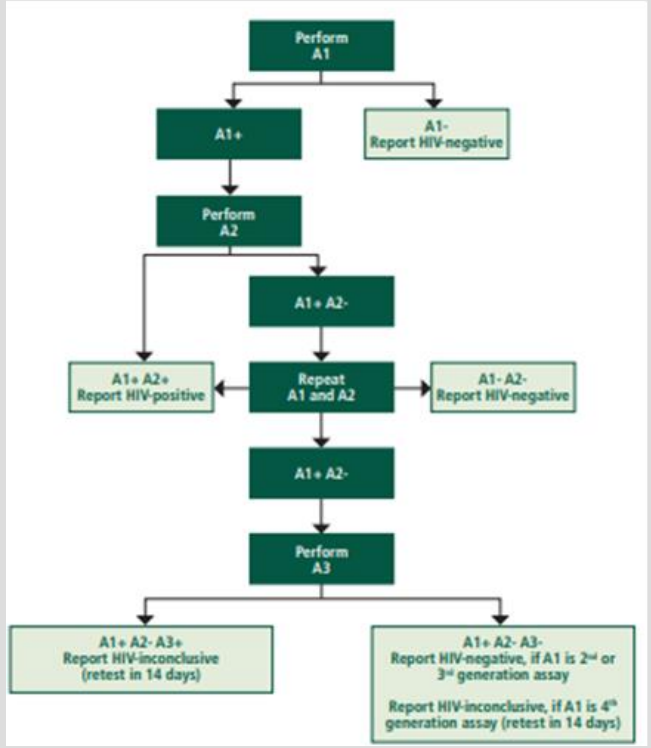
Key points

1. Chose a **testing strategy** (high or low prevalence)
2. Select products and validate the **testing algorithm**
3. Ensure **post-market surveillance** of products used

WHO recommended HIV testing strategies

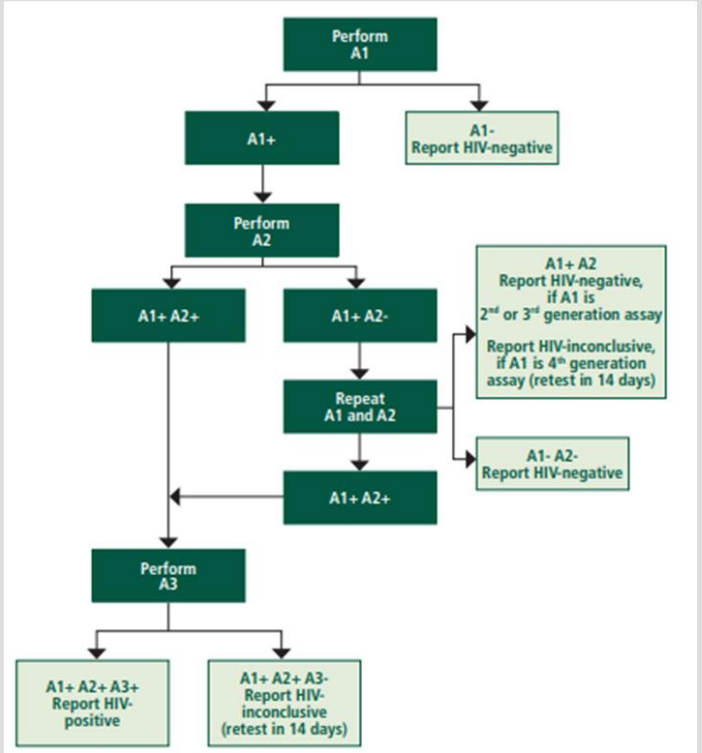
Using combination of RDTs and EIAs

High prevalence settings ≥5%
(2 consecutive reactive tests = positive)



- *A1- = negative*
- ***A1+; A2+ = positive***
- *A1+; A2-; A3- = negative*
- *A1+; A2-; A3+ = inconclusive*

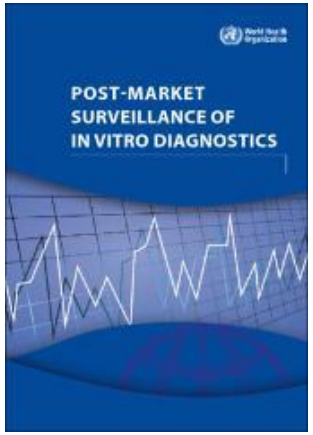
Low prevalence <5%
(3 consecutive reactive tests = positive)

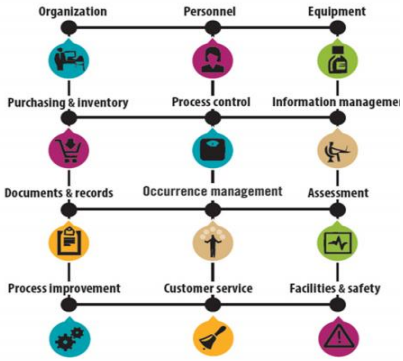


- *A1- = negative*
- *A1+; A2- = negative or inconclusive*
- ***A1+; A2+; A3+ = positive***
- *A1+; A2+; A3- = inconclusive*

Implementation for Accurate Diagnosis

- One A1 with superior sensitivity
- One each for A2 and A3 with
- superior specificity
- Be sure to have completed validation study demonstrating algorithm achieves
- Have a validated **back-up** algorithm in place
- Assure quality of HIV testing





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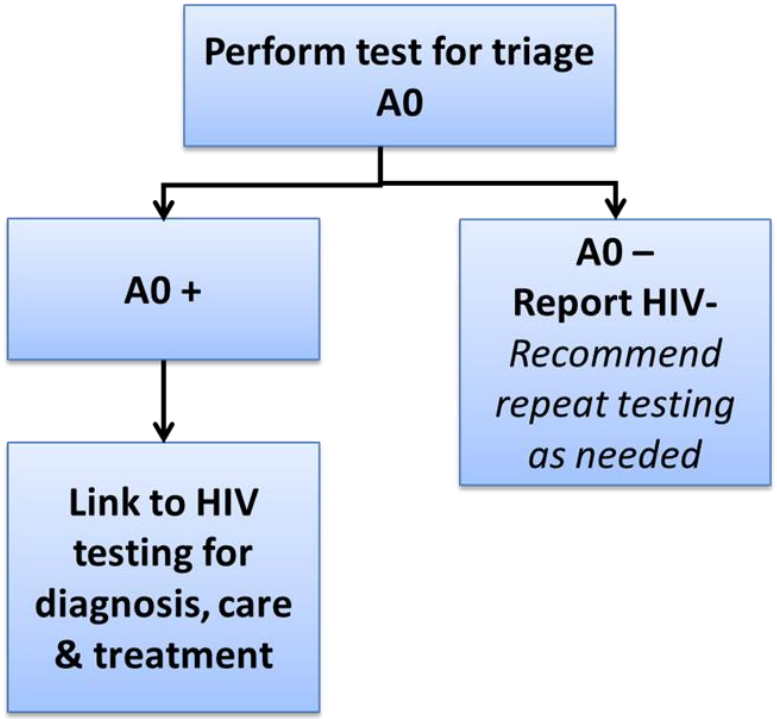
WHO recommended test for triage strategy

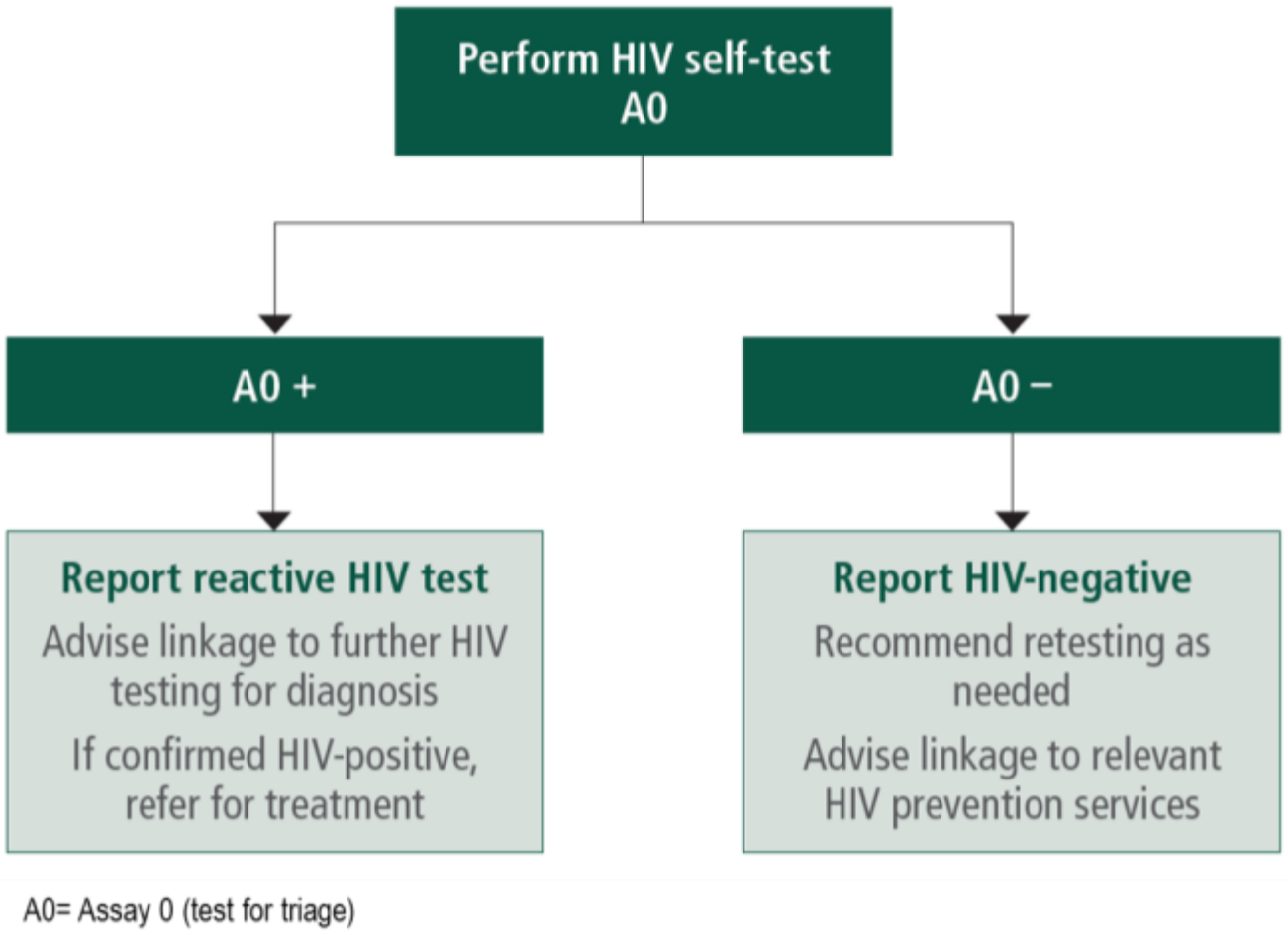


- Recommended strategy by WHO
- **A single rapid diagnostic test in community setting**
- **A0 = Assay 0; not a definitive HIV+ test result**
- Emphasis on HIV diagnosis by trained tester – facility or specific community settings (start at A1)
- ***Triage*** – prioritize linkage following testing as appropriate

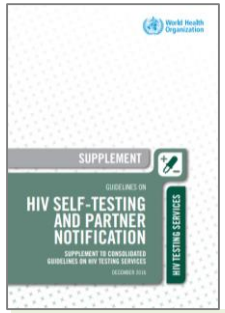
Potential benefits and considerations

- Already standard practice in many countries and settings in all regions
- Helpful way to start task sharing testing to clients and lay providers and to reach populations in need of HIV testing services but who not routinely come to existing services, e.g. young people, men, key populations.
- Emphasis on linkage is critical – as risk for loss to follow-up is real without immediate offer of HIV prevention and treatment
- Ideal to have onsite confirmation and treatment in some settings, but not feasible in all, especially where prevalence is declining, yet scale-up of testing is still needed
- May improve testing quality and PPV in health facilities – to be discussed

WHO recommended HIV self-testing strategy



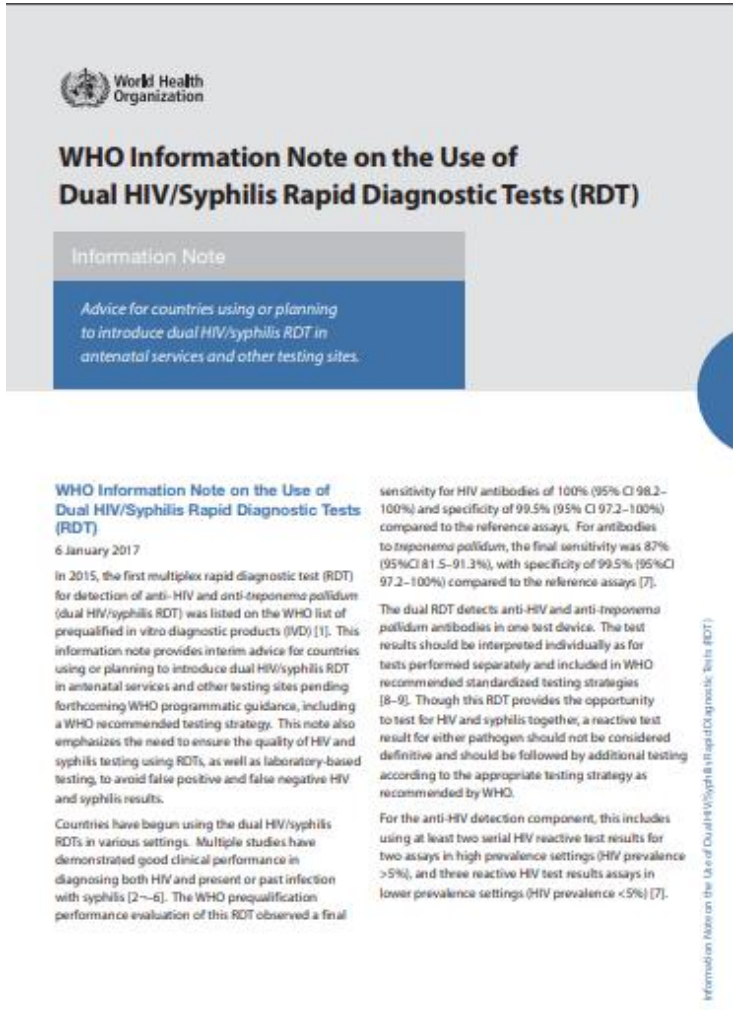
A0= Assay 0 (test for triage)



- HIVST requires self-testers with a **reactive** result to receive **further testing** from a trained provider using a validated national testing algorithm.
- All self-testers with a **non-reactive** test result should retest if they might have been exposed to HIV in the preceding six weeks, or are at high ongoing HIV risk.
- HIVST is **not** recommended for people taking anti-retroviral drugs, as this may cause a false non-reactive result.

*Any person **uncertain** about how their self-test result, should be encouraged to access facility- or community-based HIV testing

WHO recommended strategies for dual HIV/Syphilis RDTs



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WHO Information Note on the Use of Dual HIV/Syphilis Rapid Diagnostic Tests (RDT)

Information Note

Advice for countries using or planning to introduce dual HIV/syphilis RDT in antenatal services and other testing sites.

WHO Information Note on the Use of Dual HIV/Syphilis Rapid Diagnostic Tests (RDT)

6 January 2017

In 2015, the first multiplex rapid diagnostic test (RDT) for detection of anti- HIV and anti-*treponema pallidum* (dual HIV/syphilis RDT) was listed on the WHO list of prequalified in vitro diagnostic products (IVD) [1]. This information note provides interim advice for countries using or planning to introduce dual HIV/syphilis RDT in antenatal services and other testing sites pending forthcoming WHO programmatic guidance, including a WHO recommended testing strategy. This note also emphasizes the need to ensure the quality of HIV and syphilis testing using RDTs, as well as laboratory-based testing, to avoid false positive and false negative HIV and syphilis results.

Countries have begun using the dual HIV/syphilis RDTs in various settings. Multiple studies have demonstrated good clinical performance in diagnosing both HIV and present or past infection with syphilis [2–6]. The WHO prequalification performance evaluation of this RDT observed a final sensitivity for HIV antibodies of 100% (95% CI 98.2–100%) and specificity of 99.5% (95% CI 97.2–100%) compared to the reference assays. For antibodies to *treponema pallidum*, the final sensitivity was 87% (95%CI 81.5–91.3%), with specificity of 99.5% (95%CI 97.2–100%) compared to the reference assays [7].

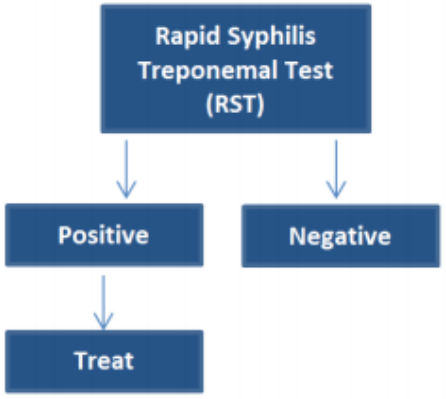
The dual RDT detects anti-HIV and anti-*treponema pallidum* antibodies in one test device. The test results should be interpreted individually as for tests performed separately and included in WHO recommended standardized testing strategies [8–9]. Though this RDT provides the opportunity to test for HIV and syphilis together, a reactive test result for either pathogen should not be considered definitive and should be followed by additional testing according to the appropriate testing strategy as recommended by WHO.

For the anti-HIV detection component, this includes using at least two serial HIV reactive test results for two assays in high prevalence settings (HIV prevalence >5%), and three reactive HIV test results assays in lower prevalence settings (HIV prevalence <5%) [7].

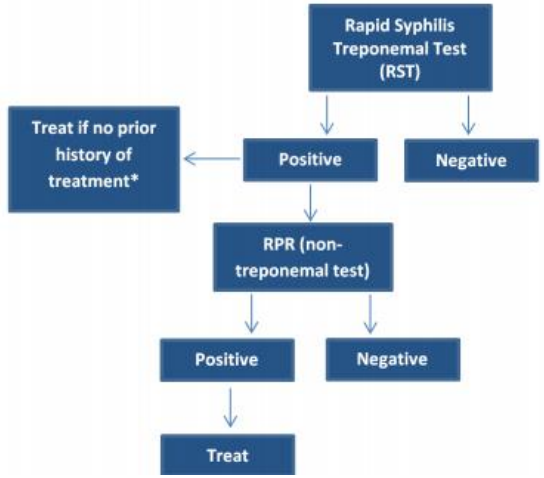
Information Note on the Use of Dual HIV/Syphilis Rapid Diagnostic Tests (RDT)

- **Use as A0 or A1 in HIV testing strategy.**
  - Currently not designed or available for self-testing
- **Important not to use on individuals previously diagnosed with HIV**
- Not for use in groups reporting past syphilis infection and treatment – unless pregnant women
  - Pregnant women who have tested syphilis positive and received treatment during a previous pregnancy should be considered for re-treatment upon receiving a positive syphilis test result in subsequent pregnancies

Low syphilis prevalence (<5%)



High syphilis prevalence (≥5%)

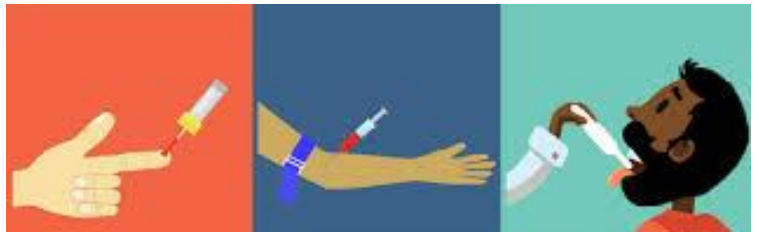


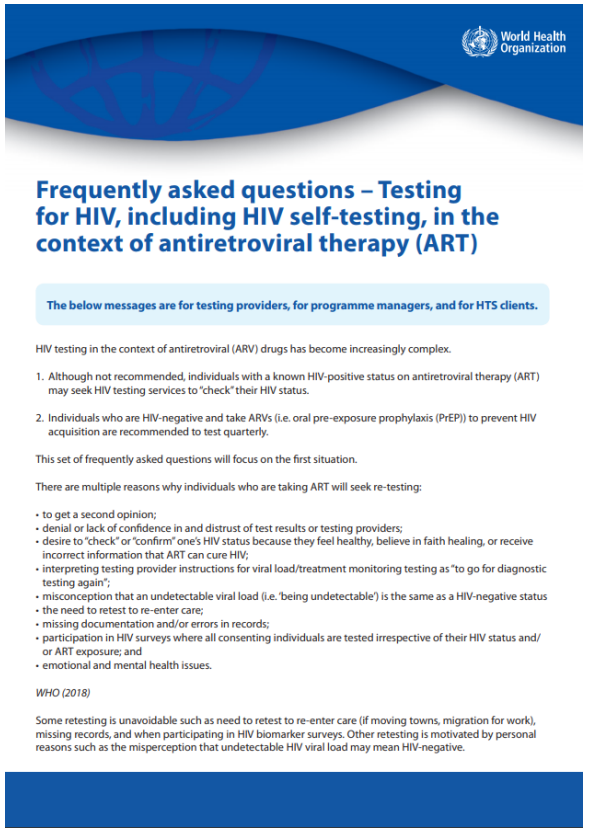
ARVs for treatment or prevention can impact test results

- ARV drugs work to suppress the HIV virus and can impact the production of HIV antibodies.
- People with HIV who are on ART (or those who acquire HIV while taking PrEP) may have a false nonreactive (negative) self-test result.
- Important people are made aware and those on ART and PrEP can be directed to appropriate services.
- WHO recommends people on ART should not retest or self-test – important to deliver clear messages to PLHIV on ART
- Individuals on PrEP need quarterly retesting – initial false reactive results (A1+) should not be cause to stop PrEP. Important to confirm and consider application of low prevalence testing strategy
- WHO New WHO FAQs:

  https://apps.who.int/iris/bitstream/handle/10665/276226/WHO-EMP-SAV-2018.06-eng.pdf

  http://apps.who.int/iris/bitstream/handle/10665/276228/WHO-EMP-SAV-2018.05-eng.pdf

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Frequently asked questions – Testing for HIV, including HIV self-testing, in the context of antiretroviral therapy (ART)

The below messages are for testing providers, for programme managers, and for HTS clients.

HIV testing in the context of antiretroviral (ARV) drugs has become increasingly complex.

1. Although not recommended, individuals with a known HIV-positive status on antiretroviral therapy (ART) may seek HIV testing services to "check" their HIV status.
2. Individuals who are HIV-negative and take ARVs (i.e. oral pre-exposure prophylaxis (PrEP)) to prevent HIV acquisition are recommended to test quarterly.

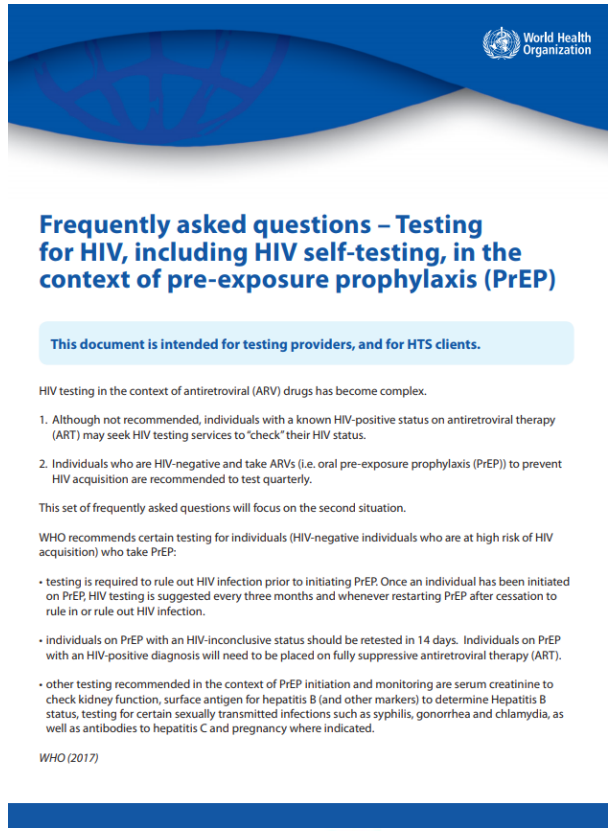
This set of frequently asked questions will focus on the first situation.

There are multiple reasons why individuals who are taking ART will seek re-testing:

- to get a second opinion;
- denial or lack of confidence in and distrust of test results or testing providers;
- desire to "check" or "confirm" one's HIV status because they feel healthy, believe in faith healing, or receive incorrect information that ART can cure HIV;
- interpreting testing provider instructions for viral load/treatment monitoring testing as "to go for diagnostic testing again";
- misconception that an undetectable viral load (i.e. 'being undetectable') is the same as a HIV-negative status
- the need to retest to re-enter care;
- missing documentation and/or errors in records;
- participation in HIV surveys where all consenting individuals are tested irrespective of their HIV status and/or ART exposure; and
- emotional and mental health issues.

WHO (2018)

Some retesting is unavoidable such as need to retest to re-enter care (if moving towns, migration for work), missing records, and when participating in HIV biomarker surveys. Other retesting is motivated by personal reasons such as the misperception that undetectable HIV viral load may mean HIV-negative.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Frequently asked questions – Testing for HIV, including HIV self-testing, in the context of pre-exposure prophylaxis (PrEP)

This document is intended for testing providers, and for HTS clients.

HIV testing in the context of antiretroviral (ARV) drugs has become complex.

1. Although not recommended, individuals with a known HIV-positive status on antiretroviral therapy (ART) may seek HIV testing services to "check" their HIV status.
2. Individuals who are HIV-negative and take ARVs (i.e. oral pre-exposure prophylaxis (PrEP)) to prevent HIV acquisition are recommended to test quarterly.

This set of frequently asked questions will focus on the second situation.

WHO recommends certain testing for individuals (HIV-negative individuals who are at high risk of HIV acquisition) who take PrEP:

- testing is required to rule out HIV infection prior to initiating PrEP. Once an individual has been initiated on PrEP, HIV testing is suggested every three months and whenever restarting PrEP after cessation to rule in or rule out HIV infection.
- individuals on PrEP with an HIV-inconclusive status should be retested in 14 days. Individuals on PrEP with an HIV-positive diagnosis will need to be placed on fully suppressive antiretroviral therapy (ART).
- other testing recommended in the context of PrEP initiation and monitoring are serum creatinine to check kidney function, surface antigen for hepatitis B (and other markers) to determine Hepatitis B status, testing for certain sexually transmitted infections such as syphilis, gonorrhea and chlamydia, as well as antibodies to hepatitis C and pregnancy where indicated.

WHO (2017)

Source: WHO 2016; WHO 2017

WHO re-testing recommendations

1. HIV-negative individuals at high ongoing risk, such as key populations, serodiscordant couples, pregnant and post-partum women in high incidence and high burden settings
   - Depending on risk can be annual – or every 3 months (e.g. PrEP users) to 6 months (e.g. sex workers)
   - Pregnant women at 1st and 3rd ANC visit for high risk groups (SDC and KP) and those in high incidence and high burden settings

2. HIV-negative individuals reporting a risk in the preceding 6-12 weeks prior to testing i.e. window period

3. Retesting all newly diagnosed PLHIV to verify HIV status to prevent unnecessary initiation of life-long ART

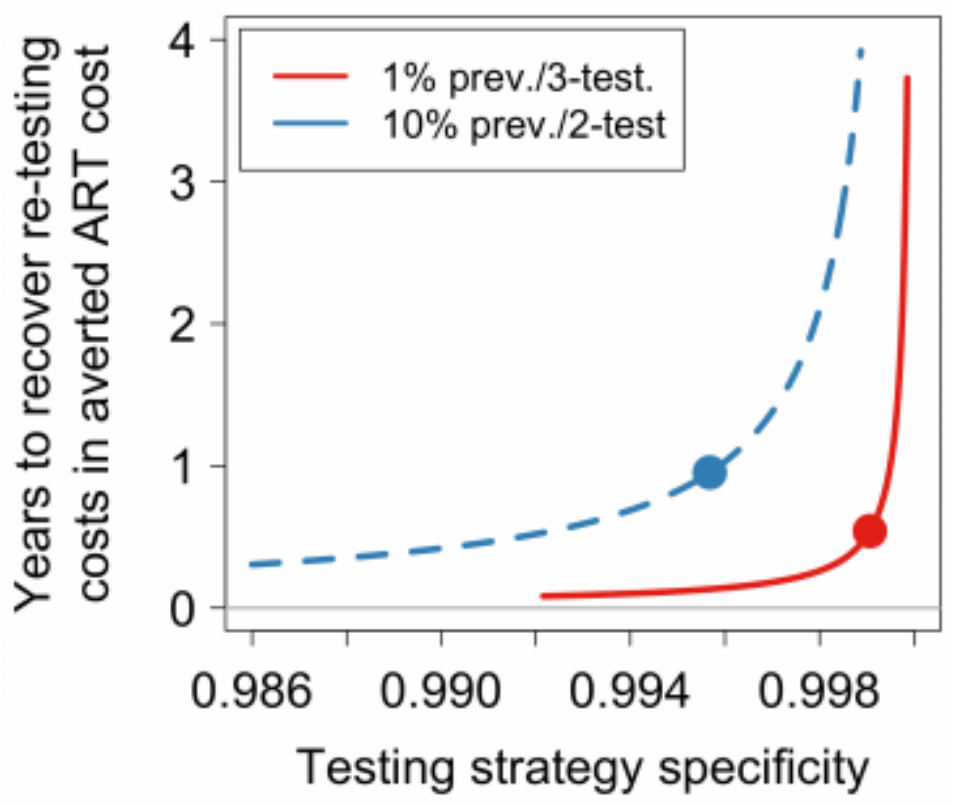
4. PLHIV who are on ART should not be retested

5. People taking PrEP should be retested for HIV quarterly at community or facility settings as part of broader health and SRH services - at this time self-testing is not recommended to replace quarterly visits using standard HIV testing services

Re-testing costs and expected ART costs for misclassified *HIV-negative adults*

results per 10,000 tested

	Low prevalence example	High prevalence example
HIV prevalence among testers:	1.0%	10.0%
Serial testing strategy:	3-test	2-test
'Real-world' testing strategy specificity:	99.9%	99.6%
Positive predictive value:	91.3%	96.2%
Total cost per 10,000 tested:	$82,628	$87,020
Number HIV-negative initiated on ART:	9.2	38.9
Expected lifetime ART cost for HIV-negative:	$57,832	$243,399
Total re-testing cost:	$2,011	$14,020
Expected savings from re-testing:	**$55,634**	**$225,751**
Time to recover re-testing costs by averted ART costs:	**0.5 years**	**0.8 years**



Source: Eaton et al 2017

Misclassification of HIV status – largely due to suboptimal testing strategy and algorithm

Johnson CC et al. Journal of the International AIDS Society 2017, 20(Suppl 6):21755
http://www.jiasociety.org/index.php/jias/article/view/21755 | http://dx.doi.org/10.7448/IAS.20.7.21755

JIAS Journal of the International AIDS Society

Review article

To err is human, to correct is public health: a systematic review examining poor quality testing and misdiagnosis of HIV status

Cheryl C. Johnson[1,2§], Virginia Fonner[3], Anita Sands[4], Nathan Ford[1], Carla Mahklouf Obermeyer[5], Sharon Tsui[6], Vincent Wong[7] and Rachel Baggaley[1]

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Abstract

Introduction: In accordance with global testing and treatment targets, many countries are seeking ways to reach the "90-90-90" goals, starting with diagnosing 90% of all people with HIV. Quality HIV testing services are needed to enable people with HIV to be diagnosed and linked to treatment as early as possible. It is essential that opportunities to reach people with undiagnosed HIV are not missed, diagnoses are correct and HIV-negative individuals are not inadvertently initiated on life-long treatment. We conducted this systematic review to assess the magnitude of misdiagnosis and to describe poor HIV testing practices using rapid diagnostic tests.

Methods: We systematically searched peer-reviewed articles, abstracts and grey literature published from 1 January 1990 to 19 April 2017. Studies were included if they used at least two rapid diagnostic tests and reported on HIV misdiagnosis, factors related to potential misdiagnosis or described quality issues and errors related to HIV testing.

Results: Sixty-four studies were included in this review. A small proportion of false positive (median 3.1%, interquartile range (IQR): 0.4-5.2%) and false negative (median: 0.4%, IQR: 0-3.9%) diagnoses were identified. Suboptimal testing strategies were the most common factor in studies reporting misdiagnoses, particularly false positive diagnoses due to using a "tiebreaker" test to resolve discrepant test results. A substantial proportion of false negative diagnoses were related to retesting among people on antiretroviral therapy.

Conclusions: HIV testing errors and poor practices, particularly those resulting in false positive or false negative diagnoses, do occur but are preventable. Efforts to accelerate HIV diagnosis and linkage to treatment should be complemented by efforts to improve the quality of HIV testing services and strengthen the quality management systems, particularly the use of validated testing algorithms and strategies, retesting people diagnosed with HIV before initiating treatment and providing clear messages to people with HIV on treatment on the risk of a "false negative" test result.

Keywords: HIV; HIV testing; misdiagnosis; misclassification; diagnostic error; false positive; healthcare; patient safety

To access the supplementary material to this article please see Supplementary Files under Article Tools online.

- False positive and false negative results identified – largely due to suboptimal testing strategies, poor test selection and use etc.
- Review could not identify the specific causes of misdiagnosis, it did find common & avoidable errors:
  1. **Suboptimal testing strategy**
  2. Inadequate management and supervision of testers,
  3. User errors particularly when interpreting weak reactive lines
  4. Issue of testing on ART warrants further investigation
- Consequences of misdiagnoses are serious at an individual & public health level.
  - False positive = unnecessary ART initiation
  - False negative = missed opportunity
- With the momentum to increase diagnosis of PLHIV & link them to ART, a parallel push to improve the quality, prevent errors & misdiagnosis is essential.

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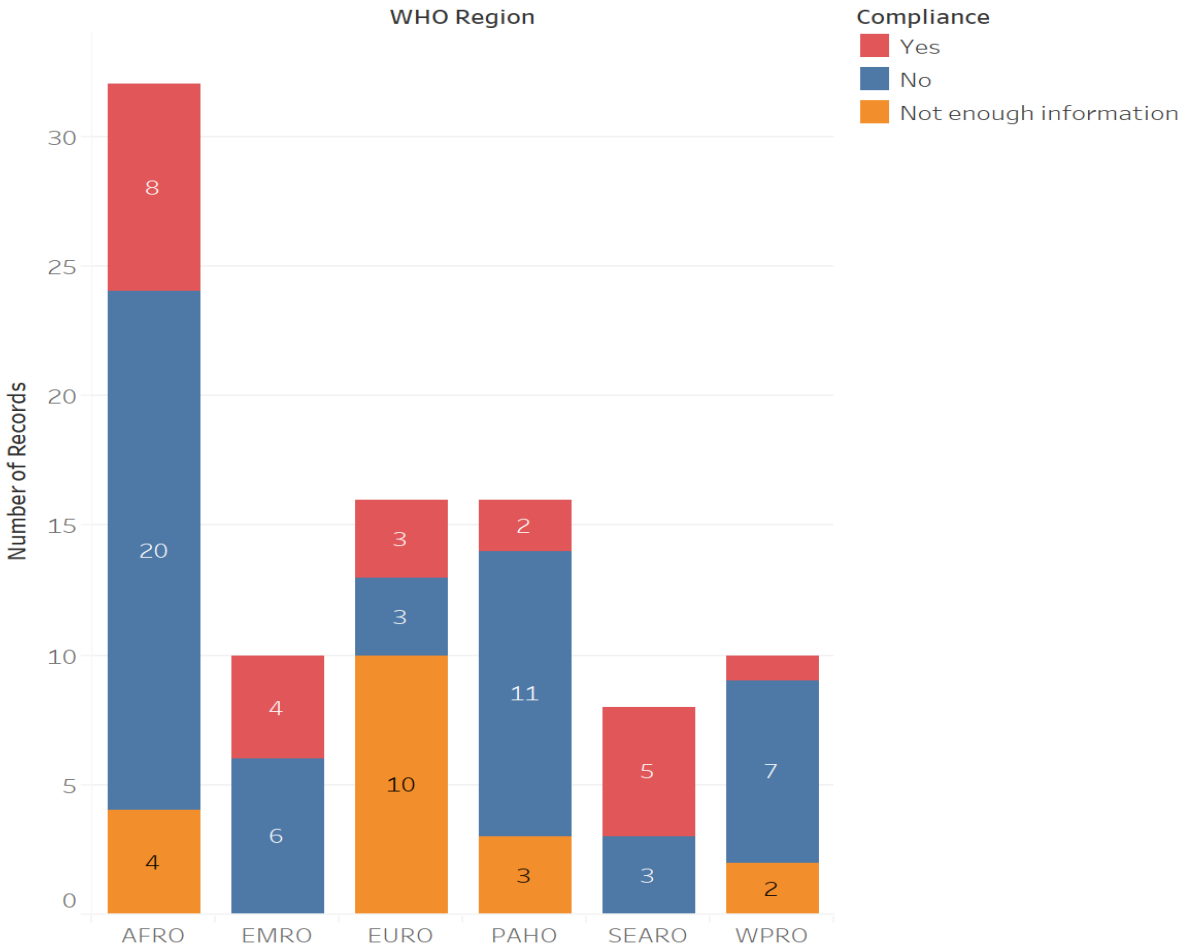
2018 Policy Review on uptake of WHO recommended strategies and algorithms



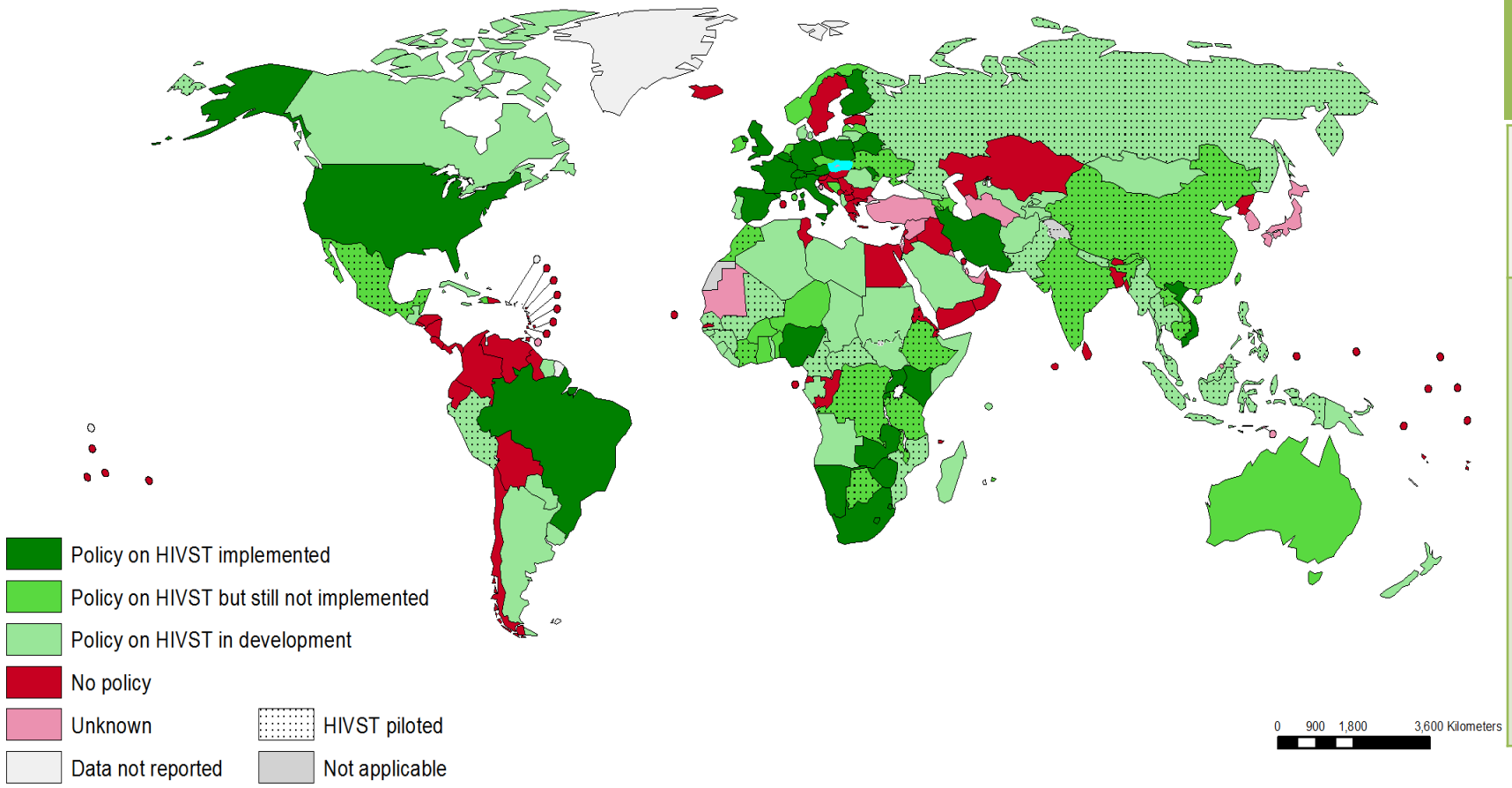
- Of 92 testing strategies:
  - 23/92 aligned with WHO rec (25%)
  - 50/92 did not align with WHO rec (54%)
  - 19/92 did not have sufficient information to make determination (21%)
- Excluding policies without sufficient information, 23/73 (32%) were in compliance
- Improvements from 2014 review (17% compliance):
  - Less use of tie-breaker to rule-in HIV infection
  - Some countries adapted policies to be more in compliance with WHO rec

Efforts still needed to improve uptake and compliance

HIVST policy and implementation map

Ongoing review

59 Countries with HIVST policies – 28 countries fully implementing - additional 53 countries report policy on HIVST under development.



Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and WHO HIV Country Intelligence Tool, 2018

WHO ongoing policy review identified 19 HTS policies including HIVST – 9 with operational manuals

Detailed Guidance on HIVST	Guidelines include HIVST
South Africa, Kenya, Viet Nam, Zimbabwe, Zambia, Swaziland, Benin, Malawi and Senegal	Lesotho, Cote d'Ivoire, Mali, Pakistan, Somalia, South Sudan, Brazil, Cameroon, France, Ghana, Australia, Luxembourg, Netherlands, Uganda and UK

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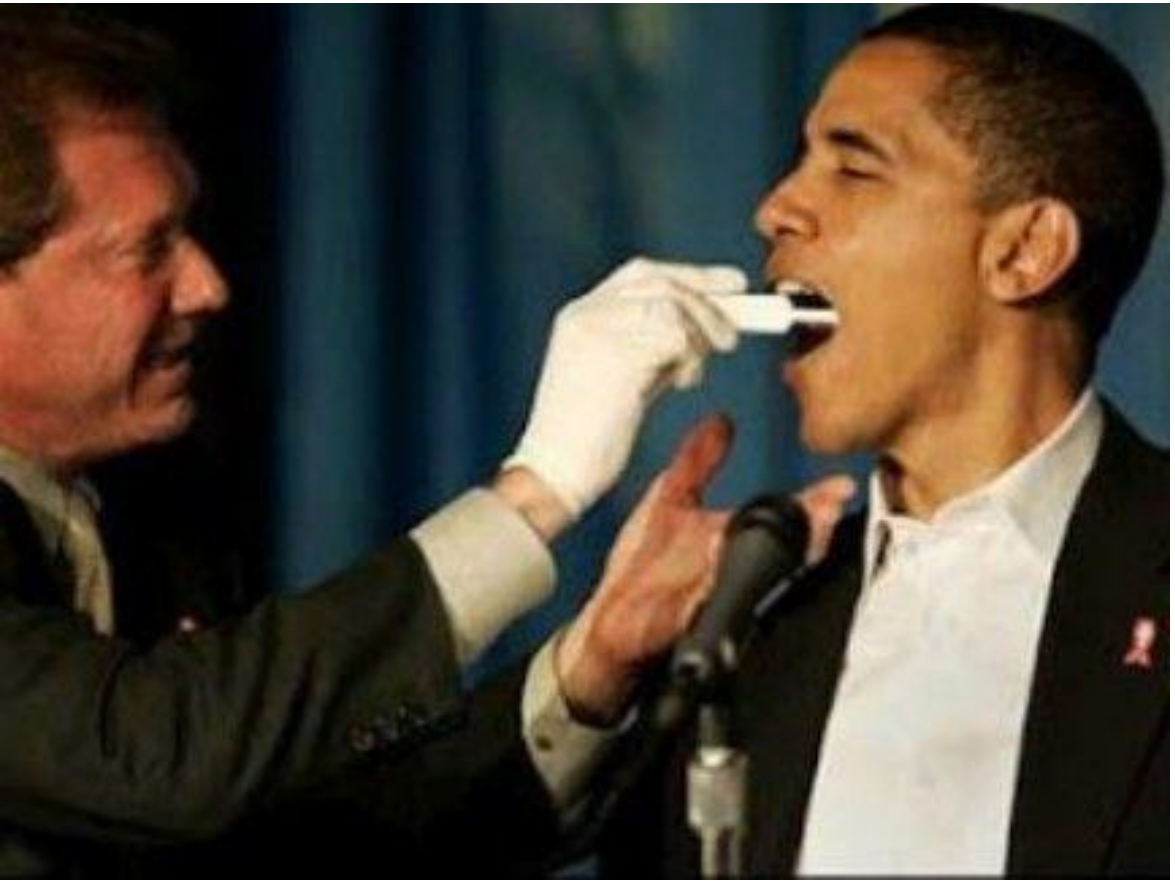
WHO recommended HIV rapid diagnostic tests (RDT)



- Rapid serology assays using (fingerprick or oral fluid specimen) can be used at point of care and detect HIV-1/2 antibodies
- All WHO PQ tests must pass review and approval – and RDTs for professional use must achieve ≥99% sensitivity and ≥98% specificity
- No single HIV test, including RDTs, can provide an HIV-positive diagnosis. Use at least 2-3 tests together in algorithm with ≥99% PPV

Products approved for use

In vitro diagnostics and laboratory technology

WHO list of prequalified in vitro diagnostic products

The WHO list of prequalified in vitro diagnostic products helps countries to easily make evidence-based selections when purchasing IVDs. By referencing the list when making purchasing decisions, countries can easily select IVDs that are safe, effective and cost-efficient. This promotes equitable access to IVDs.

Evidence-based selection – promoting informed choices and improved resource allocation through use of Health Technology Assessment, the Essential Medicines List, priority lists of products/devices (including diagnostics) and technologies

List of prequalified in vitro diagnostic products
pdf, 181kb

Disclaimer for WHO list of prequalified diagnostic products
pdf, 90kb

WHO prequalification of in vitro diagnostics public reports

- HIV serology
- HIV Self-Test
- Hepatitis C assays
- Hepatitis B assays
- Malaria rapid diagnostics tests
- HIV virological technologies
- HPV virological technologies
- CD4 assays

- 20 HIV RDTs listed by WHO PQ

  (17 professional use, 2 HIVST, and 1 Dual HIV/Syph Dual Test)
  - Professional use HIV RDT Public reports: http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-rdts/public_report/en/
  - Self-testing HIV RDT Public reports: http://www.who.int/diagnostics_laboratory/evaluations/pq-list/self-testing_public-report/en/
  - Dual HIV/Syphilis RDT public report
  - https://www.who.int/diagnostics_laboratory/evaluations/170620_amended_final_pqpr_0179_012_00_v4.pdf?ua=1
- Additional non-WHO PQ (CE or ERPD risk category products) listed by
  - Global Fund Oct 2018 list: https://www.theglobalfund.org/media/5878/psm_productshiv-who_list_en.pdf
- Additional information on HIVST
  - Unitaid-WHO 2018 landscape: https://unitaid.org/assets/HIVST-landscape-report.pdf

HIV RDTs WHO prequalified for professional use (Dec 2018)

Product (manufacturer)	Product (manufacturer)	Product (manufacturer)
ABON HIV-1/2/O Tri-line HIV RDT (ABON Biopharm, China)	**First Response HIV-1.2.0 Card Test** (Premier Medical Corporation, India)	**Rapid Test for Antibody to HIV (Colloidal Gold Device)** (Beijing Wantai, China)
Alere Determine HIV-1/2 (Alere Medical Co, Japan)	**Genie Fast HIV 1/2** (Bio-Rad, France)	**SD BIOLINE HIV-1/2 3.0** (Standard Diagnostics, Korea)
Alere HIV Combo (Alere Medical Co, Japan)	**HIV 1/2 STAT-PAK Dipstick** (Chembio Diagnostics Systems, USA)	**SURE CHECK HIV 1/2 Assay** (Chembio Diagnostics Systems, USA)
Alere HIV/Syphilis Duo (Standard Diagnostics, Korea)	**HIV 1/2 STAT-PAK** (Chembio Diagnostics Systems, USA)	**Uni-Gold HIV** (Trinity Biotech, Ireland)
Diagnostic Kit for HIV (1+2) (Colloidal Gold) V2 (Shanghai Kehua Bio-engineering, China)	**Insti HIV-1/HIV-2 Antibody Test** (BioLytical Laboratories, Canada	**Vikia HIV 1/2** (bioMörieux, France)
DPP HIV 1/2 Assay (Chembio Diagnostics Systems, USA)	**One Step HIV1/2 Whole Blood/Serum/Plasma Test** (Guangzhou Wondfo Biotech, China)	**Geenius™ HIV 1/2 Confirmatory Assay** (Bio-Rad, France)

HIVST products with WHO PQ, ERPD or approval from founding member of IMDRF*

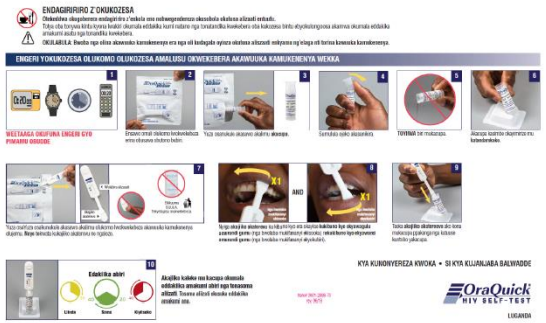
Test (manufacturer)	Specimen	Approval	SENS	SPEC	Price per test (US$)
atomo HIV Self Test (Atomo Diagnostics, Australia)	Blood	TGA; CE mark ERPD- Risk Category 3	99.7%	99.7%	Public sector: $ 3
autotest VIH® ** (AAZ Labs, France)	Blood	CE mark	100.0%	99.8%	HIC retail: $ 20–28 Distributors/NGOs: $ 8–15
BioSURE HIV Self Test ** (BioSURE, United Kingdom Ltd)	Blood	CE mark ERPD- Risk Category 3	99.7%	99.9%	HIC retail: $ 42–48 HIC public sector: $ 7.5–15 LMIC retail: $ 11.75
Exacto® Test HIV (Biosynex, France)	Blood	CE mark	99.99%	99.99%	Not available
INSTI® HIV Self Test ** (bioLytical Lab., Canada)	Blood	WHO PQ	99.8%	99.5%	Price: $ 3–12 MSRP: $ 7–36
OraQuick® In-Home HIV Test (OraSure Technologies, USA)	Oral fluid	FDA, CE Mark	FDA: 91.7% CE: 100.0%	FDA: 99.98% CE: 99.8%	HIC retail: $ 40 Public sector prices vary.
OraQuick® HIV Self Test (OraSure Technologies, USA)	Oral fluid	WHO PQ	99.4%	99.0%	LMIC ex-works: $ 2 for 50 countries
SURE CHECK® HIV Self Test (Chembio Diagnostic Systems Inc., USA)	Blood	ERPD- Risk Category 3	NA	NA	NA

HIC, high-income countries; **FDA**, Food and Drug Administration; **ERPD,** Expert Review Panel for Diagnostics; **Gen,** test generation; **LMIC**, low- and middle-income countries, **MRSP**: maximum suggested retail price; **NA**, not available.
* Includes products prequalified by WHO, approved by a regulatory authority in one of founding-member countries of the International Medical Device Regulators Forum or eligible for procurement on recommendation of Unitaid/Global Fund Expert Review Panel for Diagnostics. ** These products sold in more than one packaging format.
Note: Product details based on information provided by the manufacturers at the time of report preparation.

Updated 3 Dec 2018 - Unitaid 2018

Professional test

Self-test



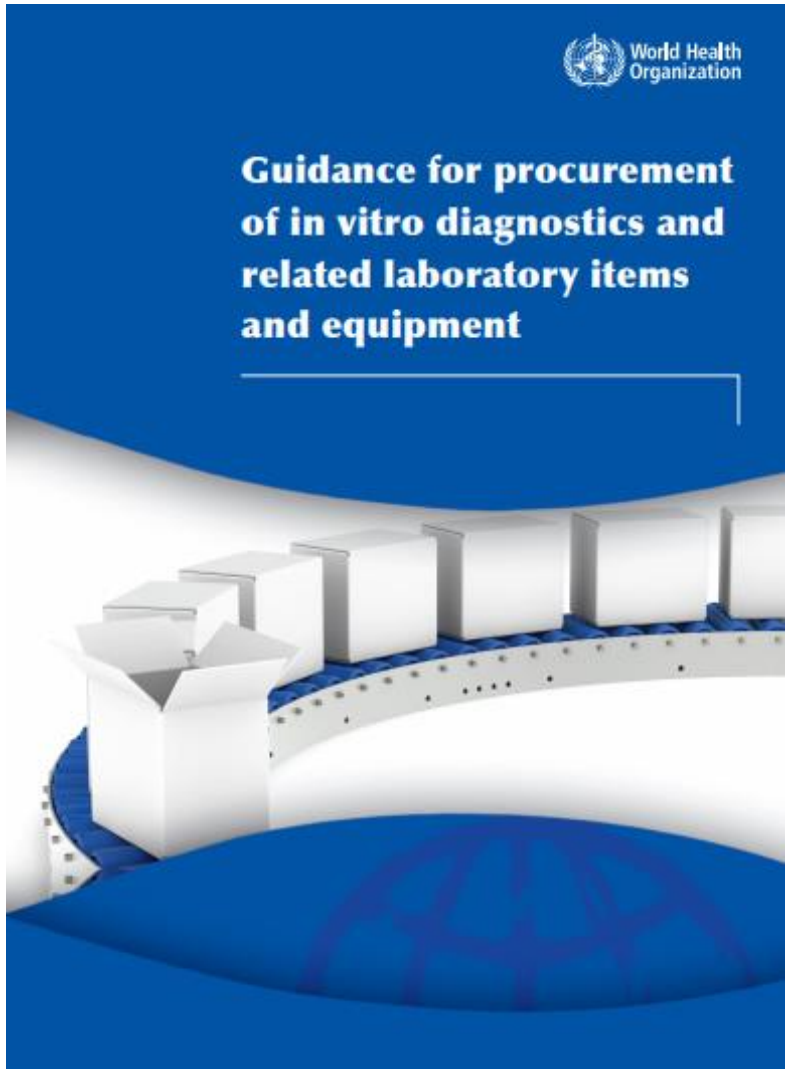
Dual HIV/Syphilis rapid diagnostic test

Alere™ HIV/Syphilis Duo
to be renamed SD BIOLINE HIV/Syphilis
(WHO PQed)

- 1 dual HIV/Syphilis test WHO PQed – 2 others in the pipeline
- All detect HIV antibodies; does not discriminate between current or past Syphilis infection
- Products required to meet ≥99% sensitivity and ≥ 98% specificity for HIV

How to select products for HIV testing algorithms

- **A testing strategy** describes a testing sequence for a specific objective, based on the desired positive/negative predictive values (≥99%)
- Whereas, a **testing algorithm** describes the specific branded products (IVDs) that will be used within a given testing strategy.
- To build and verify a HIV testing algorithm
  - Select from the list of WHO prequalified IVDs
  - Ensure Assay 1 is most sensitive and Assays 2 and 3 are most specific
    - Data is given in PQ Public Report and product IFU
    - Ensure that the combination of assays doesn't produce cross-reactivity



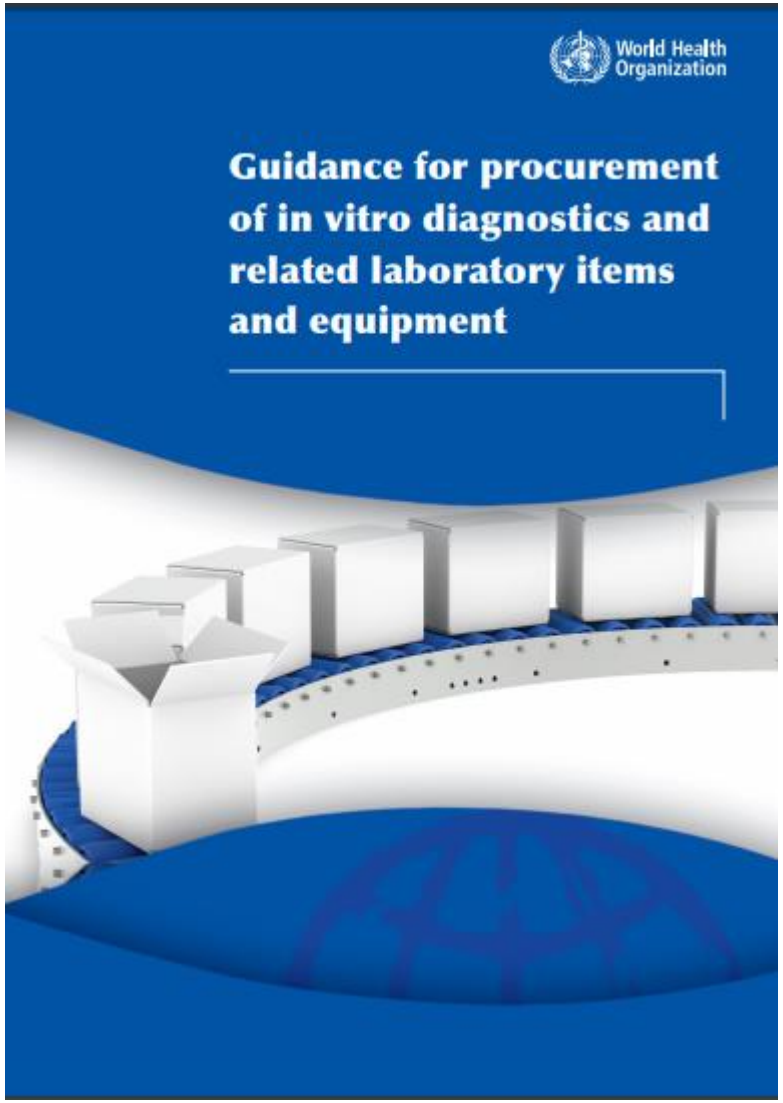
Specificity cross-walk – WHO prequalification data

- 27 RDTs, 7 EIAs were tested on the same specimen panel
- Of the 658 HIV-negative specimens tested
  - Overall **22 patients** would have been misclassified because of non-verified testing algorithms
  - 15 specimens showed false reactive results for at least two of 34 IVDs tested.
  - A further 7 specimens were false reactive on four or more IVDs.

WHO number	Product names							
990922	SD Bioline HIV Ag/Ab*	ImmunoComb II HIV 1&2 Bispot*						
991028	SD Bioline HIV Ag/Ab*	ImmunoComb II HIV 1&2 Bispot*						
WHO3-0513	SD Bioline HIV Ag/Ab*	SKB Diagnostic kit for HIV (1+2) antibody (colloidal gold) V2						
WHO3-0310	SD Bioline HIV Ag/Ab*	BioTracer™ HIV 1/2 Rapid Card						
WHO3-0201	SD Bioline HIV Ag/Ab	First Response® HIV 1·2·0 Card						
WHO3-0295	SD Bioline HIV-1/ 3.0	First Response® HIV 1·2·0 Card						
WHO3-0004	Alere Determine HIV-1/2	ABON™ HIV 1/2/O Tri-Line HIV Rapid Test Device						
WHO3-0006	Alere Determine HIV-1/2	Alere Determine HIV-1/2 Ag/Ab Combo*						
WHO3-0406	Alere Determine HIV-1/2 Ag/Ab Combo*	Retrocheck HIV						
WHO3-0054	SKB Diagnostic kit for Antibody to HIV (ELISA)	AID™ anti-HIV 1+2 ELISA						
WHO3-0098	Wantai Rapid Test for Antibody to HIV (Colloidal Gold Device)	Uni-Gold™ HIV						
WHO3-0069	Wantai Rapid Test for Antibody to HIV (Colloidal Gold Device)	Genie™ Fast HIV 1/2						
WHO3-0224	Wantai Rapid Test for Antibody to HIV (Colloidal Gold Device)	Genie™ Fast HIV 1/2						
WHO3-0291	Wantai Rapid Test for Antibody to HIV (Colloidal Gold Device)	Genie™ Fast HIV 1/2						
WHO3-0777	Wantai Rapid Test for Antibody to HIV (Colloidal Gold Device)	Genie™ Fast HIV 1/2						
WHO3-0010	Wantai Rapid Test for Antibody to HIV (Colloidal Gold Device)	Genie™ Fast HIV 1/2	DS-EIA-HIV-AGAB-SCREEN	SKB Diagnostic kit for Antibody to HIV (ELISA)				
WHO3-0468	DoubleCheckGold Ultra HIV 1&2	First Response® HIV 1·2·0 Card	Genscreen™ ULTRA HIV Ag-Ab					
990946	HIV 1/2 STAT-PAK®	HIV 1/2 STAT-PAK® Dipstick	DPP® HIV 1/2 Assay	SURE CHECK® HIV 1/2 Assay	OraQuick HIV 1/2 Rapid Antibody Test			
990973	Alere Determine HIV- 1/2	ImmunoComb II HIV 1&2 Bispot*	Genscreen ULTRA HIV Ag-Ab	VIKIA HIV 1/2	Enzygnost HIV Integral	Alere™ HIV Combo		
WHO3-0446	Retrocheck HIV	SKB Diagnostic kit for Antibody to HIV (ELISA)	DS-EIA-HIV-AGAB-SCREEN	AID anti- HIV 1+2 ELISA	BioTracer™ HIV 1/2 Rapid Card	Murex HIV Ag/Ab Combination		
WHO3-0008	Genscreen™ ULTRA HIV Ag-Ab	SKB Diagnostic kit for Antibody to HIV (ELISA)	DS-EIA-HIV-AGAB-SCREEN	AID™ anti-HIV 1+2 ELISA	AID™ anti-HIV 1+2 ELISA	Murex HIV Ag/Ab Combination	Enzygnost HIV Integral	
WHO3-0006	Alere Determine HIV-1/2 Ag/Ab Combo*	Retrocheck HIV	One Step HIV 1/2 Whole Blood/ Serum/ Plasma Test	Wantai Rapid Test for Antibody to HIV (Colloidal Gold Device	DS-EIAHIV-AGAB	Genie™ Fast HIV 1/2	Biselisa HIV 1+2 Ag/Ab	BioTracer™ HIV 1/2 Rapid Card

ASLM2018 abstract 3056475, Sands A et al.

Verification of HIV testing algorithms

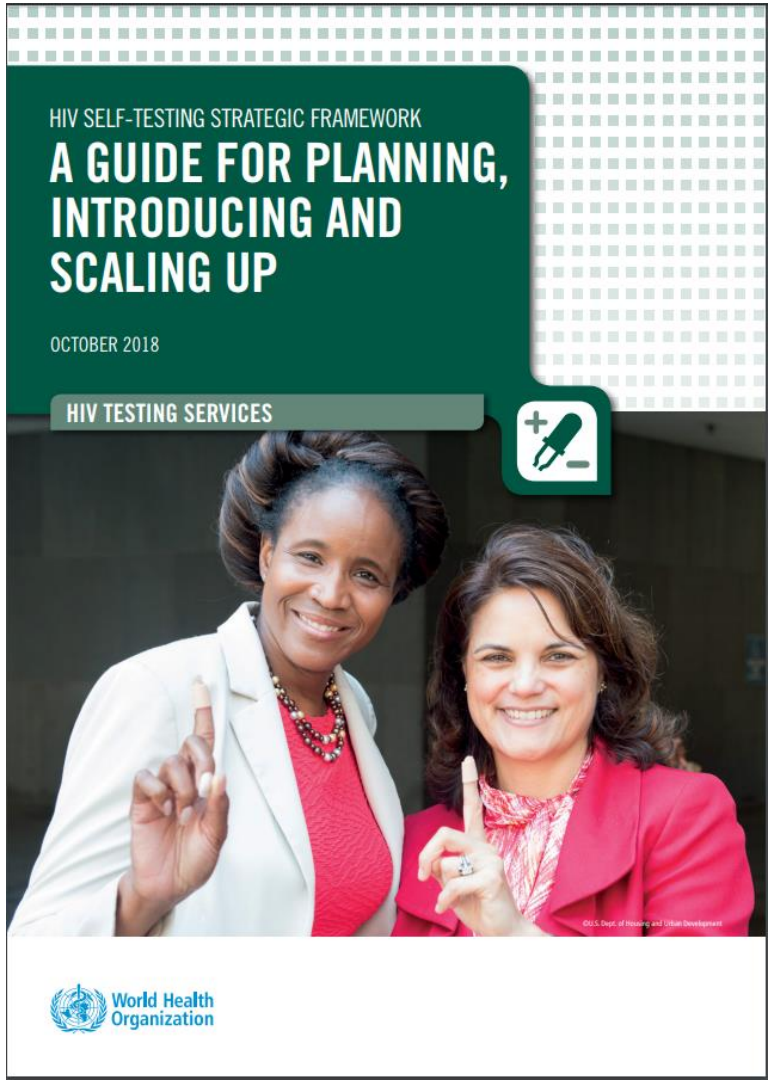


- WHO recommends a verification study
- This is not a study to re-confirm sensitivity and specificity.
  - ***See annex 2 of WHO guidance on procurement of IVDs***
- Specimen panel
  - One specimen with +1 reactivity intensity on a scale of 0 to 3 (near to LoD).
  - One specimen with inconclusive (+/-) reactivity intensity on a scale of 0 to 3.
  - One specimen with +2 reactivity intensity on a scale of 0 to 3. (well above LoD)
  - HIV negative specimens to verify cross-reactivity
- Test each specimen 40 replicates on the proposed testing algorithms and the status quo testing algorithm (except for HIV-negatives, these should be tested in duplicate only).
- More than one operator should conduct testing , over more than one day, in more than one testing site .

Ensure HIVST products are quality assured

Choose *products with acceptable specifications*

- **HIVST products should be:**
  - accurate (acceptable sensitivity and specificity);
  - simple to use;
  - have necessary consumables (such as swabs and plasters);
  - provide results that are easy to read/interpret and that are available in a short period of time (1–20 minutes after the test is conducted);
  - disposable in general waste system
- **HIVST should be accompanied with:**
  - contain clear pictorial instructions, support tools, info on what to do and where to go after self-testing
  - Products that include support tools – such as instructional videos, hotlines, websites and referral information – should be prioritized.
  - Products that do not have good stability (that cannot sustain suboptimal storage) or that are not robust (for example cannot sustain common user errors) may not be ideal for self-testing.
- **Other considerations**
  - Cost – consider cost of full service not just unit cost of kit
  - Options (offering blood and oral)



A clinical utility risk-benefit analysis for HIV self-testing

AUTHORS:

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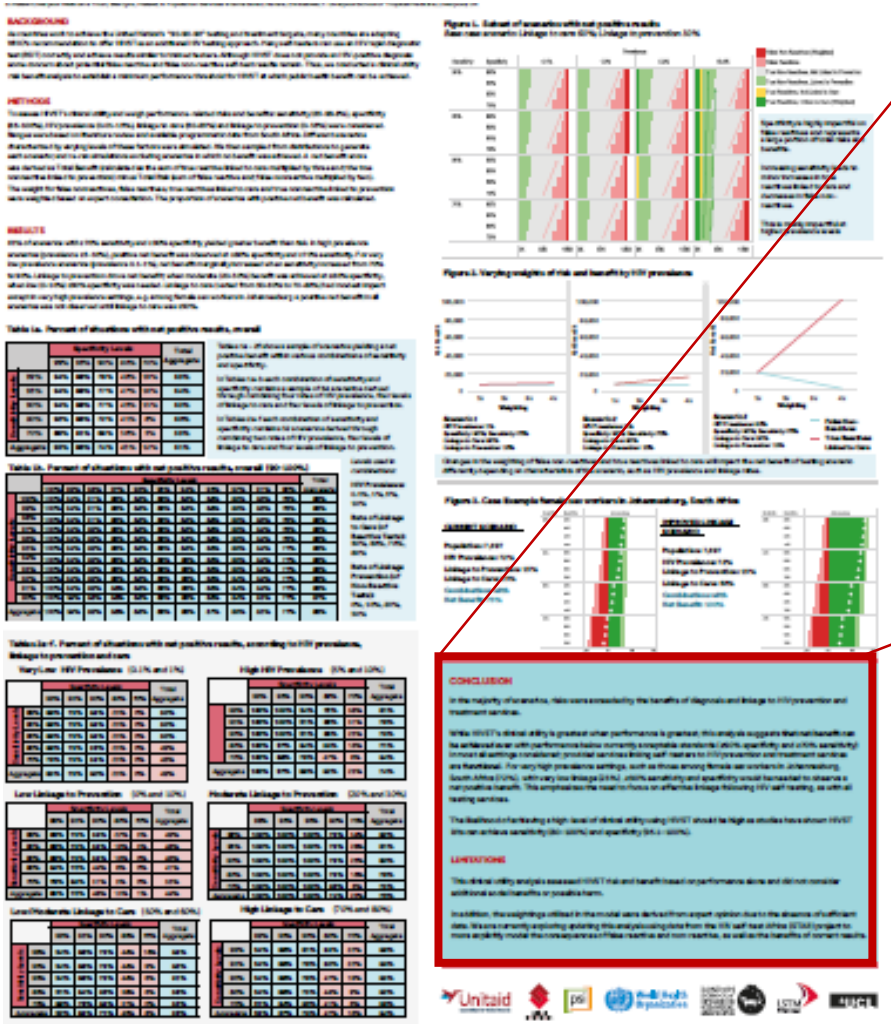


In the majority of scenarios, risks were exceeded by the benefits of diagnosis and linkage..

Analysis suggests that net benefit can be achieved even with **≥90% specificity and ≥70% sensitivity** in most all settings considered; provided services linking self-testers to HIV prevention and treatment services are functional.

For very high prevalence settings, e.g. sex workers in Johannesburg (72%), with very low linkage (23%) , **≥90% sensitivity and specificity** would be needed.

The likelihood of achieving a high-level of clinical utility using HIVST should be high as studies have shown HIVST kits can be correctly and accurately used by lay people (sensitivity: 80–100% and specificity: 95.1–100%).

WHO PREQUALIFICATION TEAM: DIAGNOSTICS — World Health Organization

Technical Specifications Series for submission to WHO Prequalification – Diagnostic Assessment

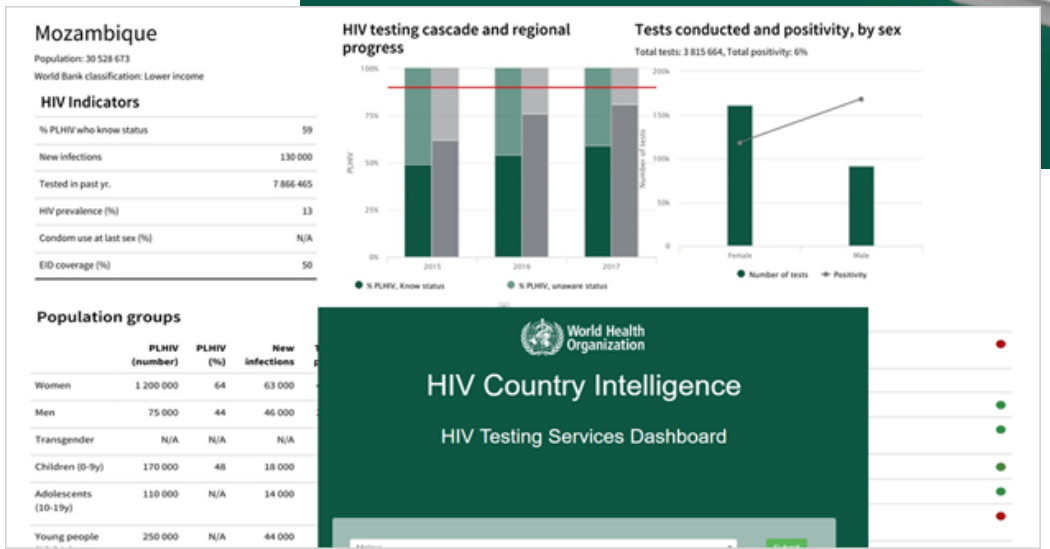
TSS-1 Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional use and/or self-testing

WHO PQ for HIVST doesn't set a defined bench mark

Acknowledges HIVST when evaluated in hands of untrained lay users will likely be less sensitive than professional use RDTs evaluated in laboratory setting

Dual HIV/Syphilis RDTs implementation considerations

- When adding test into national algorithm verification of the new algorithm is needed – cannot just swap out current A1 – need to ensure no cross-reactivity between tests and that combination achieves ≥99% PPV
- Important to consider clinical utility and integration of service delivery, e.g. both HIV and Syphilis treatment available and affordable?
- Current use is focused primarily in ANC settings for pregnant women
    - Use in key populations is ongoing in some pilot programmes
- Support to ensure procurement is planned correctly is key, as well as additional tester training and monitoring as increases complexity of testing algorithm
- WHO working on modelling on the most cost-effective application and use of the dual HIV/Syphilis test in settings with high and low HIV and syphilis burden.
- More guidance available for Q4 2019



French, Russian, Spanish, Chinese coming soon!

Download now!

New Data Viz feature

Search “WHO HTS Info”

In App Store / Google Play

Or Try the link:

http://www.who.int/hiv/mediacentre/news/hts-info-app/en/

WHO 2019 Guidelines Update

1 Dec 2019 Release

Recommendations Planned

- Demand creation for HTS & linkage
- HIVST service delivery approaches – incl linkage
- Partner notification and social network approaches – focus on KP
- **Western Blot vs RDT/EIA algorithms**

Modelling

- HIV testing strategies – 3 tests vs 2 tests, test for triage/HIVST, NAT technologies
- Optimal repeat testing in pregnancy, labour/delivery, post-partum
- **HIV/Syphilis Dual test**

Literature reviews

- HIV testing in presumptive TB patients
- Community-based HTS best practices
- HIV testing in context of ARVs
- Retesting issues
- Screening tools to optimise HTS
- Best practices reaching SDC
- Sexual behaviour change
- Counselling messages

Policy reviews

- Integration of HIV testing and TB screening
- Screening tools to optimise HTS
- HIVST operational guidance
- Lay providers
- HIV testing strategies / algorihtms
- Age of consent for HTS
- Repeat testing in pregnant and post-partum women

Other

- Case examples collection on HTS best practices
- HTS using data and surveillance

Key takeaways

- Scaling-up and focusing differentiated HIV testing services are critical – but important to ensure quality of testing to ensure greatest public health impact

- Verification of testing algorithms essential – as well as adherence to other WHO HIV testing recommendations

- Guidelines updates on HIV testing services for 2019 – and ongoing efforts needed to ensure and increase compliance and correct results

- New technologies and challenges may = new opportunities
  - Considering product optimisation to address issues of retesting among PLHIV on ART, as well as needs for PrEP users
  - Dual HIV/Syphilis, HIV self-test, viral hepatitis, other multi-analyte testing

Acknowledgements

Questions? Contact Cheryl Johnson johnsonc@who.int

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- Muhammad Shahid Jamil
- Irena Prat

World Health Organization

Malaria Diagnostic Testing

Jane Cunningham
Prevention, Diagnosis & Treatment Unit

Meeting of Diagnostic Manufacturers and Procurers

11 December 2019

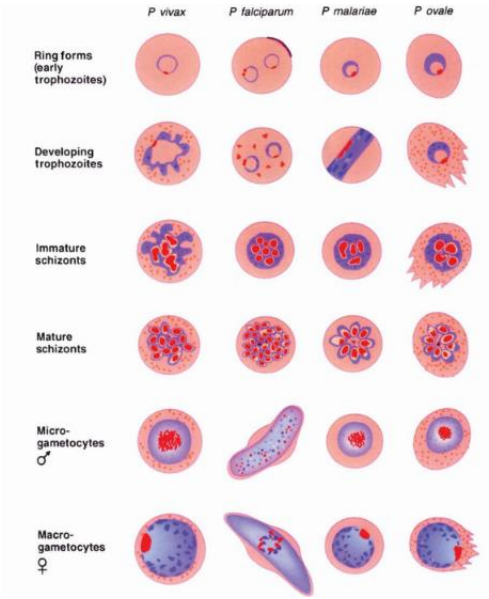
Global **Malaria** Programme

World Health Organization

Malaria

- 5 main species of malaria (Plasmodium) infecting humans:
  - ***P. falciparum***
  - ***P. vivax (relapsing)***
  - *P. malariae*
  - *P. ovale (relapsing)*
  - *P. knowlesi*

Anopheles stephensi in flight © Hugh Sturrock Wellcome Images



- Malaria is transmitted through bite of a female *Anopheles sp*. mosquito
- 30-40 species transmit malaria
- Life span – up to 1 month (1-2 weeks)
- Malaria parasites need 10-21 days to develop
- Active dusk and dawn or nocturnal

Serious public health problem

- 219 million cases of malaria occurred worldwide (95% CI: 203–262 million)
- Five countries accounted for nearly half of all malaria cases worldwide: Nigeria (25%), Democratic Republic of the Congo (11%), Mozambique (5%), India (4%) and Uganda (4%)
- 435 000 deaths – children <5 yrs account for 61%

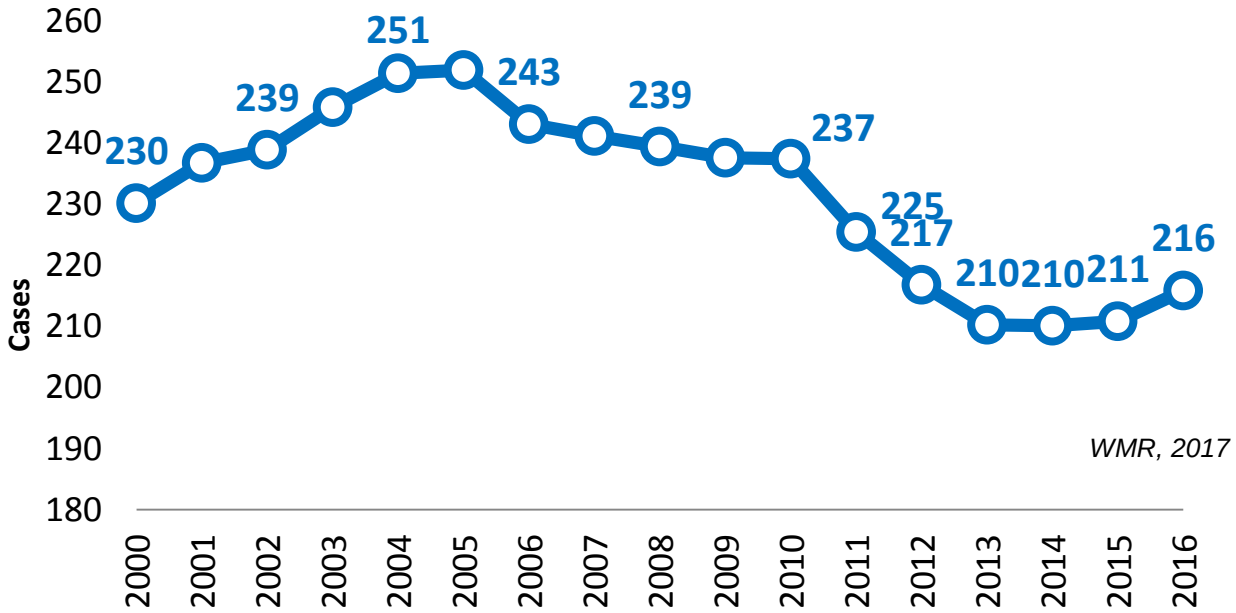
WHO Global Technical Strategy (2016-2030)

- **Pillar 1. Ensure <u>universal access</u> to malaria prevention, <u>diagnosis</u> and treatment**
- **Pillar 2. Accelerate efforts towards elimination and attainment of malaria-free status**
- **Pillar 3. Transform malaria surveillance into a core intervention**

Diagnosis central role in case management, surveillance, elimination and in assessing efficacy of various interventions under research

Vision – A world free of malaria

Goals	Milestones 2020	Targets 20
1. Reduce malaria mortality rates globally compared with 2015	≥40%	%
2. Reduce malaria case incidence globally compared with 2015	≥40%	%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria-free	Re-establishment prevented	Re-establishment prevented



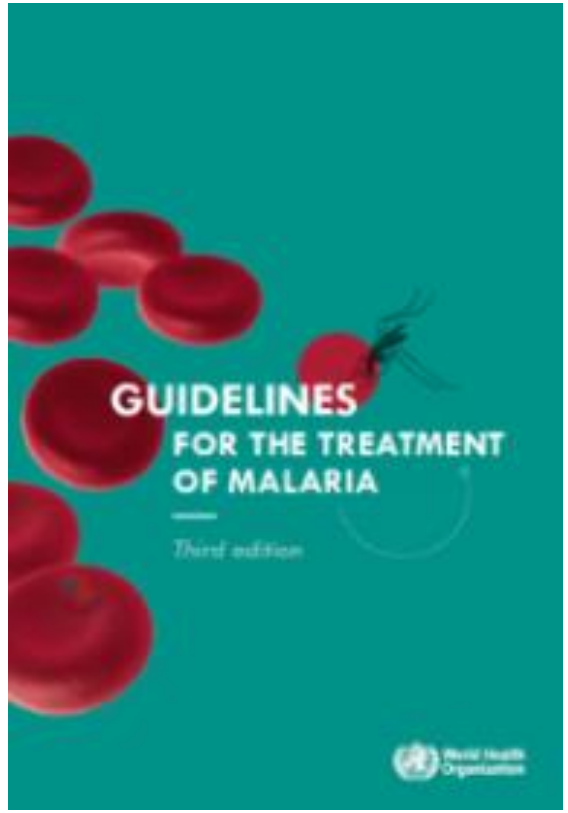
WMR, 2017

Global **Malaria** Programme

Recommendations for malaria diagnosis

- Prompt parasitological confirmation by microscopy or alternatively by rapid diagnostic tests (RDTs) is recommended in all patients suspected of malaria

- Both microscopy and RDTs should be supported by a quality assurance plan



Modalities for malaria diagnosis in all settings

Microscope

- Detect and quantifies all human malaria species
- 'gold' standard for case management

Ag detecting malaria RDT

- Antigens are species specific eg. HRP2, Pf-LDH and non-specific (pLDH, aldolase)

Clinical assessment & Clinical diagnosis if > 2hrs for testing or severe malaria

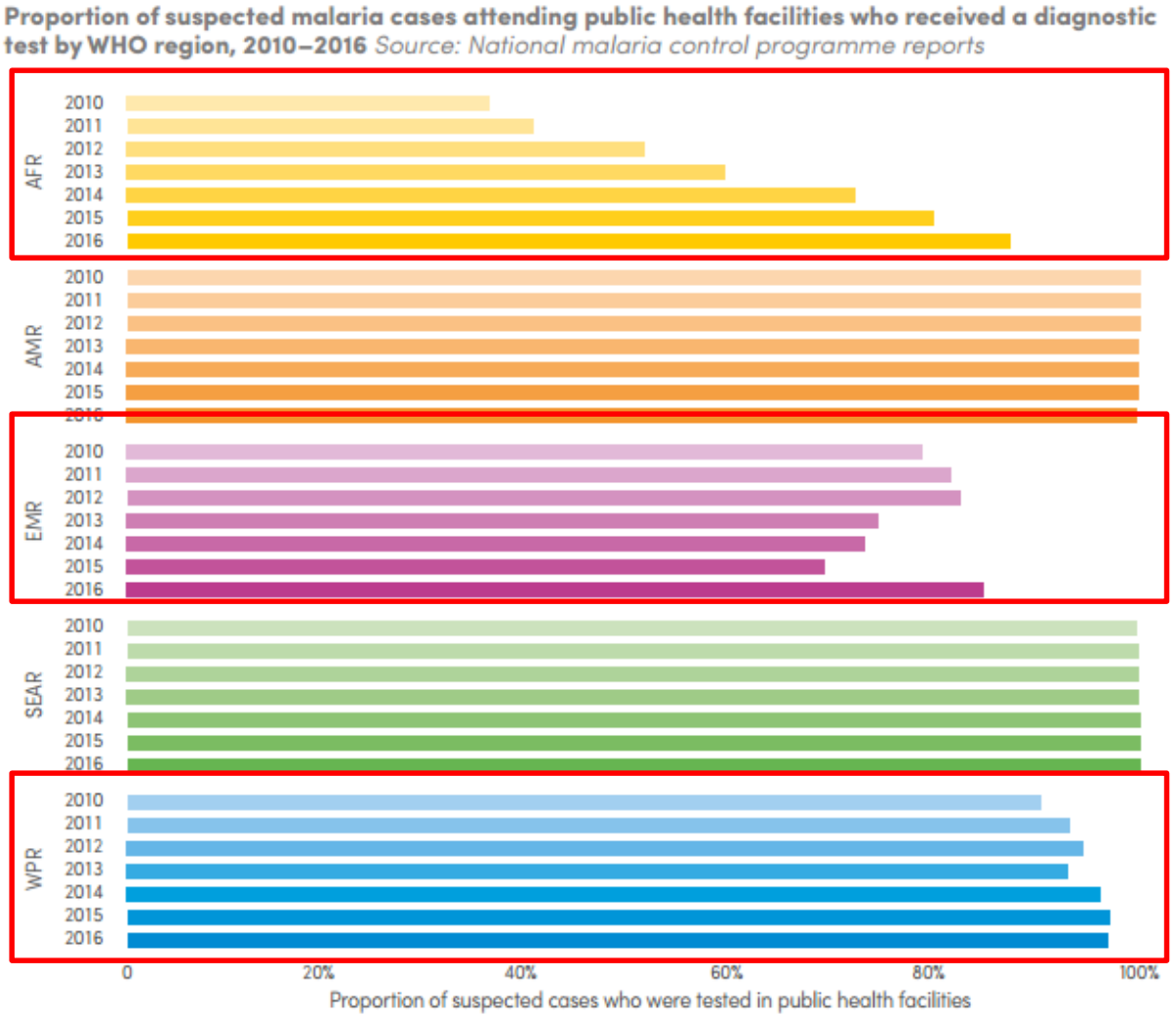
Microscopy vs RDT

Table 2. Technical strengths and constraints of RDTs and microscopy to be taken into account in selecting the best options for different clinical situations and settings

Criterion	Characteristic of diagnostic test	Target cases and clinical setting	Recommended diagnostic test	
			RDT	Microscopy
Parasite density	**RDTs** give only a positive or a negative result, while **Microscopy** can also show parasite density.	Uncomplicated malaria cases	Yes	Yes
		Severe cases upon admission	Not alone[a]	Yes
		Follow-up of admitted patients[b]	No	Yes
Antigen persistence	**RDTs** detect persisting antigens after parasite clearance,[c] while **Microscopy** gives negative result as soon as the parasite is cleared from the patient's blood.	Confirmed malaria cases with persisting fever despite antimalarial treatment	No	Yes
		Cases of persisting fever not previously tested for malaria	Yes	Yes
		Cases of persisting fever in people who did not receive antimalarial treatment	Yes	Yes
Electricity supply	**RDTs** do not require electricity, while **Microscopy** requires a reliable electricity supply.	Health centres and hospitals	Yes	Yes
		Health workers in the community and at health posts	Yes	No
Time for test completion	**RDTs** can be performed comparatively quickly, while **Microscopy** requires more time.	Settings with low work load per health worker, e.g. small health facilities and facilities in areas of low endemicity	Yes	Yes
		Settings with high work load per health worker, e.g. outpatient departments of hospitals or health centres in areas of high endemicity	Yes	Not alone[a]
Competence and training requirements	**RDTs** are comparatively easy to perform, while **Microscopy** is more complex and requires the competence of a trained microscopist.[d]	Health workers with limited training in laboratory skills or settings with limited resources for supervision[d]	Yes	No
		Settings where specific training in malaria microscopy is possible and a laboratory quality management system is functioning[e]	Yes	Yes

Progress towards universal access

- Between 2010 and 2016 access to diagnosis has dramatically increased in AFRO (36 to 87%) and gains in EMRO and WPRO
- "Optimistic" estimate
  - ? those who report more likely to test
  - # RDT should be >> ACTs courses
    - 1 (312 M) RDT sold to 1.3 (409M) ACT treatment courses procured *(WMR, 2017)*



Source: World Malaria Report, WHO, 2017

RDT market transformation

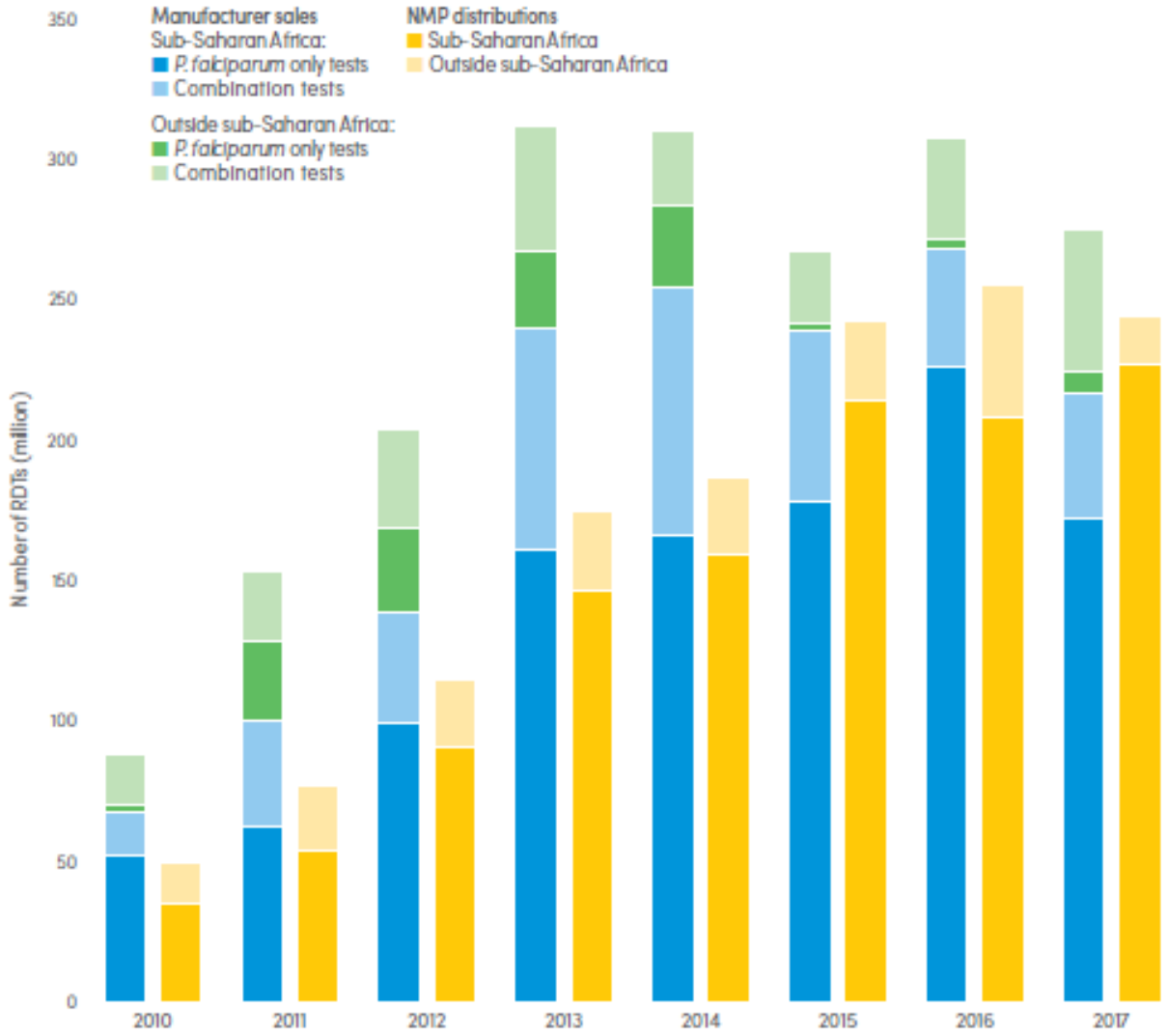
- Expansion of diagnostic testing largely attributable to expansion of accurate, affordable RDTs, particularly in SSA
- In 2017, 276M RDTs sold; 66% Pf only sold to SSA

- Improvements in performance and alignment of performance requirements

Room for expansion:

- new manufacturer coming on board
- WHO Prequalification pipeline full

Number of RDTs sold by manufacturers and distributed by NMPs for use in testing suspected malaria cases,[a] 2010–2017 *Sources: NMP reports and sales data from manufacturers eligible for WHO's Malaria RDT Product Testing Programme.*



NMP: national malaria programme; *P. falciparum*: *Plasmodium falciparum*; RDT: rapid diagnostic test; WHO: World Health Organization.

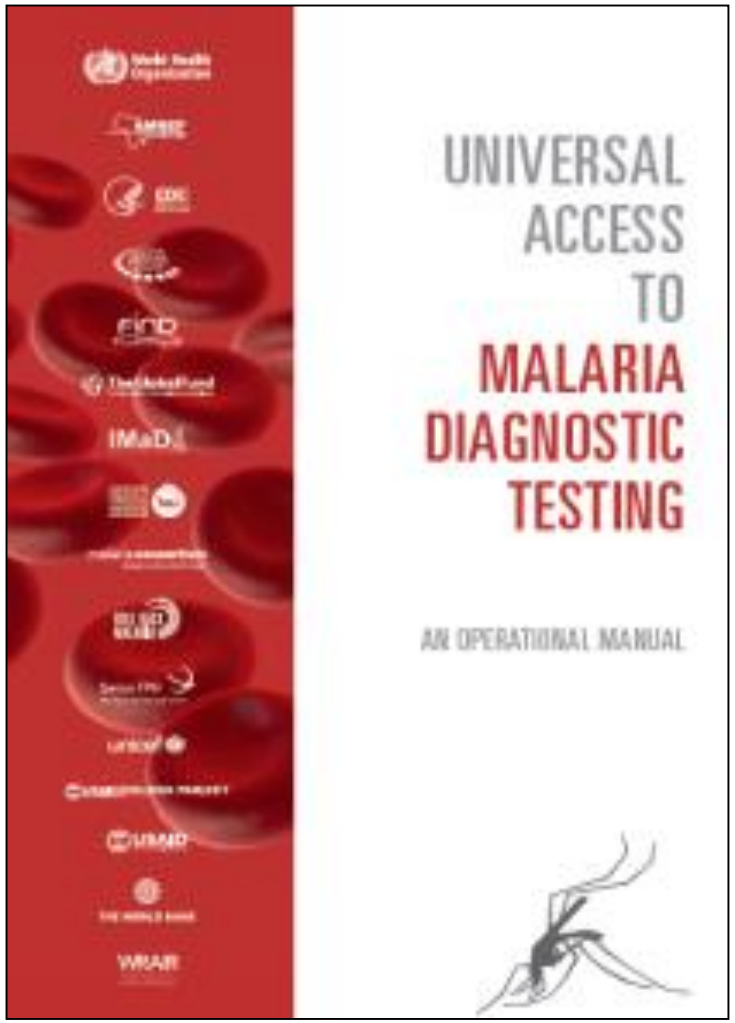
[a] NMP distributions do not reflect RDTs that may still be in storage and have yet to be delivered to health facilities and community health

Source: World Malaria Report, WHO, 2017

Global **Malaria** Programme

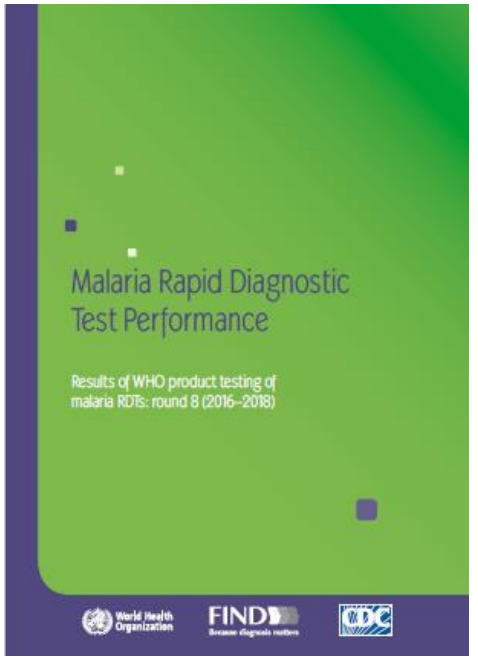
Guidance on implementation (2011)

- Programme planning
- Policies and technical guidelines
- Procurement and logistics
- Quality Management system
- Training
- Supervision
- M&E



RDT Selection and Procurement

- Manual to guide selection and procurement of malaria RDTs
- Eight rounds of product evaluations - 332 RDTs evaluated
- Performance criteria requirements
- New requirements for WHO prequalification in 2018; expanding in 2019



Box 3: WHO selection criteria for the procurement of RDTs

As of 1 January 2018, all RDTs for diagnosing *P. falciparum*–only malaria by detection of HRP2 are required to be prequalified for WHO procurement.[1]

All other products should have active applications with the WHO prequalification programme and be selected in line with the following criteria, based on the results of the assessment in the WHO malaria RDT product testing Programme:

(a) For the detection of *P. falciparum* in all transmission settings, the PDS should be at least 75% at 200 parasites/µL.

(b) For the detection of *P. vivax* in all transmission settings, the PDS should be at least 75% at 200 parasites/µL.

(c) The false positive rate should be less than 10%.

(d) The invalid rate should be less than 5%.

Only products that meet these performance criteria are recommended for procurement.

[1] http://www.who.int/malaria/news/2017/rdt-procurement-criteria/en, accessed 21 August 2018.

Post market surveillance

- Given weak to non-existent PMS in endemic countries
- WHO recommends and coordinates lot testing services based on well characterized materials at specific laboratories (RITM, NIMR, ANDI-UL) - accepts requests for pre, post shipment and post deployment testing based on concerns/complaints
- approximately 800 lots tested per year

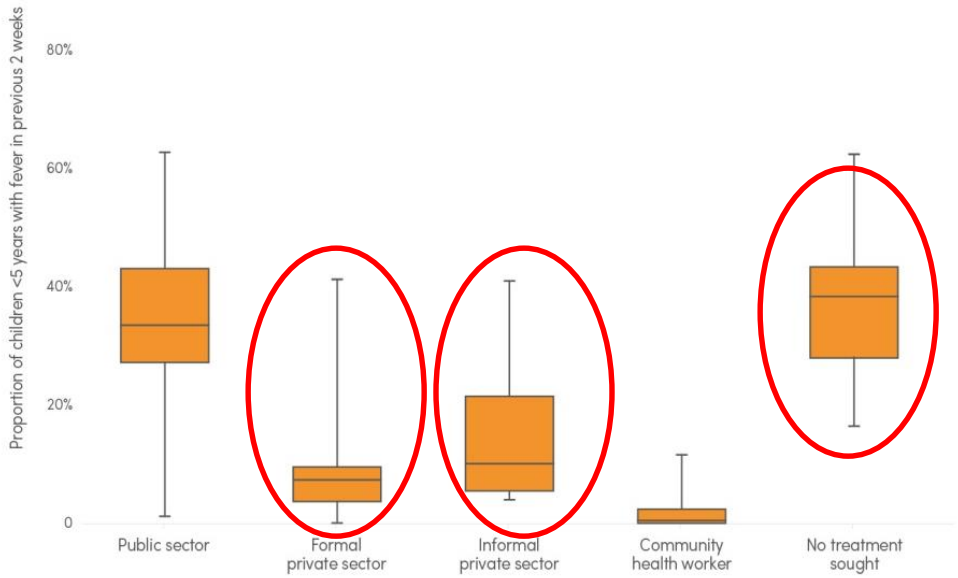
Control materials for malaria RDTs

- Due to extreme environments and lack of confidence in RDT results amongst some providers: point of care controls have been a “long term goal”
- Unable to develop and validate a universal (single threshold), recombinant based control
- Recently developed ‘preferred product characteristics’ and a set of protocols for development and validation of control materials
- Seeking manufacturers interested in piloting these protocols
- Anticipate countries will implement in high risk areas along the supply chain and based on range of algorithms in clinical care settings

Challenges to achieving universal access ?

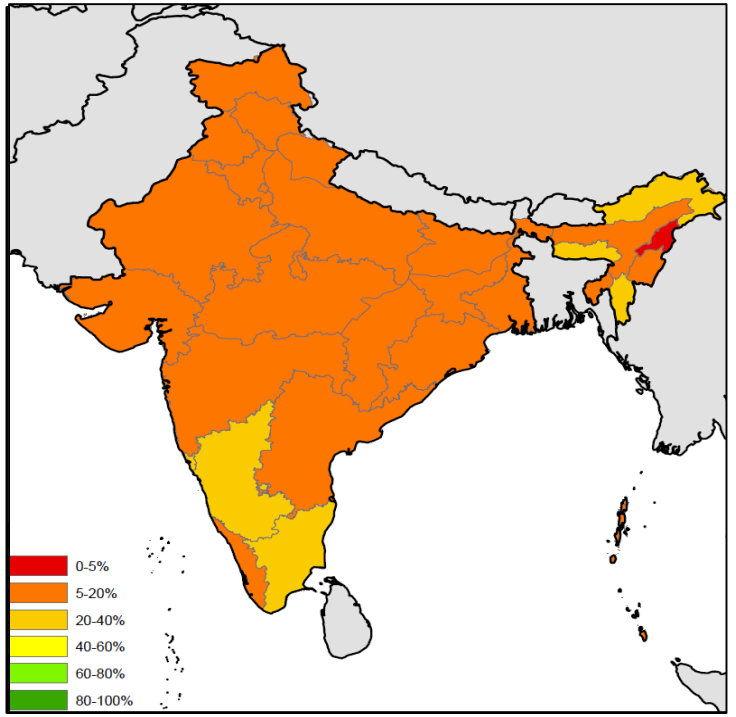
1 Access to care

Proportion of children under five with fever for whom care was sought in sub-Saharan Africa, 2014-2016



2 Access to appropriate care

Percentage of symptomatic children U5 who had blood taken, for whom care was sought



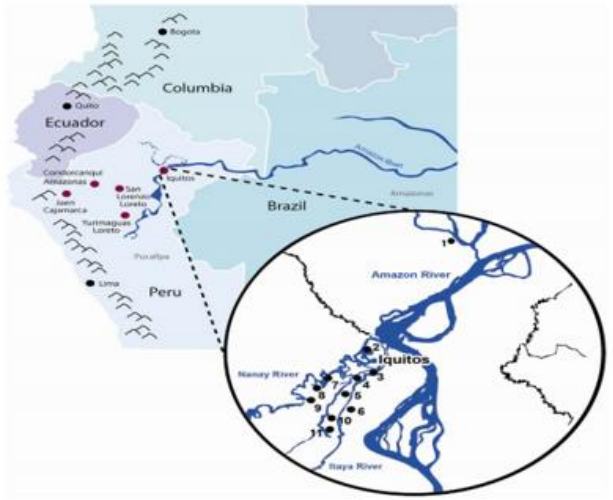
Source: WHO calculation using Demographic and Health Surveys and Malaria Indicator Surveys as of 16 January 2018.

3 Incomplete reporting in surveillance system

pfhrp2/3 deletions

- *P.falciparum* parasites have deleted *pfhrp2* +/- *pfhrp3* genes
- Leads to negative RDTs
- Non HRP2 detecting RDTs are limited and generally have poorer performance - miss low density infections
- Malaria Threat Maps

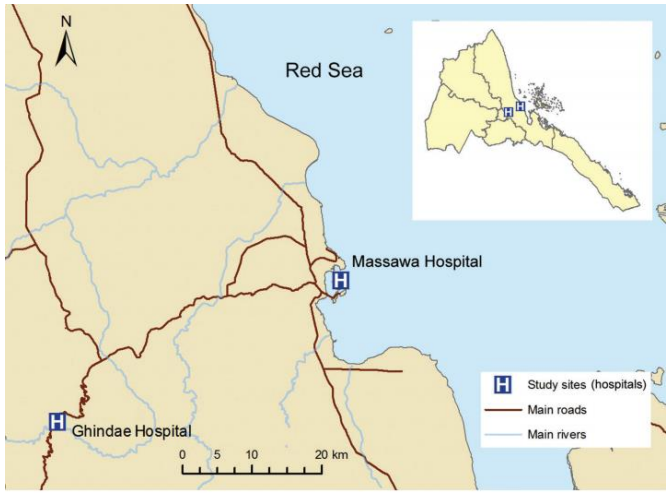
Peru, 2010



- 41% (61/148) of isolates lacked *pfhrp2;*
- 21% lacked both *pfhrp2 and 3*

PLoS One Gamboa et al. January 2010; 5(1)

Eritrea, 2016



Ghindae: 80.8% (21/26); 92.3% (24/26) pfhrp2-neg, pfhrp3-negative parasites; respectively.
Massawa: 41.7% (10/24); 70.8% (17/24) pfhrp2-negative and pfhrp3-negative, respectively.

Berhane et al EID, Vol. 24, No. 3, March 2018

G6PD tests

Preventing relapse in *P. vivax* or *P. ovale* malaria

The G6PD status of patients should be used to guide administration of primaquine for preventing relapse.
Good practice statement

To prevent relapse, treat *P. vivax* or *P. ovale* malaria in children and adults (except pregnant women, infants aged < 6 months, women breastfeeding infants aged < 6 months, women breastfeeding older infants unless they are known not to be G6PD deficient, and people with G6PD deficiency) with a 14-day course (0.25-0.5 mg/kg bw daily) of primaquine in all transmission settings.
Strong recommendation, high-quality evidence

In people with G6PD deficiency, consider preventing relapse by giving primaquine base at 0.75 mg/kg bw once a week for 8 weeks, with close medical supervision for potential primaquine-induced haemolysis.
Conditional recommendation, very low-quality evidence

When G6PD status is unknown and G6PD testing is not available, a decision to prescribe primaquine must be based on an assessment of the risks and benefits of adding primaquine.
Good practice statement

Prior to 2015: all recommendations implied that G6PD status and level of activity was known

Currently no prequalified point of care G6PD test (1 in pipeline)

- Quantitative tests recently registered in Thailand, India

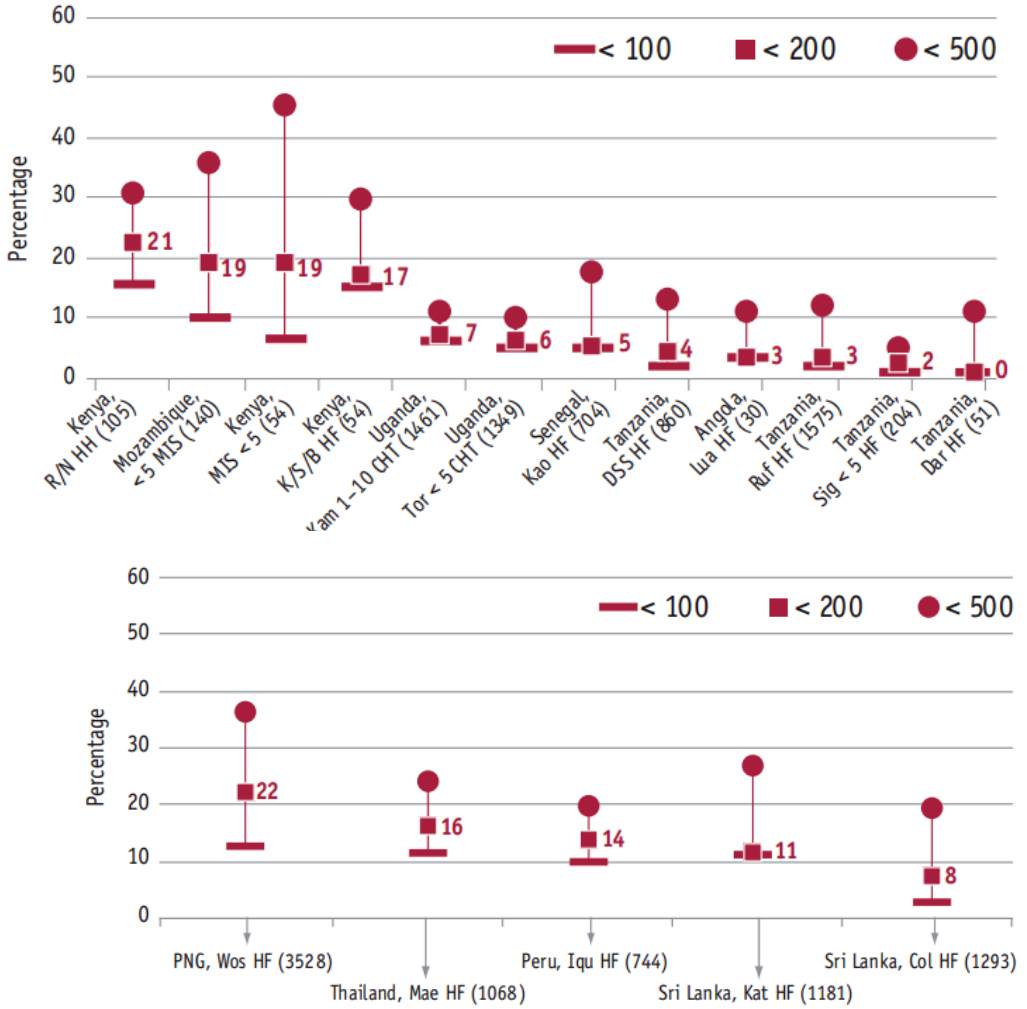
- Review of POC qualitative tests in 2014 consistent with FST results
- Cochrane systematic review planned for 2019
-

Source: Malaria Treatment Guidelines 3rd Edition 2015

Role or more sensitive malaria tests ?

- Under and over diagnose with current tools because the thresholds for clinical malaria vary
- RDTs and field microscopy have only one 'typical' threshold 100-200 p/µL
- No min and max performance requirements; just minimum
- Greater proportion of clinical *P. vivax* malaria < 100-200 p/µL

Cumulative proportions of symptomatic patients with Pf or Pv densities below 100, 200 and 500 p/µL

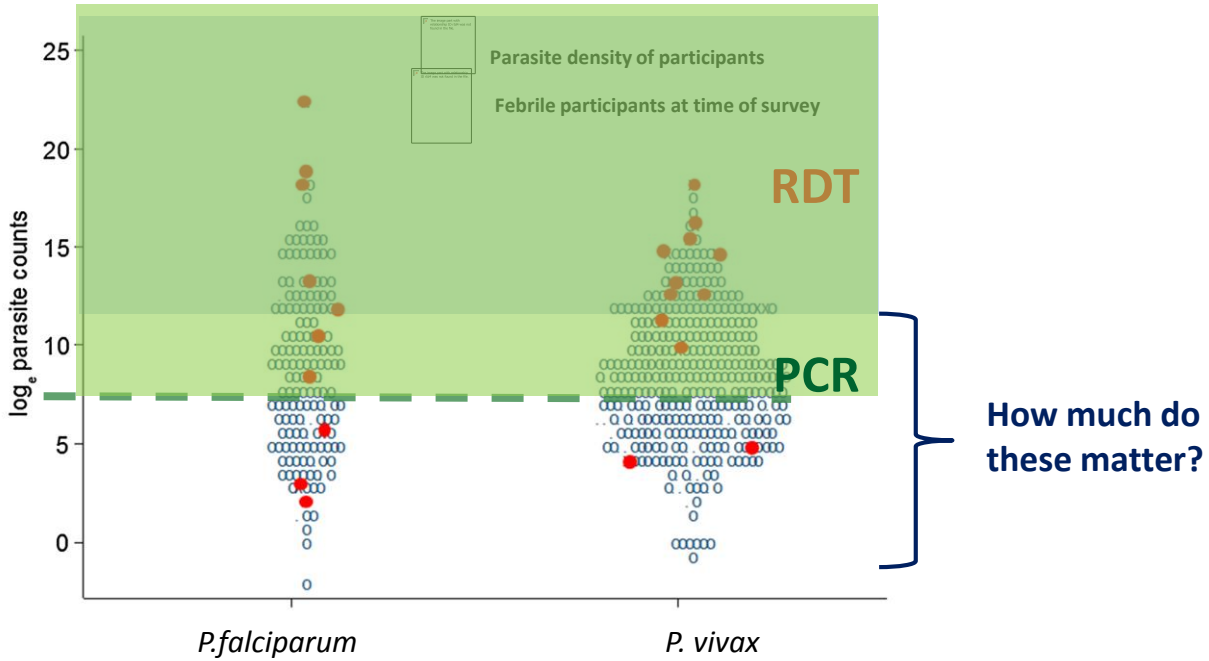


Source: 18 studies (12 Africa; 6 non-Africa). Parasitological confirmation of malaria diagnosis: WHO technical consultation, Geneva, 6-8 October 2009

Low density infections: how sensitive do tests need to be ?

A high proportion of *P. falciparum* and *P. vivax* infections identified in cross-sectional surveys are characterized by low parasite densities undetectable by conventional RDT and microscopy. Although limited by small sample sizes, the relative frequency of low-density infections appears to be higher in low transmission settings than in high transmission ones.

Evidence from several reports using mosquito-feeding experiments indicates that mosquitoes can be infected with low-density *P. falciparum* and *P. vivax* infections, although less efficiently than with high-density infections.



Source: Imwong et al. Malar J (2015) 14:381

<u>Conclusion:</u> Research is needed to document the public health benefits and cost–effectiveness of detecting and treating low-density infections in low transmission areas and/or specific population groups.

Conclusions

- Diagnosis central to case management, surveillance and elimination strategies
- Not on target to meet GTS targets for reductions in cases and mortality or funding
- Microscopy and antigen detecting RDTs are main modalities for dx
- Increased requirements for prequalification of RDTs and G6PD POC test for procurement
- Gaps in testing are a top priority to address
- Key threats need an urgent response: care seeking behaviour, *pfhrp2/3* gene deletions, POC quanitatitive G6PD testing
- Elimination strategies may require new tools (esp. SSA, GMS)

Update on Prequalification of in vitro diagnostics

11 December 2018

Irena Prat | Group Lead –Diagnostics Assessment | PQ Team

Update on Prequalification of in vitro diagnostics

Presentation outline

Update on Prequalification of in vitro diagnostics

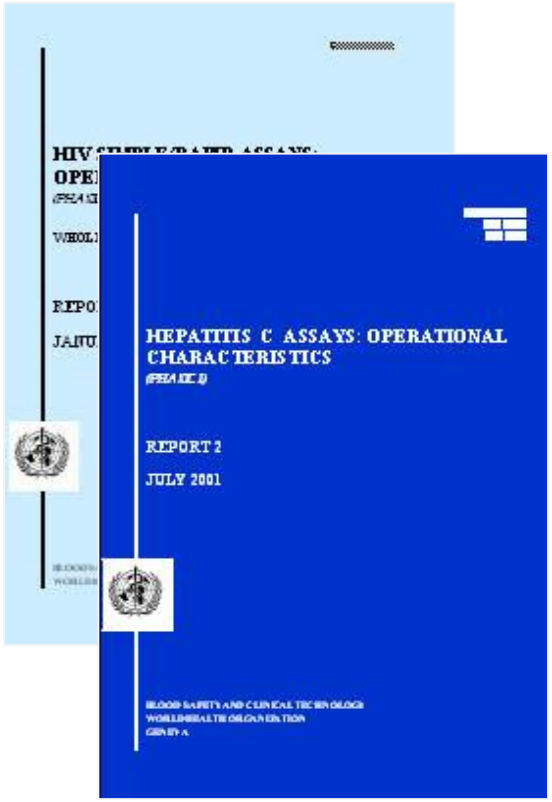
World Health Organization

Introduction to the prequalification assessment of IVDs

IVDs QA activities within WHO

World Health Organization

WHO has been assessing IVDs performance and operational characteristics since 1988



HIV assays since 1988

Hepatitis B assays since 2000

Hepatitis C assays since 2000

Syphilis assays since 2001

Chagas assays since 2002

Malaria assays since 2002

CD4 technologies ad-hoc in 1996 & 2003

Trends in IVDs

Globalised industry sectors with outsourced production

Rapid emergence of new technologies

Increasing expectations on quality, safety and performance

Increasing workload for regulators

Easy to operate tests/methods facilitate near patient testing, hard-to-reach populations, non-lab environments

PQDx: aim, scope and impact

World Health Organization

- HIV
- Malaria
- Hepatitis C
- Hepatitis B
- HPV
- G6PD
- Cholera
- Syphilis*

The aim of PQDx is to promote and facilitate access to safe, appropriate and affordable IVDs of good quality

Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings

PQDx: aim, scope and impact

The findings of PQDx generate **independent technical information** on safety, quality and performance of IVDs, principally used by other UN agencies, WHO Member States and other interested organizations.

The PQDx status, in conjunction with other procurement criteria, is used by UN agencies, WHO Member States and other interested organizations to guide their procurement of IVDs.

Prequalification components

PQDx undertakes an assessment of individual IVDs through a standardized procedure aimed at determining if the product meets WHO prequalification requirements.

- PQ reviews aspects of particular relevance for resource-limited settings
- The prequalification assessment process includes three components:

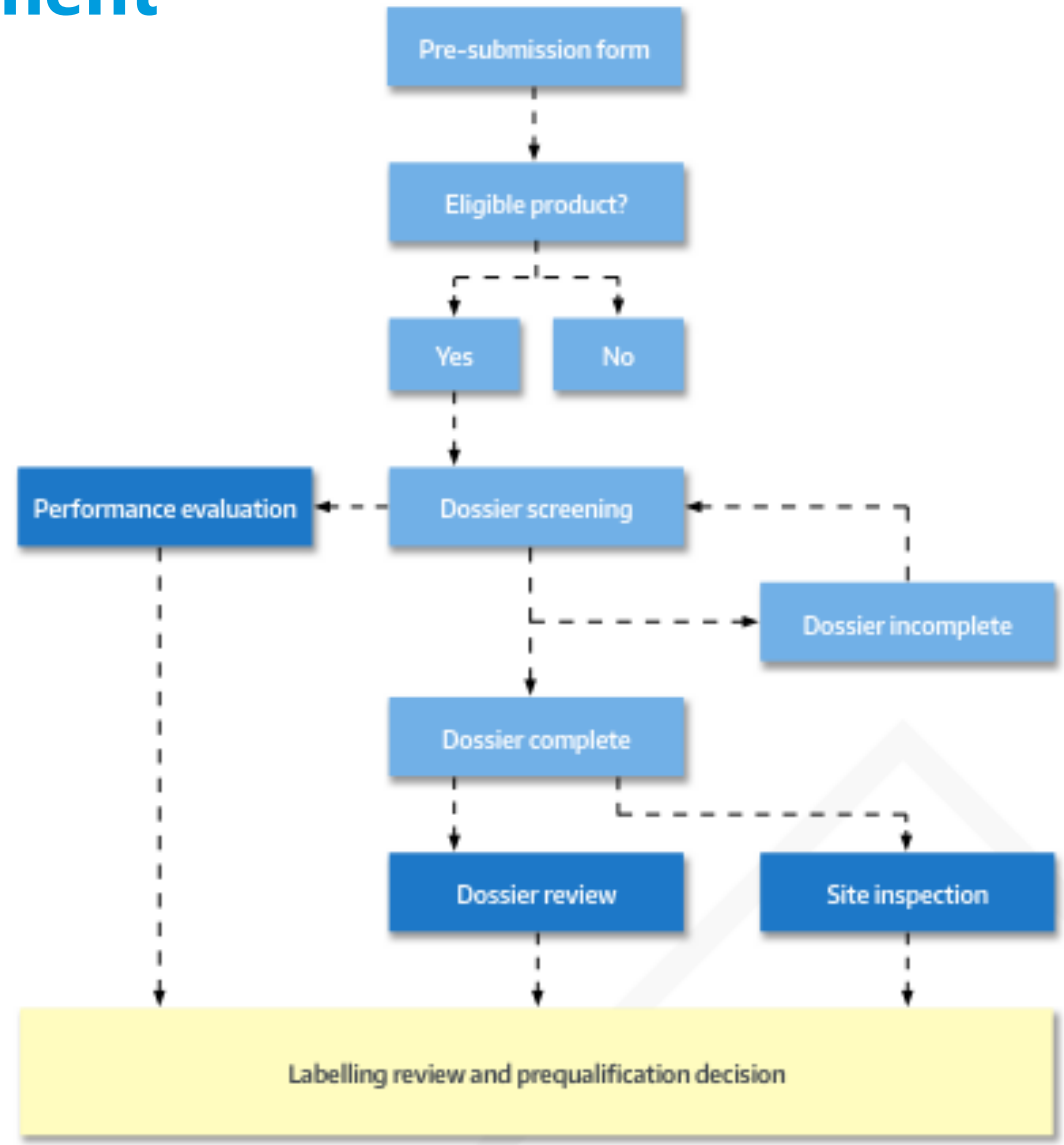
Review of a product dossier

Manufacturing site(s) inspection

Performance evaluation

WHO prequalification: Full assessment

World Health Organization



Product dossier

World Health Organization

Subset of technical documentation held by manufacturer

- Demonstrates that the IVD conforms to the "Essential Principles of Safety and Performance of Medical Devices"
- Provide information on the QMS (informs inspections team)
- Demonstrate the manufacturer has considered the safety and performance in WHO Members States
- Information to determine regulatory version
- The dossier reflects the status of the IVD at a **particular moment in time**

Manufacturing site inspection

- Fully implemented quality management system (design & development, manufacturing including quality control, storage, distribution)
- Risk management to meet ISO 14971:2007
- Robustness of the Product
- Products undergoing prequalification have to be in routine manufacturing
- Sufficient capacity to ensure reliable delivery

Performance evaluation

- Independent **verification** of the performance of IVDs submitted for prequalification assessment.
- Assays are challenged with a focus on their use in resource-limited settings and in the context of WHO guidelines (SRA review has different priorities based on local populations and product use)
- The dataset obtained complements the verification and validation data submitted by the manufacturer in the product dossier and finding in the Site inspection
- Currently takes place in a WHO Collaborating Centre (CC) and/or a site otherwise designated by WHO

Prequalification: decision

Final prequalification outcome depends on:

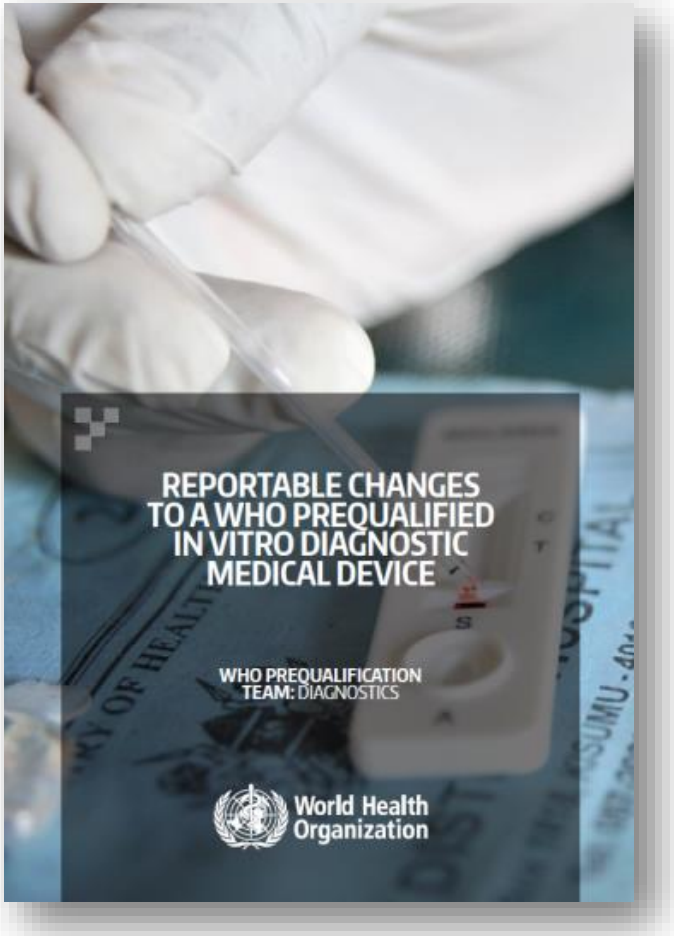
- Results of dossier assessment and acceptance of action plan
- Results of inspection(s) and acceptance of action plan
- No level 5 nonconformities outstanding for either dossier or for inspection
- Meeting the acceptance criteria for the laboratory evaluation

WHO PQDx Public Report is posted on WHO website and product is added to the list of WHO prequalified products

Product is then eligible for WHO and UN procurement

Maintenance of PQ status

Change reporting



- Guidance available

  what changes must be reported, what does not need to be reported

- Not all changes will be charged an assessment fee

Maintenance of PQ Status

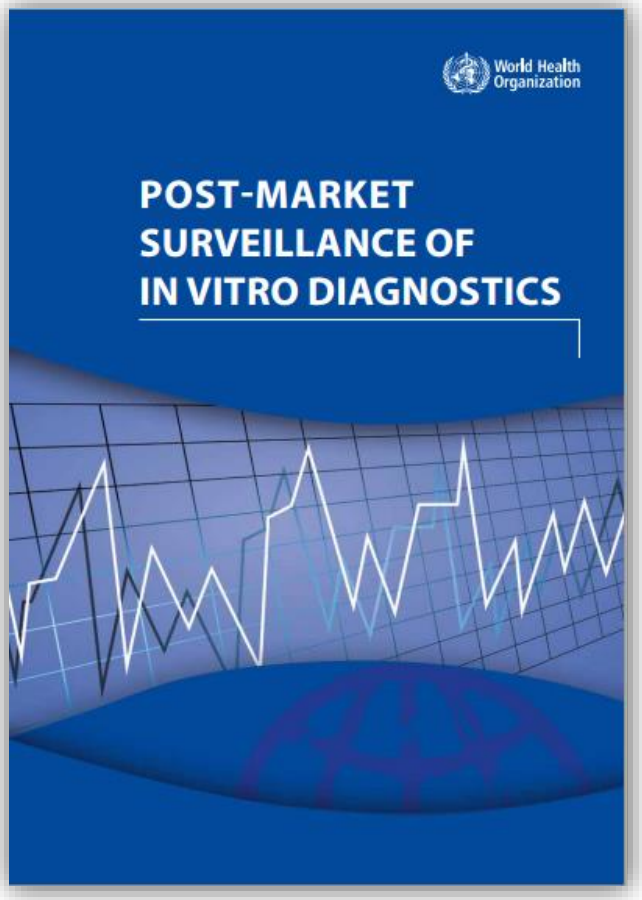
Annual reporting

- Sales data
- Number of complaints
- Number of field safety corrective actions

Maintenance of PQ Status

World Health Organization

Post Market Surveillance



Roles/responsibilities of different stakeholders

- End users, manufacturers, NRAs, NRLs

Forms

- IVD complaint report
- Manufacturer complaint investigation report
- Field Safety Corrective Action report
- Lot testing data collection & report

Notices

- Field Safety Notice

Update on Prequalification of in vitro diagnostics

World Health Organization

Eligibility for prequalification assessment

Prequalification scope

World Health Organization

PQ eligibility consultation

HIV

HCV

HPV PoC

G6PD

Cholera

Syphilis

malaria

HBV

HPV

2019

Expansion of PQDx scope over time

Consultation on PQDx eligibility

- **<u>Currently ongoing, closing 31/12/2018</u>**
- Gather input from key stakeholders in order to determine the types of in vitro diagnostics for which prequalification is most needed and for which it will have the greatest benefit:
  - burden of disease;
  - health interventions associated with particular IVDs;
  - existing WHO guidelines;
  - EDL listing.
- Based on received feedback a priority level for inclusion on the prequalification scope will be assigned for each type of IVD based on the above criteria.
- The priority level will be used to determine timelines for inclusion in the prequalification of IVDs scope.

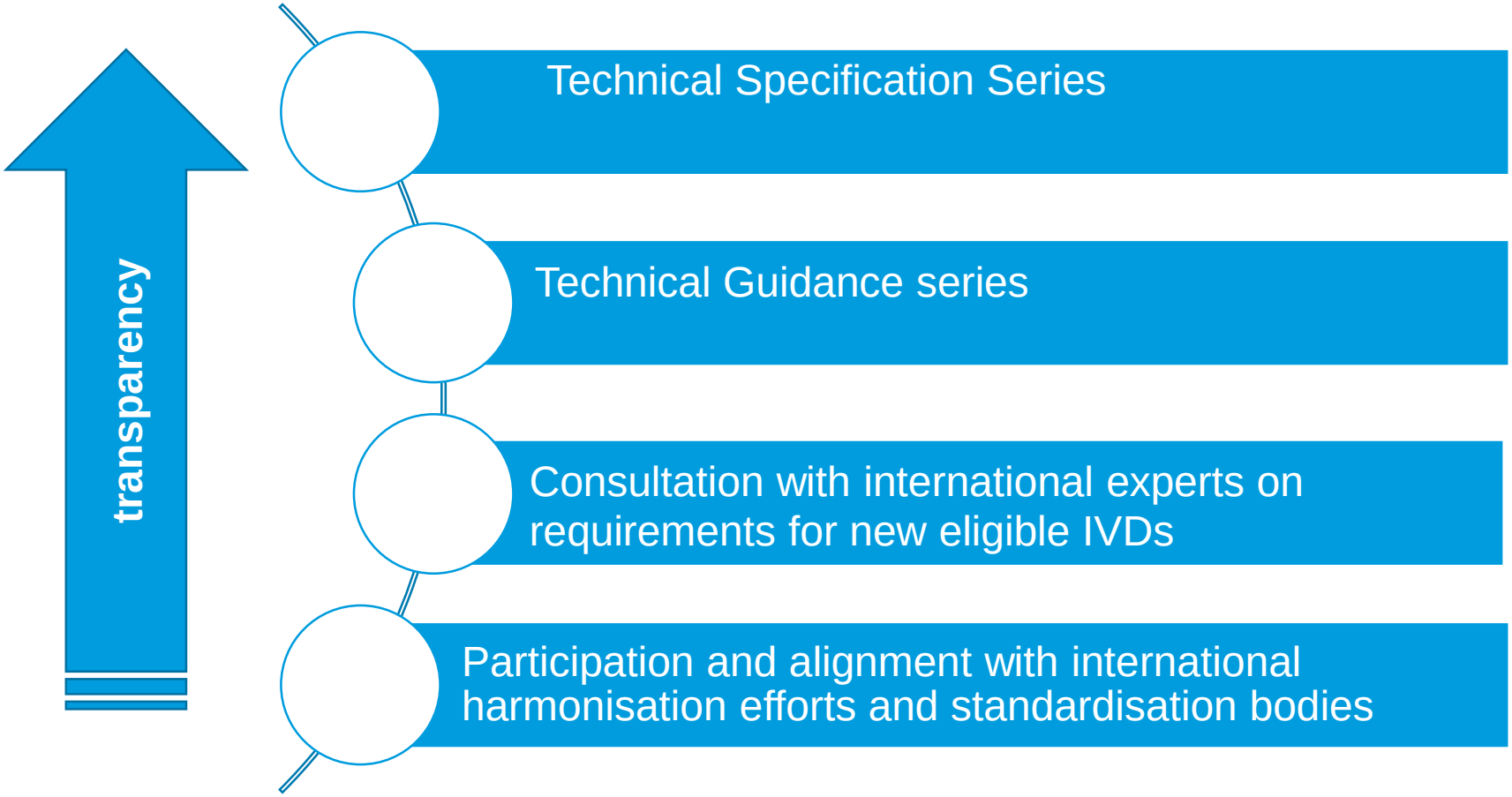
Update on Prequalification of in vitro diagnostics

World Health Organization

Product dossier: assessment requirements

Increasing transparency for applicants and increasing likelihood for success

HOW: publication of WHO requirements, revision of WHO documents and alignment with other organizations.



Dossier assessment: 2018 – 2019

PQ continuing to review and improve processes based on experience and feedback

- **Continued publication of Technical Specifications outlining the performance study criteria for eligible IVDs:**
  - Transition to TSS requirements as part of dossier assessment and prequalification follow up
- **Implementation of IMDRF "Table of Contents format:**
  - Dossiers
  - Dossier reports
  - Technical specifications and Guidance documents

Update on Prequalification of in vitro diagnostics

World Health Organization

Technical guidance, technical specifications and sample dossiers

Technical specification series (TSS)
- published -

http://www.who.int/diagnostics_laboratory/guidance/technical_specification_series/en/

- TSS 1: **HIV** RDT for professional and/or self-testing
- TSS 2: IVDs to identify **G6PD** activity
- TSS 3: **Malaria** RDT
- TSS 4: IVD used for the detection of high-risk **HPV** types in cervical cancer screening
- TSS 5: RDT used for surveillance and detection of an outbreak of **Cholera**

Technical specification series (TSS)
- in development -

World Health Organization

- TSS 6: **Syphilis** RDT (Consultancy meeting 2018 Q3, publication in Q4 2018)
- TSS 7: **HCV** RDTs (Consultancy meeting 2018 Q4, public consultation in Q1 2019)
- TSS 9: **HCV** Enzyme Immunoassays (Consultancy meeting 2018 Q4, public consultation in Q1 2019)
- TSS 8: **HIV** Enzyme Immunoassays
- TSS 10: NAT to detect **HCV** (quantitative)
- TSS 11: NAT to detect **HIV-1** (quantitative)
- TSS 12: NAT to detect **HIV-1** & **HIV-2** (qualitative)

Enforcement of new TSS documents

- Date of effect: 3 months after publication.
- Prequalified IVD products: 3 years to ensure compliance (after notification).
- New submissions (> 3months after TSS publication date): assessed against new requirements.
- New submissions (< 3 months after publication date): assessed against ‘old’ requirements and if successful have 3 years to ensure compliance with new TSS requirements.

Technical guidance series (TGS)

Final

- TGS 1 **Standards** applicable to the WHO prequalification of IVD.
- TGS 2: Establishing **stability** of an IVD for WHO prequalification (TGS2 Annex: component stability).
- TGS 3: Principles of **performance studies** of an IVD for WHO prequalification.
- TGS 4: Guidance on test method **validation** for an IVD.
- TGS 5: Designing '**instructions for use'** for IVD.
- TGS 6: **Panels** for QA and QC of IVD.
- TGS 7: **Risk management** for manufacturers of IVD.

In development

- TGS 8: Use of **biological reference materials** in the development of IVDs.
- TGS 9: **Precision** and **robustness.**
- TGS 10: **Accessories.**

Sample Product Dossiers

- Fictitious IVDs:
  - CD4 IVD.
  - Qualitative NAT for the detection of HIV1 & HIV2 RNA.
  - Quantitative NAT for the detection/measurement of HIV1 RNA.
  - IVD intended for HIV self-testing (under review).

- Provides examples of:
  - formatting and reporting details required.
  - how to complete an "Essential Principles" checklist.
  - risk assessment.

Update on Prequalification of in vitro diagnostics

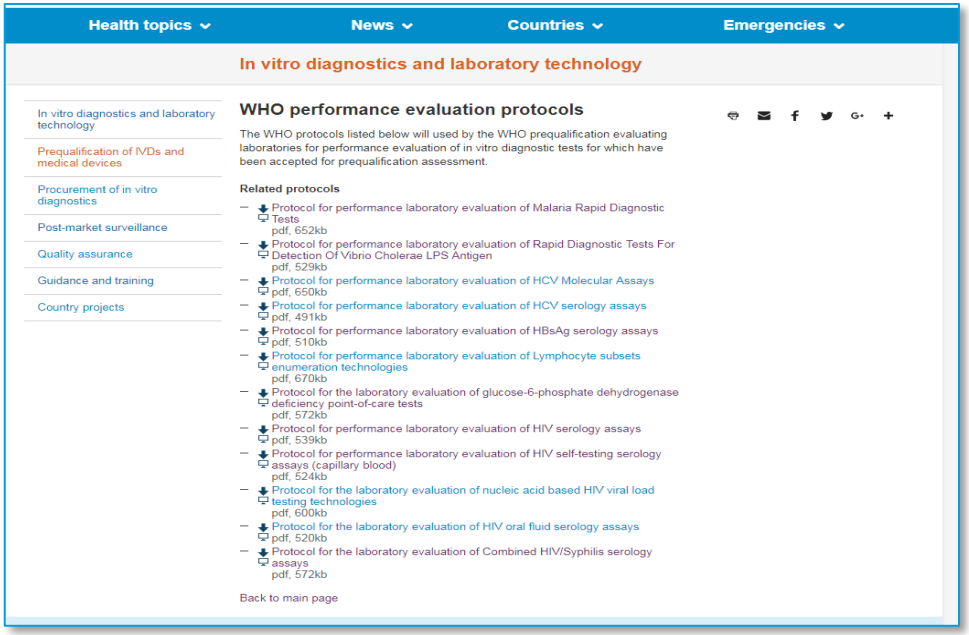
World Health Organization

Alternative performance evaluation pathway

Alternative mechanism for WHO PQ performance evaluation

Manufacturers free to choose one of two performance evaluations pathways:

- Option 1: The performance evaluation scheduled and coordinated by WHO
- Option 2: Performance evaluation commissioned and paid for by the manufacturer
- Both options require use of a **WHO evaluation protocol**



Key requirements for Option 2

- Manufacturers may contact a WHO Evaluating Laboratory to commission an evaluation **for the purpose of WHO Prequalification,** however the following key conditions must be fulfilled:

Conditions
Manufacturer must apply for WHO Prequalification assessment prior to beginning of the evaluation
Laboratory must be audited and listed by WHO at the time of the evaluation
Laboratory AND manufacturer must inform WHO of the upcoming evaluation
All evaluations carried out following WHO protocol
Evaluation must be conducted independently of the manufacturer
Use of WHO report templates
Report submitted to WHO directly by the laboratory to ensure independence

Implementation

- Assessment process started in September 2016:
  - 17 laboratories submitted expressions of interest.
  - 15 laboratories audited.
  - 11 laboratories successful and listed.
- Location of listed labs:
  - Australia, Belgium, Kenya, India, Nigeria, South Africa (2), Tanzania, United Kingdom (2), USA.
- 4 laboratories will be re-audited in Q1 2019.
- The call for expression of interest is still open.
- Evaluations using option 2: HCV RDT: 1 (Completed) and 4 molecular technologies (3 HIV, 1 HCV) ongoing in three laboratories, 1 HBsAg being scheduled.

Update on Prequalification of in vitro diagnostics

World Health Organization

Abridged assessments

Resources optimization: full Vs abridged assessment

World Health Organization

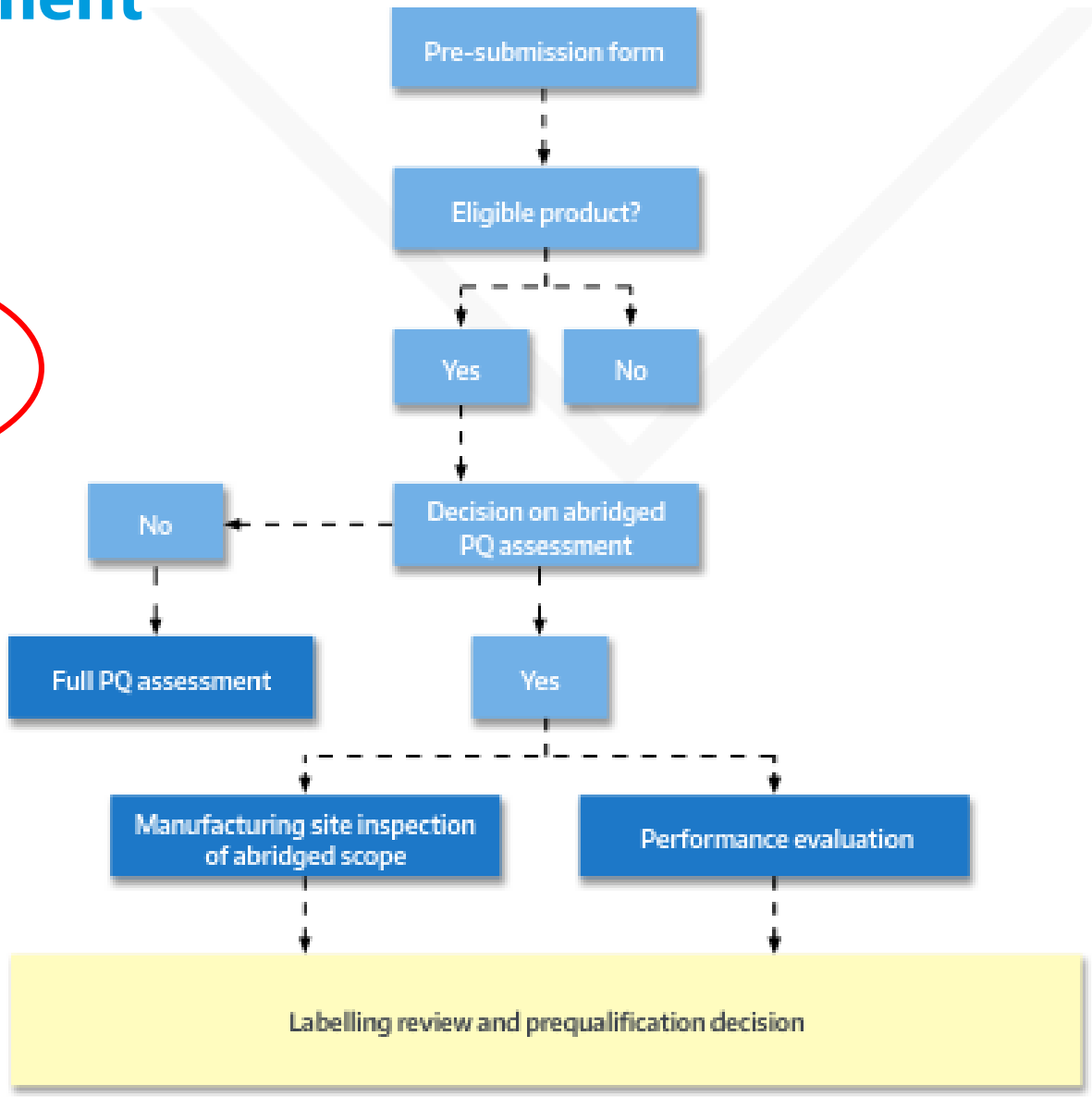
Intention: It is a harmonization initiative which:

- Leverages existing evidence of prior regulatory review (i.e. stringent pre-market reviews).
- Avoids duplication of efforts already undertaken by RAs who conduct a stringent assessment of the **same** IVD.
- (Recognition limited to stringent assessments from USA, Australia, Canada, EU and Japan).
- WHO PQ compares existing evidence and country requirements with WHO PQ requirements.
- WHO PQ makes an independent decision based on this evidence.

WHO prequalification: abridged assessment

World Health Organization

No dossier



Abridged assessment review

Eligible RDTs: HIV (except HIV ST), HCV, HBsAg

Current procedure in place since 2014:

- Need to reflect changes to regulations;
- Introduction of MDSAP;
- New jurisdictions participating to IMDRF.

Revision planned on 2019:

- Will include a consultation with stakeholders.

Update on Prequalification of in vitro diagnostics

World Health Organization

Specific information for RDTs

Specific information for RDTs

1. Malaria

- WHO procurement eligibility shift from product testing to PQ listing.
- New applications can be submitted at any time.
- Performance evaluation now coordinated by PQ:
    - CDC Atlanta
- Compliance with TSS-3.
- PQ commitments.

Specific information for RDTs cont'd

World Health Organization

2. HIV

Compliance with TSS-1:

- HIV self-testing requirements.
- 2nd ST PQ-ed.
- HIV ST: new application or change to PQ-ed professional use version.

3. HCV

- TSS in public consultation by end 2018.
- ST not recommended by WHO.

Specific information for RDTs cont'd

World Health Organization

4. HBsAg

- TSS Timeline TBD

5. Cholera

- Solicit applications
- TSS-5

6. Syphilis

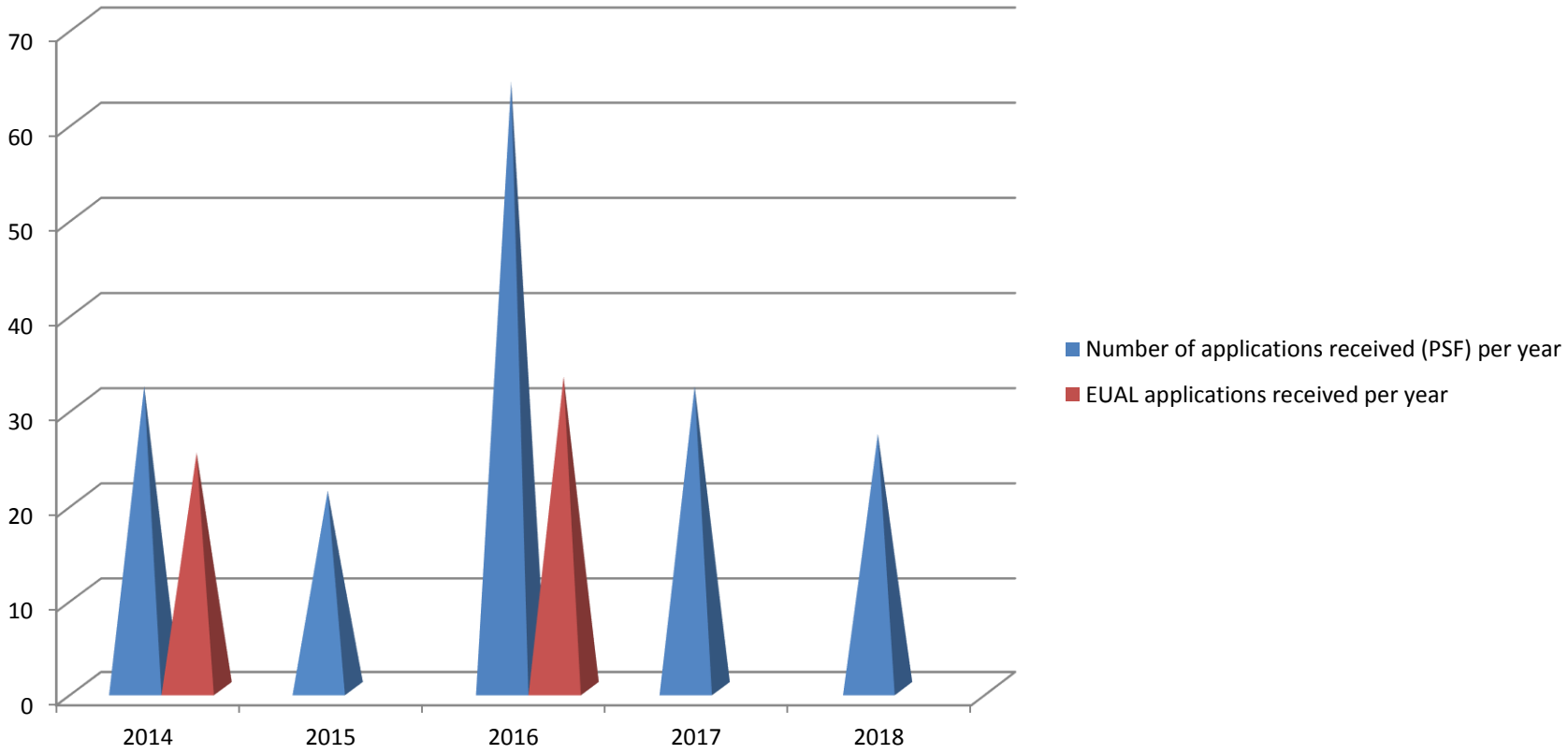
- TSS-6 public consultation closed, final by end 2018
- Eligible in early 2019 (3 months after publication of final TSS)

Update on Prequalification of in vitro diagnostics

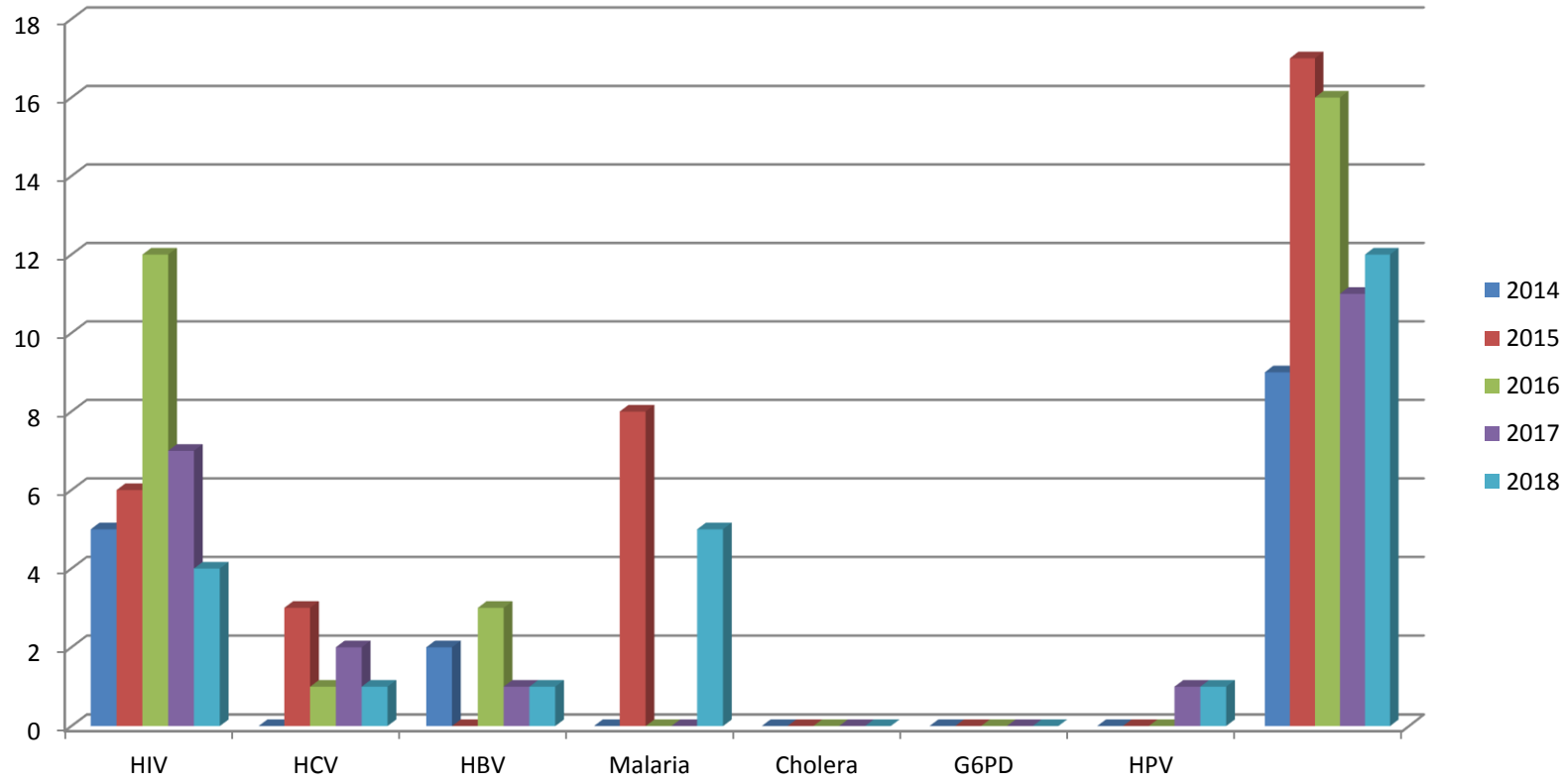
World Health Organization

PQDx in numbers

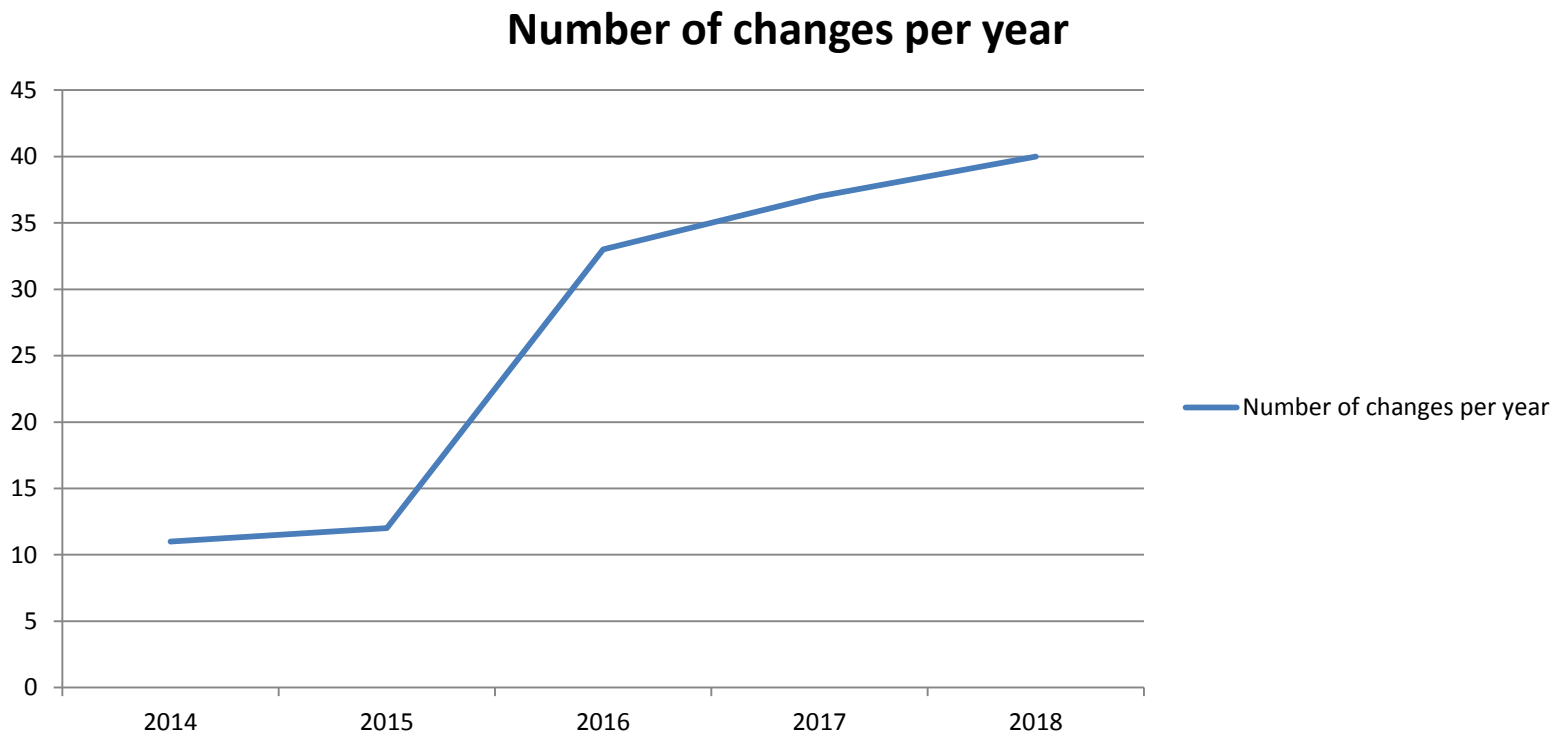
Submissions to PQDx and IVD EUAL



Number of PQ-ed products per year, since 2014



Number of change notifications



Update on Prequalification of in vitro diagnostics

World Health Organization

Prequalification financing model

PQDx financing model

PQ fees structure changed in 2016 for medicines and vaccines

For IVDs: consultation of proposed model, closed on 30 April

Model went live on 1 August 2018

What has changed:

- the type of assessment: whether a full or abridged assessment of a new application, or assessment of changes;
- an annual maintenance fee.

New application full assessment	New application abridged assessment	Annual fee	Change assessment fee
5,000 + 12,000	8,000	4,000	3,000

Update on Prequalification of in vitro diagnostics

World Health Organization

International harmonization and convergence

International harmonization and convergence

IMDRF - related convergence

- EPs: new version published 31.10.2018; to be reflected in PQ documents
- ToC and dossier restructuring:
  - Shift to ToC structure planned in 2019
  - Transition period
  - Assessment report restructuring
- GRRP:
  - Labelling
  - new reliance mechanisms
- MDSAP

AHWP

- Labelling
- Changes

Update on Prequalification of in vitro diagnostics

World Health Organization

New IT solution

Electronic Prequalification System (e-PQS)

- Expected to be launched on Q1/Q2 2019
- No more e-mails, communication on applications through a wizard
- Single user sign in
- Application tracking
- Shift to e-submission

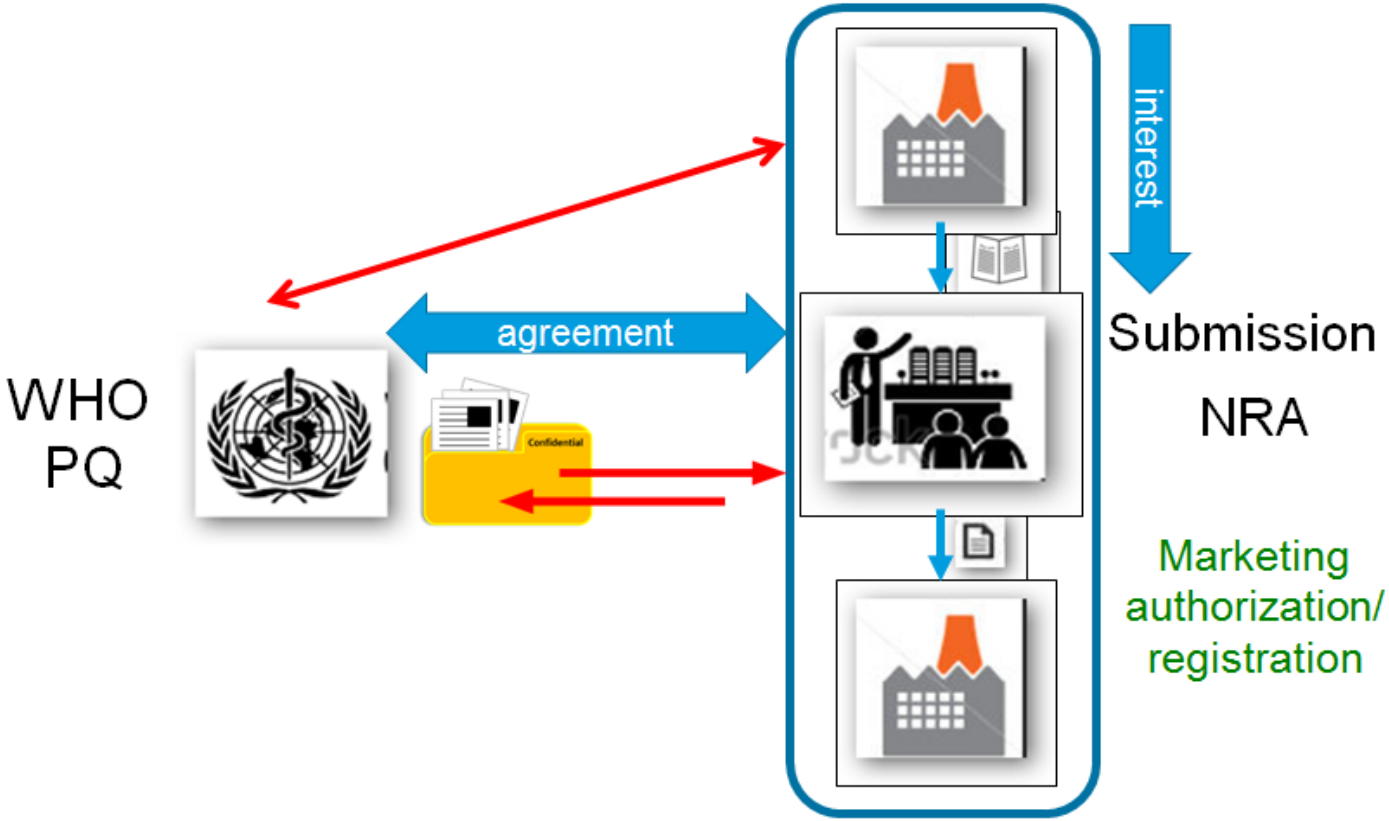
Update on Prequalification of in vitro diagnostics

World Health Organization

Collaborative registration procedure (CRP)

Providing an avenue for…

- the NRAs to reduce regulatory burden and duplication
- promote efficient use of resources by re-allocating resources to high-risk products and manufacturing sites



KEY Principles of WHO PQ CRP

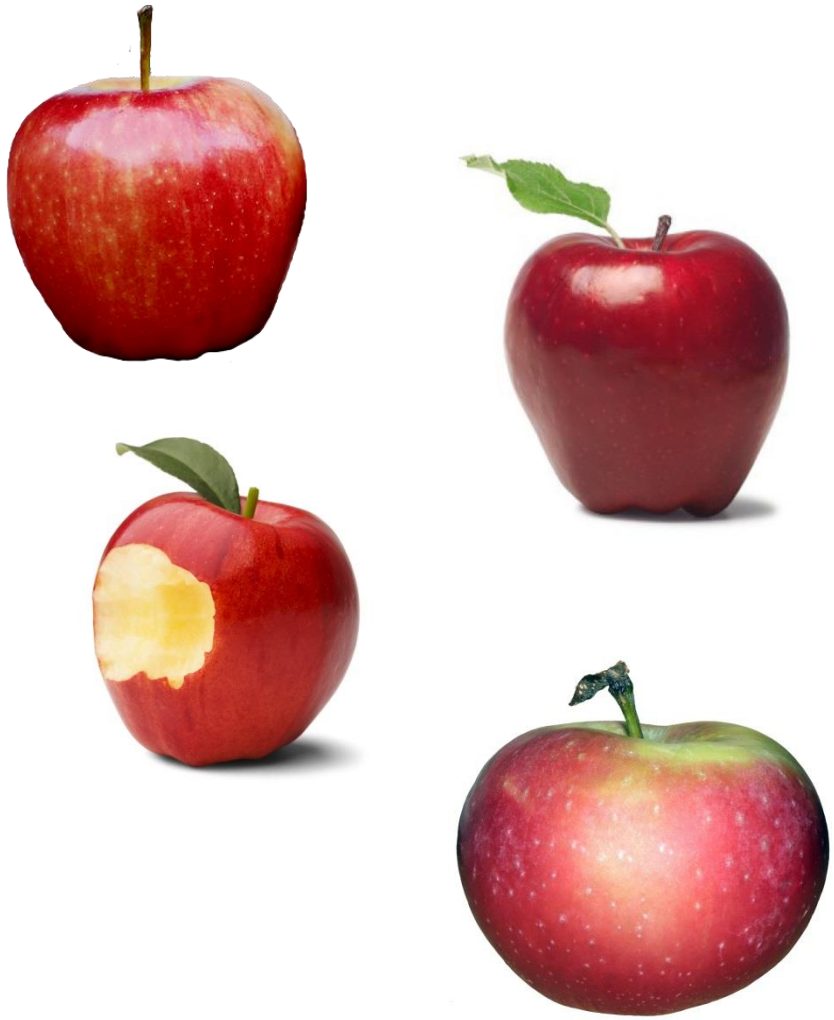
- Voluntary.
- Product is “the same” as prequalified by WHO.
- Shared confidential information to support NRA decision making in exchange for accelerated registration process.
- 'Harmonized product status' is monitored and maintained.

Elements still to be defined for IVDs

Sameness of products

World Health Organization

1. product name
2. product code
3. manufacturer
4. regulatory version



Win-win outcomes for all stakeholders

World Health Organization

Manufacturers

- Facilitated interaction with NRAs
- Accelerated and more predictable registration
- Easier post-registration maintenance

Procurers

- Time to market entry, QA, availability

NRAs

- Availability of WHO assessment and inspection outcomes to support national decisions and save internal capacities.
- Having assurance about registration of 'the same' product as PQ-ed

Collaborative registration procedure for IVDs

Procedure under development

Coordinated through RSS group at WHO

Mtg with 15 African countries held in Oct 2018

Mirror CRP for medicines with 90 days registration target timelines

Agreement with NRAs + interest from manufacturers = CRP

Pilot planned Q1/Q2 2019

Opened questions:

- Submission structure and content.
- Managing diversity of regulatory systems maturity levels.

Questions and answers

World Health Organization

WHO

20, Avenue Appia
1211 Geneva

Switzerland

diagnostics@who.int

https://www.who.int/diagnostics_laboratory/evaluations/en/

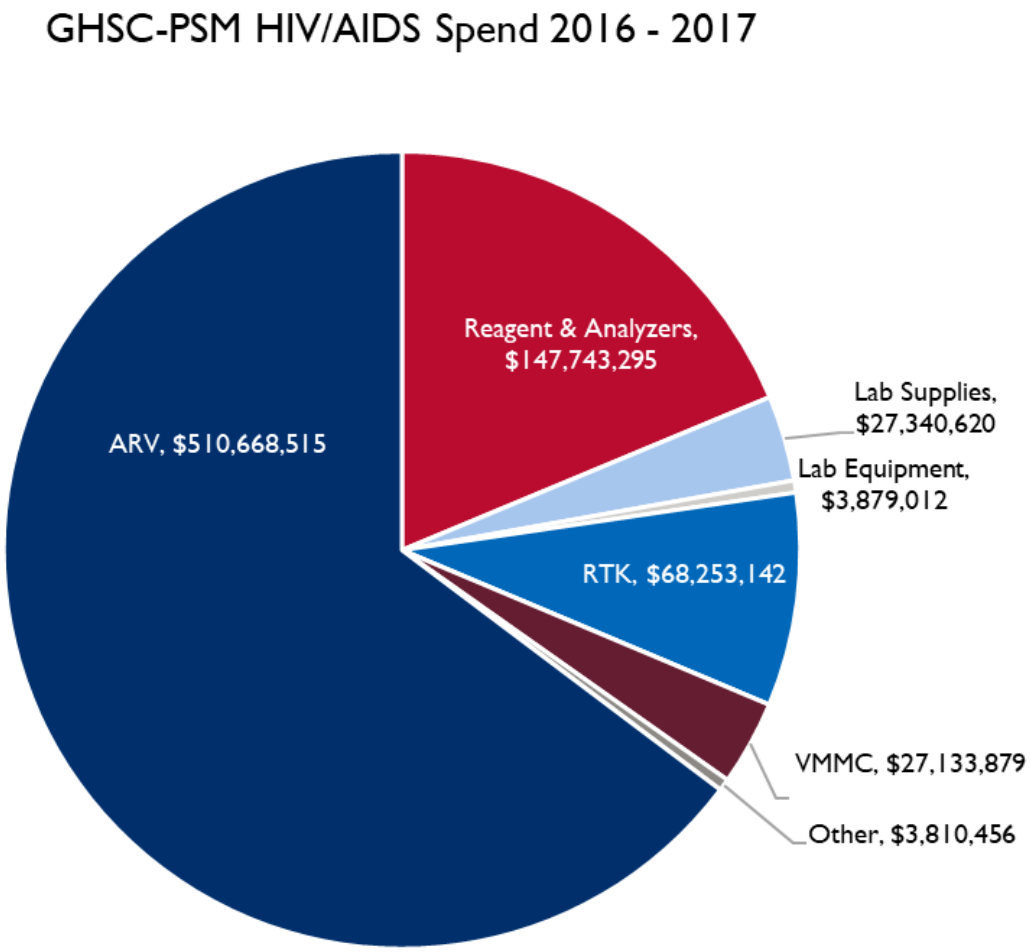
USAID
FROM THE AMERICAN PEOPLE

PEPFAR
U.S. President's Emergency Plan for AIDS Relief

Procurement of Laboratory Diagnostics with special reference to HIV RTKs

Joel Kuritsky/Peter Smith

GHSC-PSM & GHSC-RTK Aggregated Spend

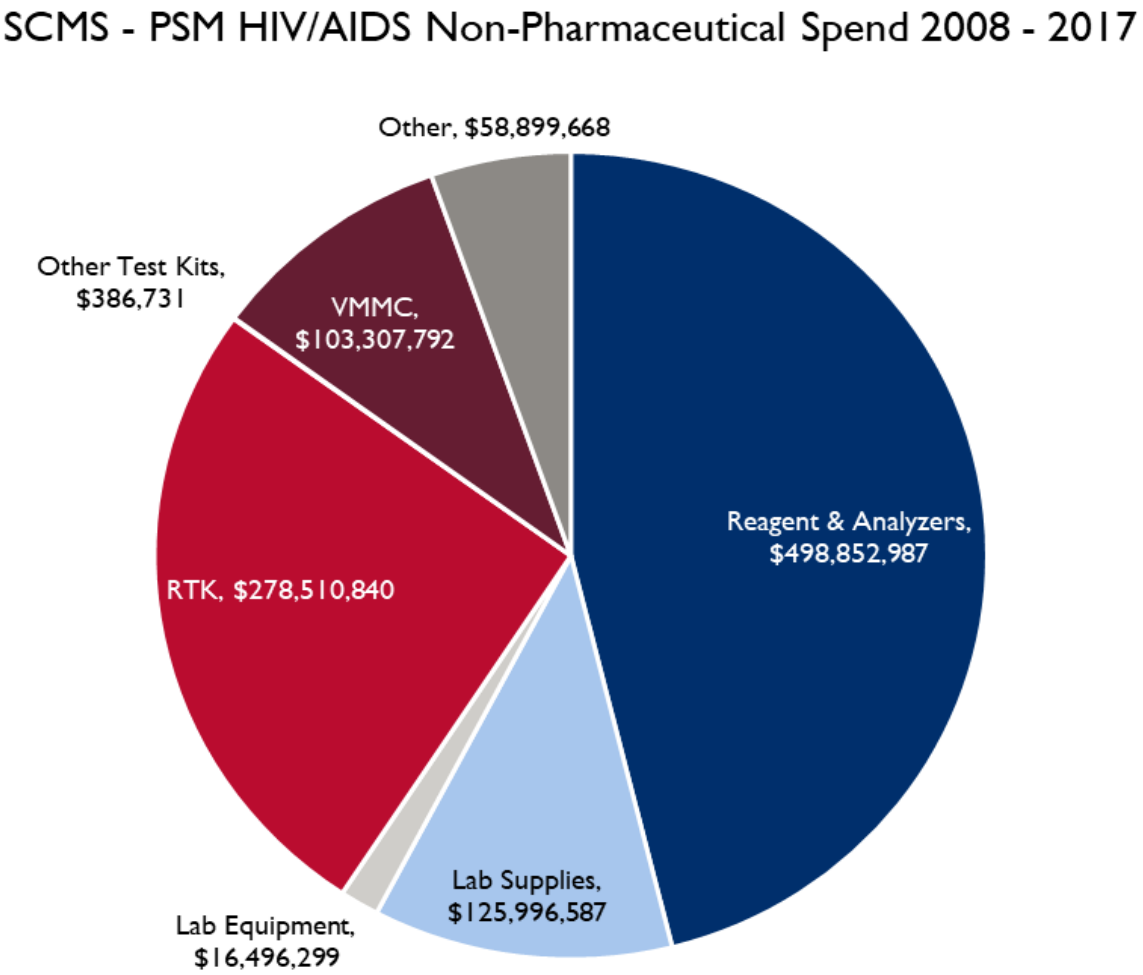


*Sources: GHSC-RTK; Plan team analysis; SCMS and PSM data; product price for most recent PO placed is used to calculate costs. Other lab commodities refers to products that can not be exclusively mapped to Molecular or CD4 categories; orders are calculated using Requested Delivery Dates

USAID FROM THE AMERICAN PEOPLE

PEPFAR U.S. President's Emergency Plan for AIDS Relief

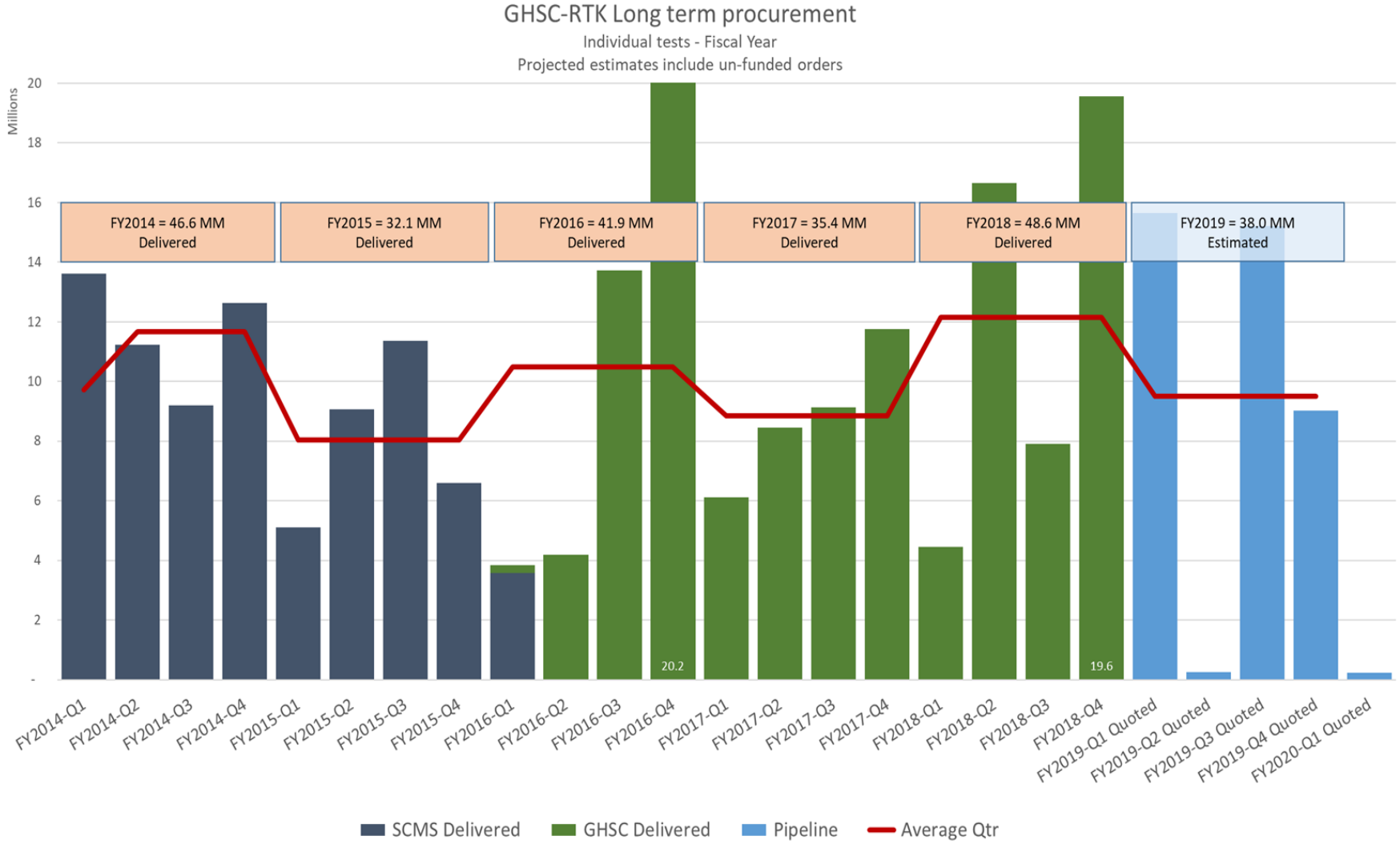
SCMS – PSM Aggregated Spend

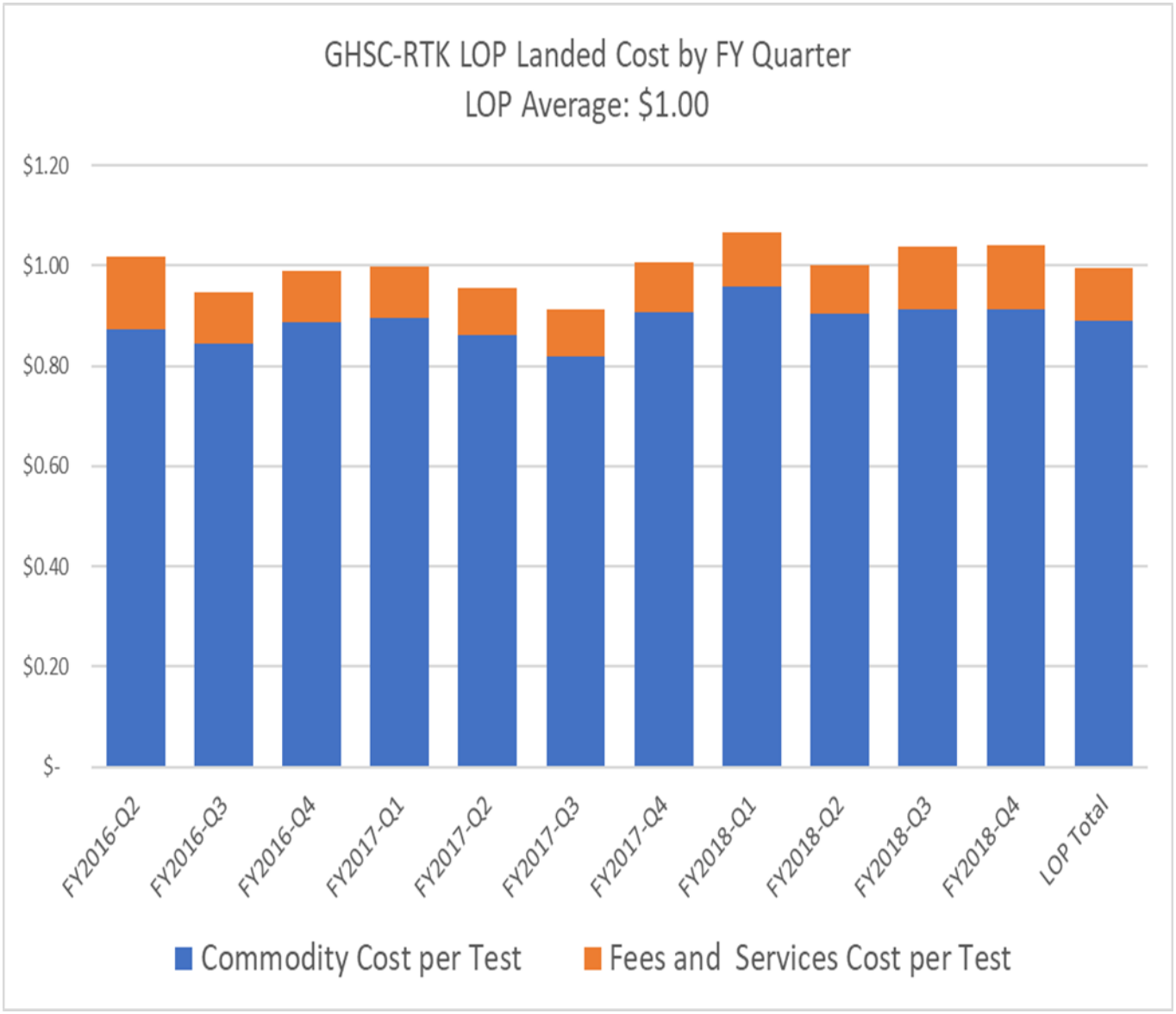


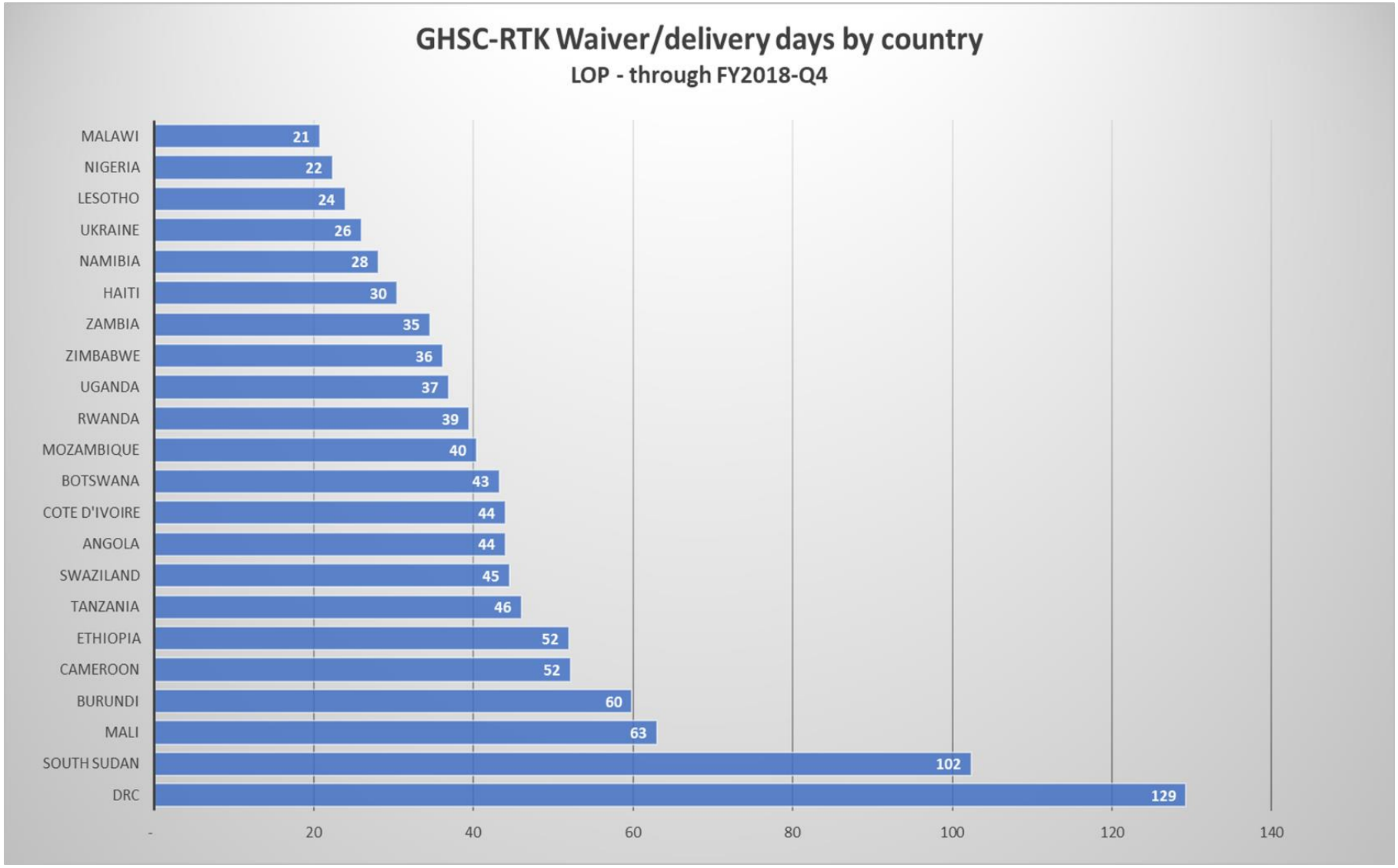
*Sources: GHSC-RTK; Plan team analysis; SCMS and PSM data; product price for most recent PO placed is used to calculate costs. Other lab commodities refers to products that can not be exclusively mapped to Molecular or CD4 categories; orders are calculated using Requested Delivery Dates
*VMMC data starts from 2010

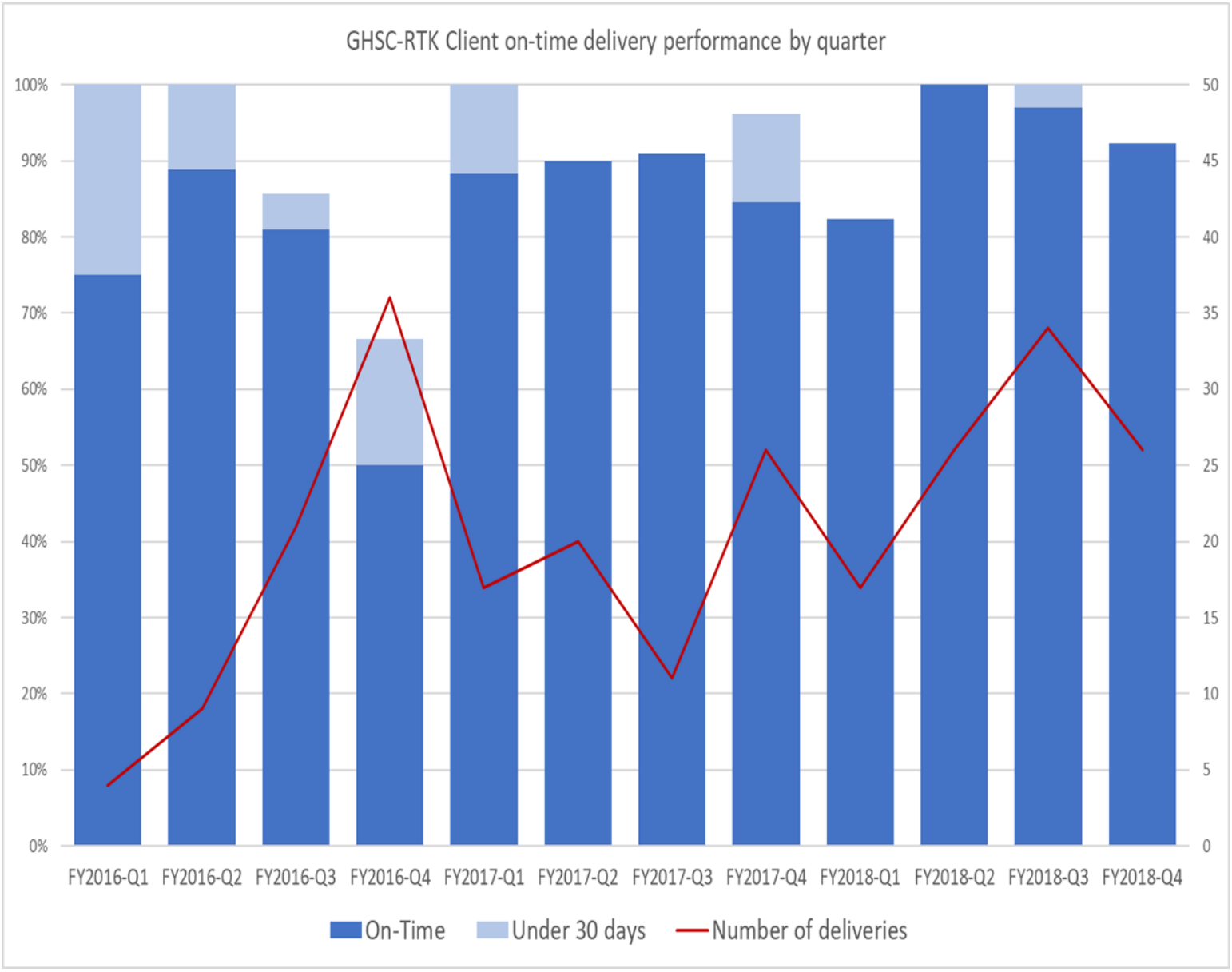
Procurement and Logistical Considerations

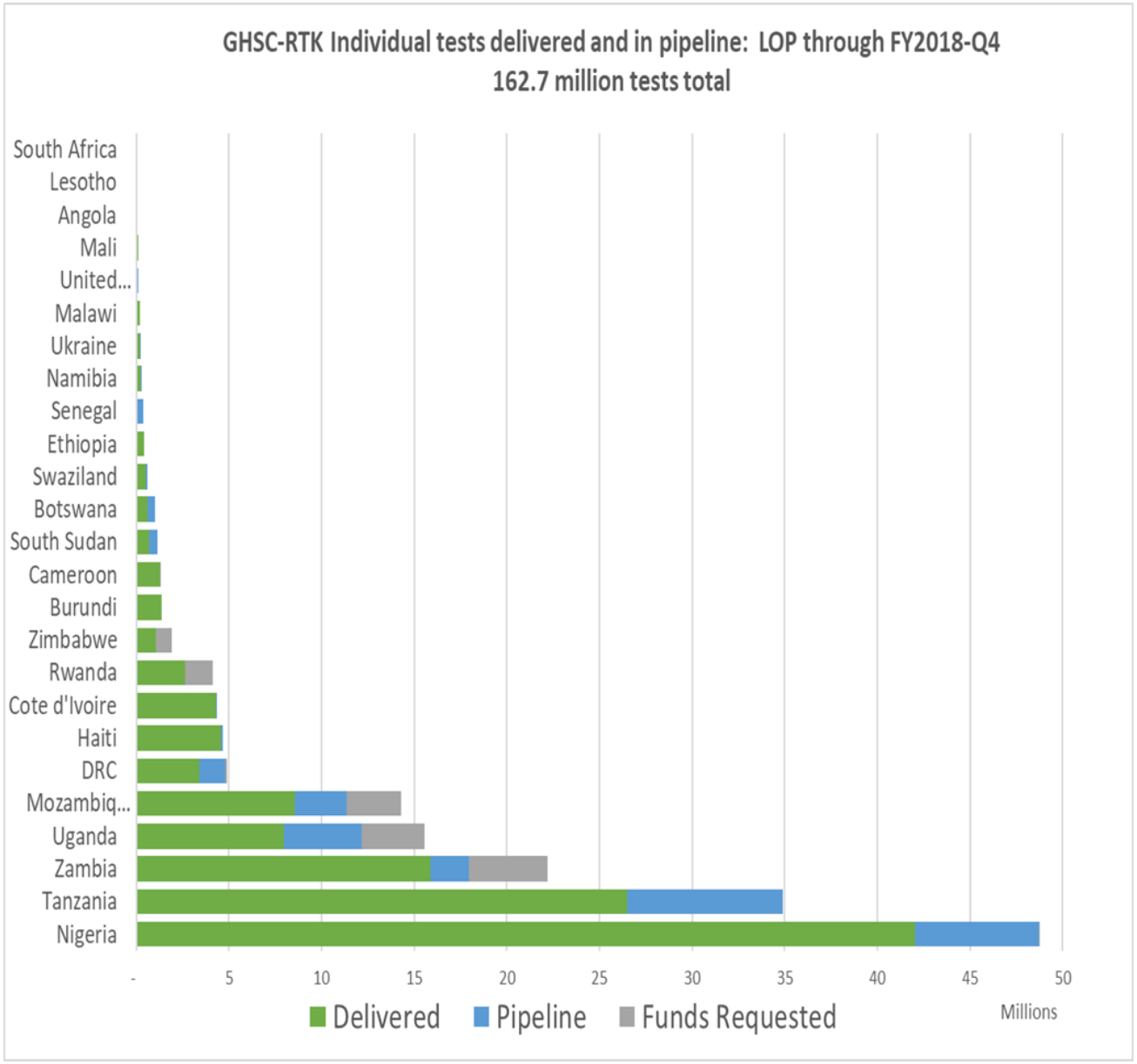
- USAID approved list of HIV Rapid Diagnostics/ WHO list of prequalified in vitro diagnostic products
- Specifications and Country Algorithm
- In country Registration / Regulatory Requirements
- Special Requirements such a Labeling, Product Inserts
- Lead times and client expectations
- Waiver Issues and supplier space/cash Flow Impact
- Product Shelf life and Shipping Mode

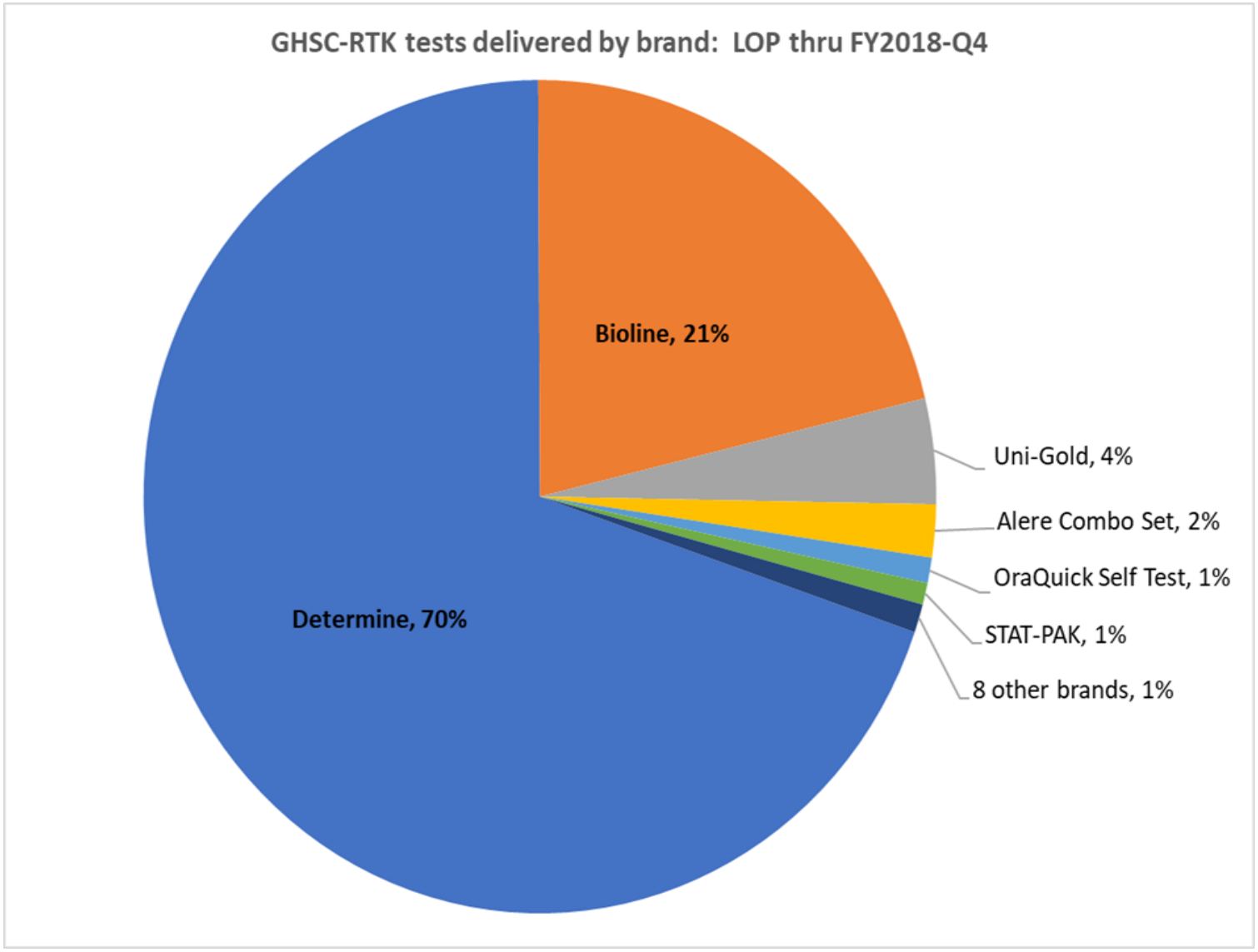

GHSC-RTK Long term procurement
Individual tests - Fiscal Year
Projected estimates include un-funded orders
Millions
20
18
16
14
12
10
8
6
4
2
-
FY2014 = 46.6 MM Delivered
FY2015 = 32.1 MM Delivered
FY2016 = 41.9 MM Delivered
FY2017 = 35.4 MM Delivered
FY2018 = 48.6 MM Delivered
FY2019 = 38.0 MM Estimated
20.2
19.6
FY2014-Q1
FY2014-Q2
FY2014-Q3
FY2014-Q4
FY2015-Q1
FY2015-Q2
FY2015-Q3
FY2015-Q4
FY2016-Q1
FY2016-Q2
FY2016-Q3
FY2016-Q4
FY2017-Q1
FY2017-Q2
FY2017-Q3
FY2017-Q4
FY2018-Q1
FY2018-Q2
FY2018-Q3
FY2018-Q4
FY2019-Q1 Quoted
FY2019-Q2 Quoted
FY2019-Q3 Quoted
FY2019-Q4 Quoted
FY2020-Q1 Quoted
SCMS Delivered
GHSC Delivered
Pipeline
Average Qtr

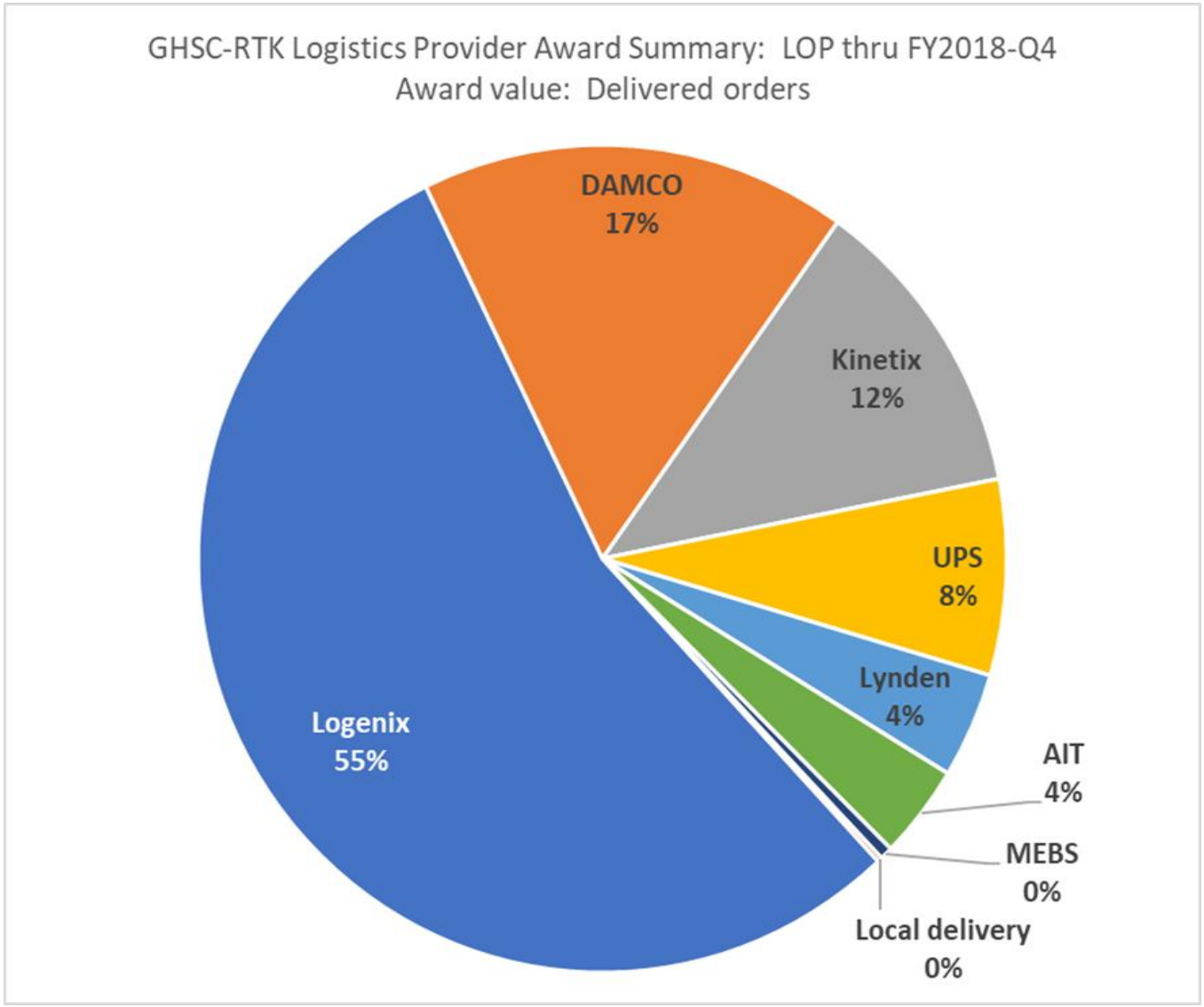

GHSC-RTK LOP Landed Cost by FY Quarter
LOP Average: $1.00
$1.20
$1.00
$0.80
$0.60
$0.40
$0.20
$-
FY2016-Q2
FY2016-Q3
FY2016-Q4
FY2017-Q1
FY2017-Q2
FY2017-Q3
FY2017-Q4
FY2018-Q1
FY2018-Q2
FY2018-Q3
FY2018-Q4
LOP Total
Commodity Cost per Test
Fees and Services Cost per Test


GHSC-RTK Waiver/delivery days by country
LOP - through FY2018-Q4
MALAWI 21
NIGERIA 22
LESOTHO 24
UKRAINE 26
NAMIBIA 28
HAITI 30
ZAMBIA 35
ZIMBABWE 36
UGANDA 37
RWANDA 39
MOZAMBIQUE 40
BOTSWANA 43
COTE D'IVOIRE 44
ANGOLA 44
SWAZILAND 45
TANZANIA 46
ETHIOPIA 52
CAMEROON 52
BURUNDI 60
MALI 63
SOUTH SUDAN 102
DRC 129
- 20 40 60 80 100 120 140


GHSC-RTK Client on-time delivery performance by quarter
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
50
45
40
35
30
25
20
15
10
5
0
FY2016-Q1
FY2016-Q2
FY2016-Q3
FY2016-Q4
FY2017-Q1
FY2017-Q2
FY2017-Q3
FY2017-Q4
FY2018-Q1
FY2018-Q2
FY2018-Q3
FY2018-Q4
On-Time
Under 30 days
Number of deliveries


GHSC-RTK Individual tests delivered and in pipeline: LOP through FY2018-Q4
162.7 million tests total
South Africa
Lesotho
Angola
Mali
United...
Malawi
Ukraine
Namibia
Senegal
Ethiopia
Swaziland
Botswana
South Sudan
Cameroon
Burundi
Zimbabwe
Rwanda
Cote d'Ivoire
Haiti
DRC
Mozambiq...
Uganda
Zambia
Tanzania
Nigeria
-
5
10
15
20
25
30
35
40
45
50
Millions
Delivered
Pipeline
Funds Requested


GHSC-RTK tests delivered by brand: LOP thru FY2018-Q4
Bioline, 21%
Uni-Gold, 4%
Alere Combo Set, 2%
OraQuick Self Test, 1%
STAT-PAK, 1%
8 other brands, 1%
Determine, 70%


GHSC-RTK Logistics Provider Award Summary: LOP thru FY2018-Q4
Award value: Delivered orders
DAMCO
17%
Kinetix
12%
UPS
8%
Lynden
4%
AIT
4%
MEBS
0%
Local delivery
0%
Logenix
55%

Malaria RDT Task Force Market Health Analysis

11 December, 2018

Malaria RDT Procurement Task Force: Focus on Market Health

Over last the 18 months, the task force met and discussed RDT market challenges:

June 2017, Geneva

- *Procurement task force meeting*
  - *Established Working Group to explore opportunities to improve market stability*
- *Follow up meetings:*

October 2017, Montreaux

  - *Side meeting GFATM strategic sourcing meeting*

November 2017, Baltimore

  - *Side meeting ASTMH*

February 2018, Geneva

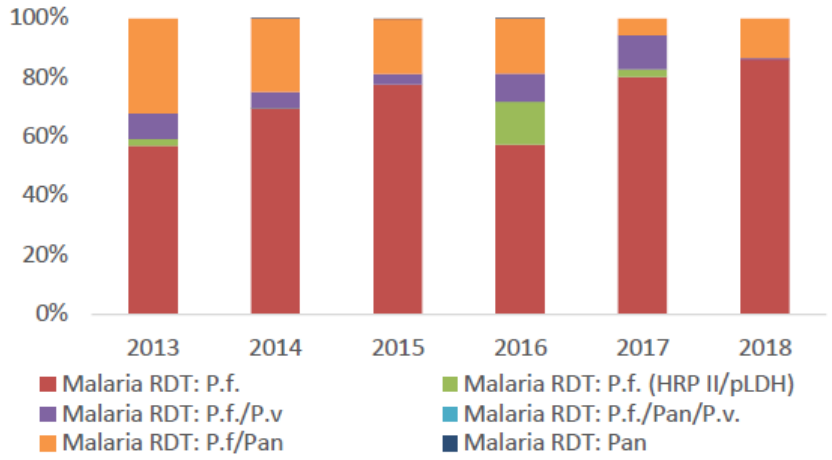
- *Procurement Task force meeting*
  - *Agreement on a market framework to assess the health of the RDT market*
  - *Present at next taskforce meeting*

July 2018, Geneva

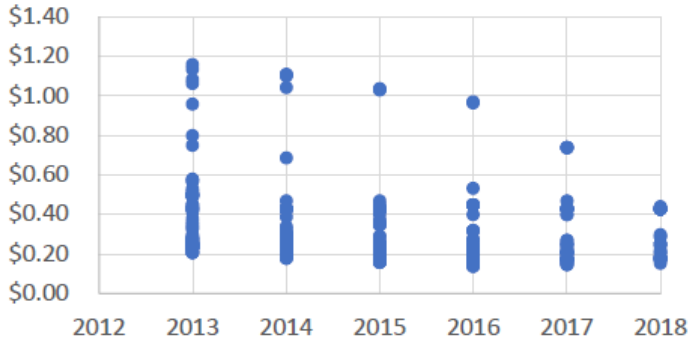
- *Procurement Task force meeting*

Malaria RDT Market Snapshot

*HRP II P. Falciparum test remains the dominant test***

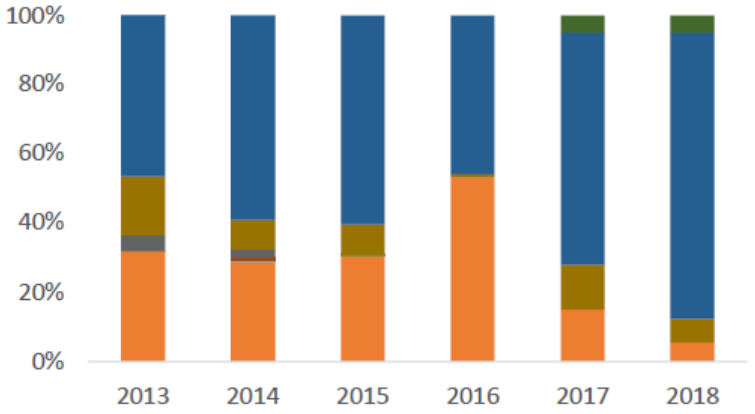


RDT prices tender have decreased, as low as $0.15 (Pf HRP II Hospital packs)



The latest available public sector procurement data* shows some fundamental dynamics have not changed

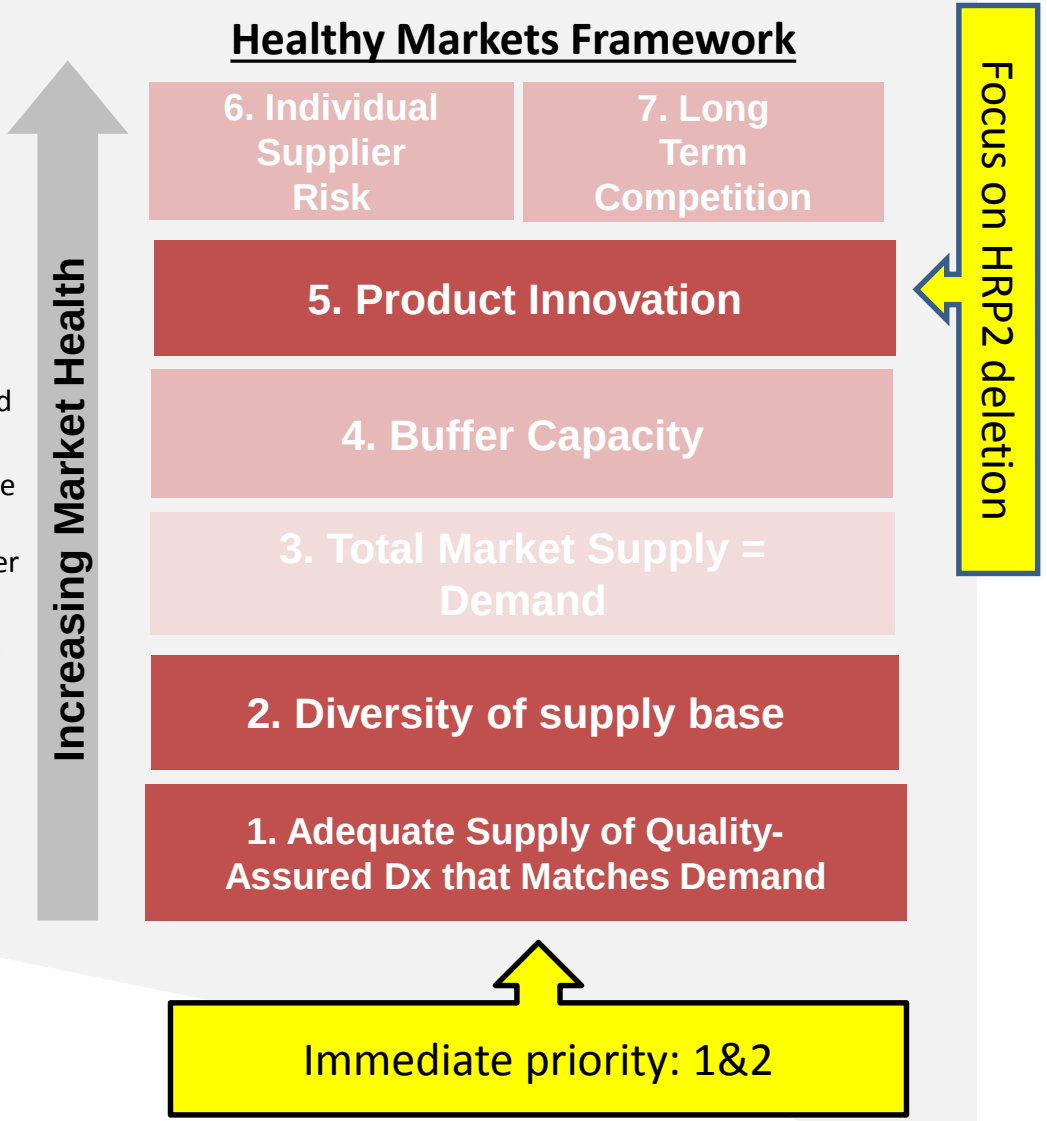
The market continues to be dominated by 2 suppliers capturing 85% or more of since 2013



*PQR (May18th 2018), PMI ** **2018 data only PMI, PQR 2017 data only ~30%**

Summary: current market health

1. There is adequate supply of RDTs for today's dominant products, but insufficient for emerging demand
2. There are 3+ PQ'd suppliers for today's dominant product, but for all other product types we are deficient
3. Private sector demand is relatively small and therefore the assessment of supply vs. demand is similar
4. If one of the largest 2 suppliers of the dominate products were to exit, limited to no buffer. For new/emerging product types, insufficient buffer for growing demand.
5. There is a significant gap in product innovation
6. Individual suppliers are at risk (medium to low volume)
7. Long term competition is at risk as market continues to consolidate



Principles for reducing market risk

- Move from spot procurement to long term agreements to help stabilize pricing and provide more visibility on demand
- Allocate demand across three or more suppliers
- Limit restricted procurement based on testing protocol. Other, malaria epidemiology-based reasons, such as multi-species prevalence is appropriate
- Encourage sustainable pricing by signaling that price is not the only factor in award and allocation determination.
- Improve performance of pLDH based RDTs and/or new targets to ensure there are options for countries with higher than 5 percent HRP2 deletions

USAID GLOBAL HEALTH SUPPLY CHAIN PROGRAM
Procurement and Supply Management

PMI/GHSC-PSM RDT Sourcing Strategy 2018/2019

Photo: Lan Andrian

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CDC
U.S. President's Malaria Initiative

We evaluate four essential dimensions in assessing a "healthy market," with specific output metrics tailored to individual markets

Good Medium Poor

Dimensions	Key questions and output metrics	2016/2017 concerns
Global capacity	**Is there sufficient supply to meet demand?** – Supply and demand gap – Existence of demand forecast – Forecast accuracy – Lead times, stock out rate	▪ Prequalified public supplier production capacity expected to meet demand
Affordability & funding	**Is pricing affordable?** – Price relative to substitute and peer markets – % Supply base utilized – Funding and demand gap – Projected funding	▪ Suppliers charging unsustainable pricing (high and low) ▪ Gap between overall need and donor funding
Supply risk	**Is there sustainable, secure supply of these products?** – Number and diversity of suppliers – Margins / price relative to cost – Product registration coverage – Scalability of capacity	▪ Unsustainable prices and high supplier concentration present risk of supply security
Product quality & appropriateness	**Are there quality products that meet user needs?** – Effective products with regulatory approvals – Quality of products – Appropriateness based on target customer needs – Incentives for innovating improved products	▪ Policy change to require WHO PQ Several ▪ Innovations (i.e. G6PD testing, increased sensitivity, less invasiveness)

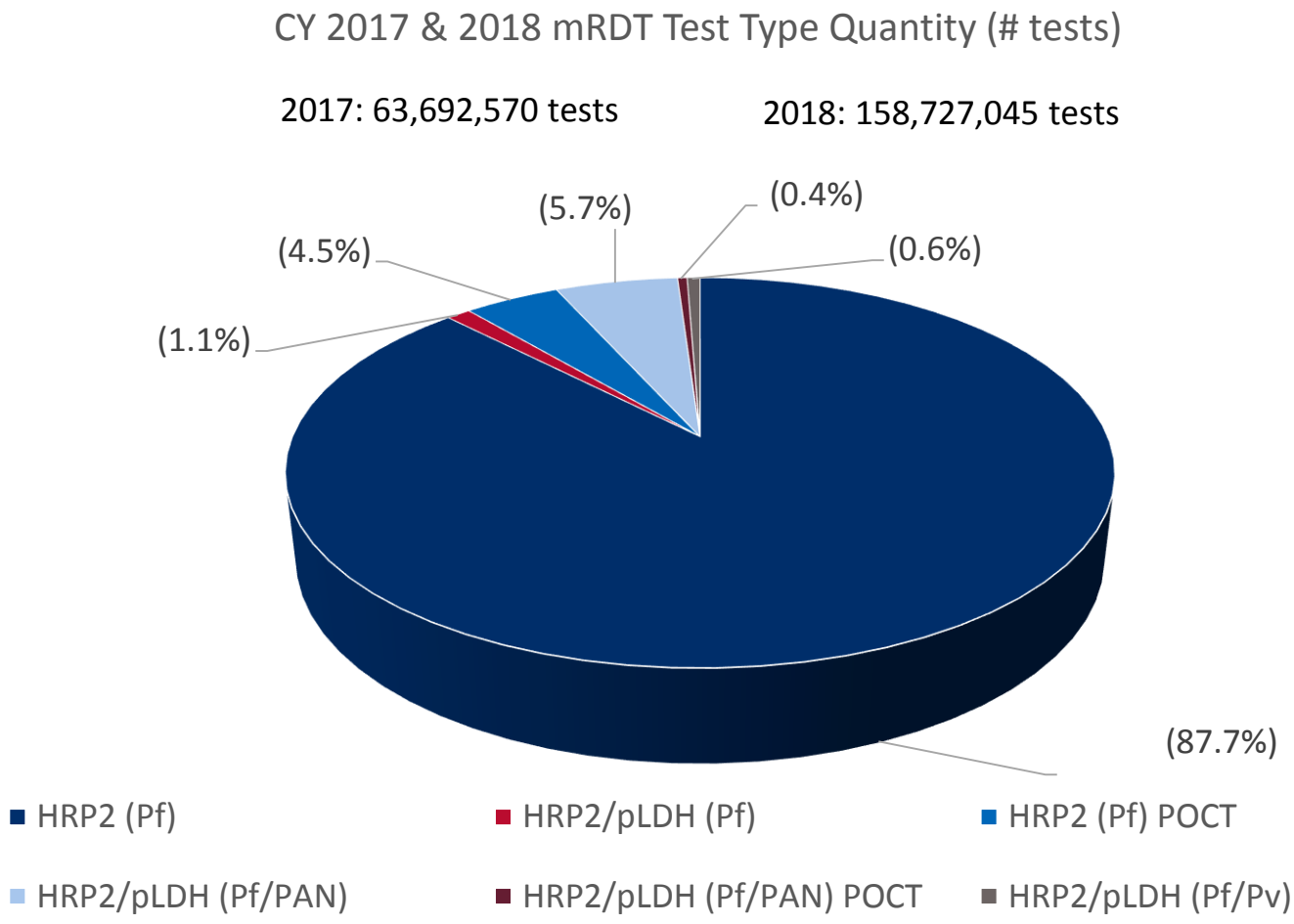
There are several levers to improve supply security for the RDT market

	Levers	Sub levers	PMI/PSM
Short-term	A Contracting strategy	▪ Develop contracting award scenarios that emphasize supply security and take into account cost barriers	✓
	B Tendering and contracting process	▪ Reduce level of effort for suppliers to respond to tenders	✓
		▪ Reduce cycle time for tender process and award notification	✓
	C Registration prioritization	▪ Provide guidance to suppliers to maximize ROI for registration and reduce sole-sourcing (2+ suppliers registered in each country; prioritize suppliers with testing protocols already accepted)	✓
Mid-term	D Demand visibility	▪ Improve demand visibility to allow for advanced planning and production leveling by manufacturers	✓
		▪ Provide transparency to suppliers on future order volumes	✓
Long-term	E Product interchange-ability	▪ Assess training requirements to reduce usage barriers and enable product switching. **In 2018 PMI revised its policy requiring countries to be able to accept RDTs from multiple suppliers.**	✓

PMI/PSM contracting strategy, implemented Summer 2018

IDIQ Element	Strategic Implementation
Pricing	▪ Country-agnostic, product-specific ceiling prices for life of contract ▪ Request for pricing tiered by order size ▪ Biannual or annual call for fixed pricing ▪ Suppliers are encouraged to submit reasonable, sustainable prices ▪ Same price for all countries
Evaluation	▪ Evaluation to determine technical eligibility and viability of business proposal ▪ Determine notional targets for order allocation in order to maintain adequate supply diversity and support market health
Order allocation and pricing	▪ GADs are confirmed with eligible suppliers prior to finalization of best value award ▪ Orders are awarded and placed against fixed prices based on overall best value determination ▪ Best value award is determined by weighing minimum eligibility requirements (like QA eligibility, ability to meet technical specifications, and country registration), as well as supplier performance, price, potential impact on other placed orders, lead time, and supply diversity.
Technical Specs	▪ WHO-PQ, country registration
Contract Length	▪ 1 base year, 3 option years
Other	▪ Regular communication on production capacity, forecast, and country registration priorities ▪ Ability to onboard new suppliers and products

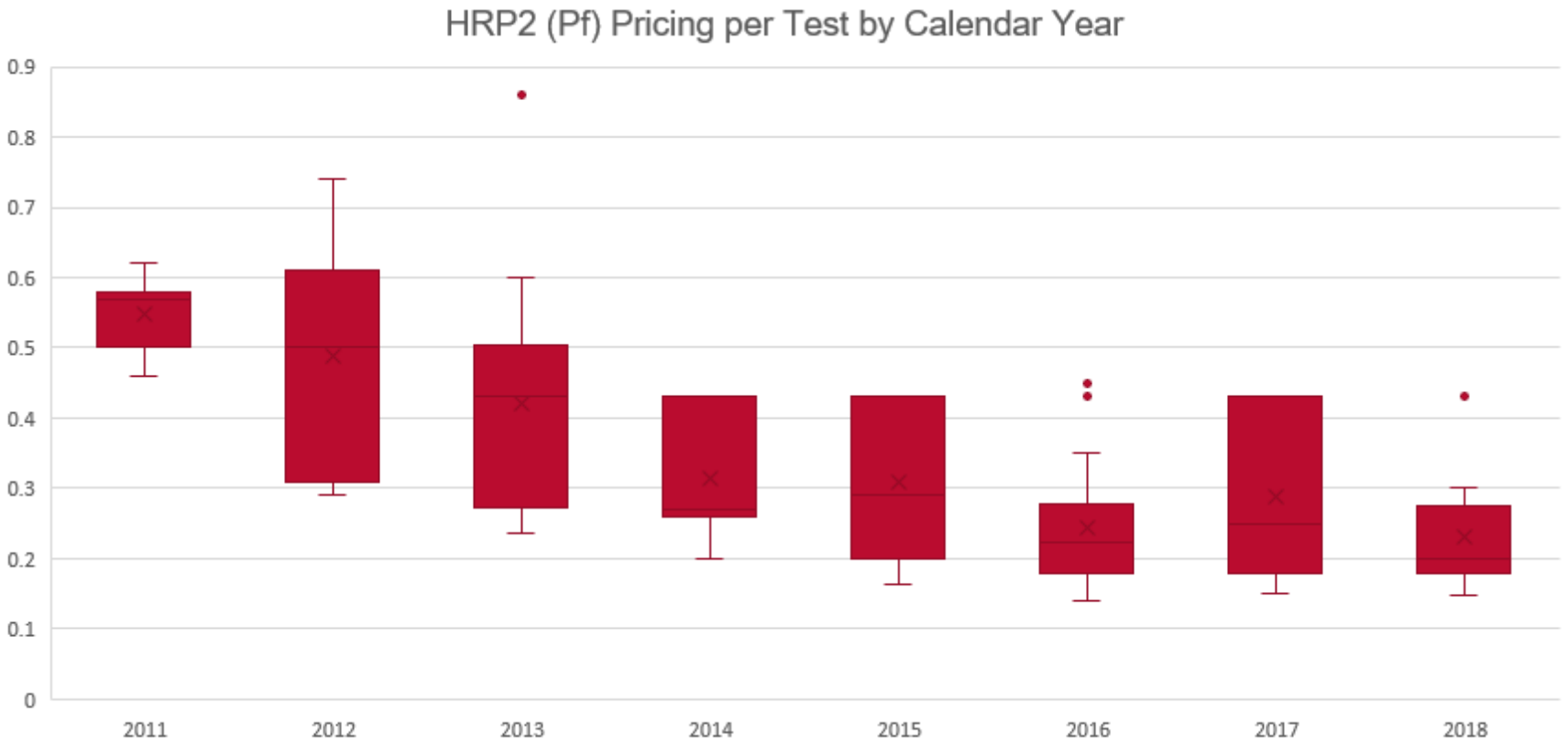
The HRP2 (Pf) test type represents the majority of mRDTs procured by PSM



In 2018, PMI countries have experienced less price variance than in prior years

PMI prices for HRP2 (Pf) mRDT procurements, not comprehensive

$USD / test*

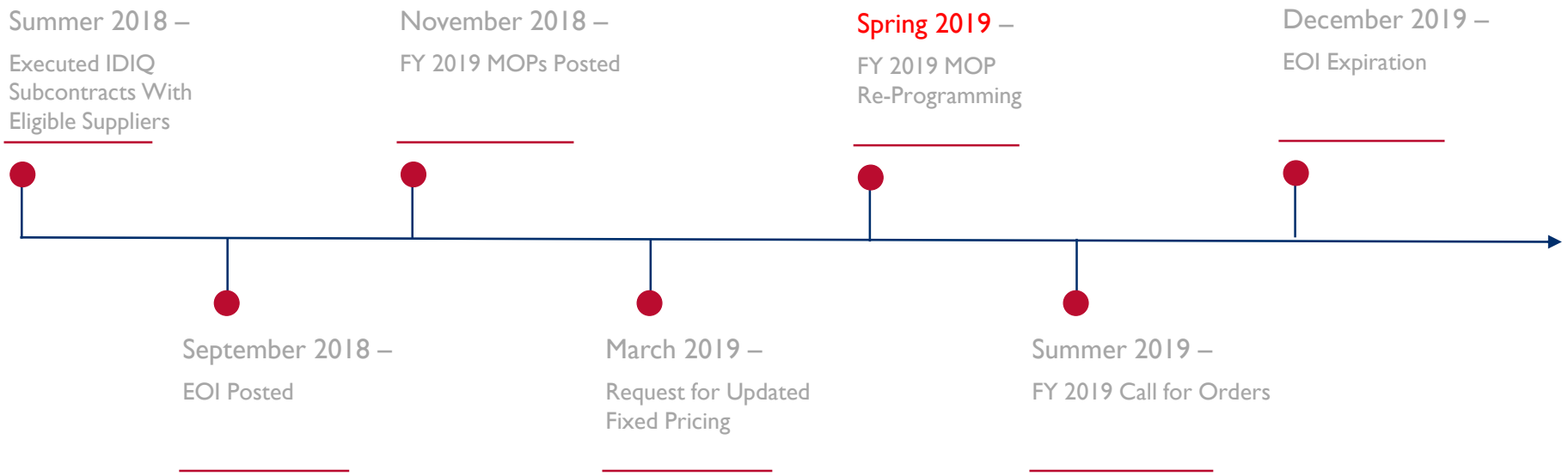


*2018 prices include procurements both before and after the establishment of LTAs with PSM RDT suppliers

PSM has solicited expressions of interest for additional RDTs to be included under IDIQ

- Posting for expressions of interest (EOI) is currently available with expiration date of December 31, 2019
- EOI provides opportunity for vendors currently under contract to incorporate newly eligible products into existing contracts
- Suppliers that are not currently under contract with GHSC-PSM can submit products via an EOI and, following evaluation, be awarded in the form of an IDIQ subcontract

GHSC-PSM RDT Sourcing Timeline



The USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project is funded under USAID Contract No. AID-OAA-I-15-0004. GHSC-PSM connects technical solutions and proven commercial processes to promote efficient and cost-effective health supply chains worldwide. Our goal is to ensure uninterrupted supplies of health commodities to save lives and create a healthier future for all. The project purchases and delivers health commodities, offers comprehensive technical assistance to strengthen national supply chain systems, and provides global supply chain leadership. For more information, visit ghsupplychain.org.

December 2018

Rapid Diagnostics Tests (RDT) Suppliers Meeting

UNICEF Procurement Update and Joint UN Tender

Lama Suleiman

Contracts Manager, Health Technology center

unicef | for every child

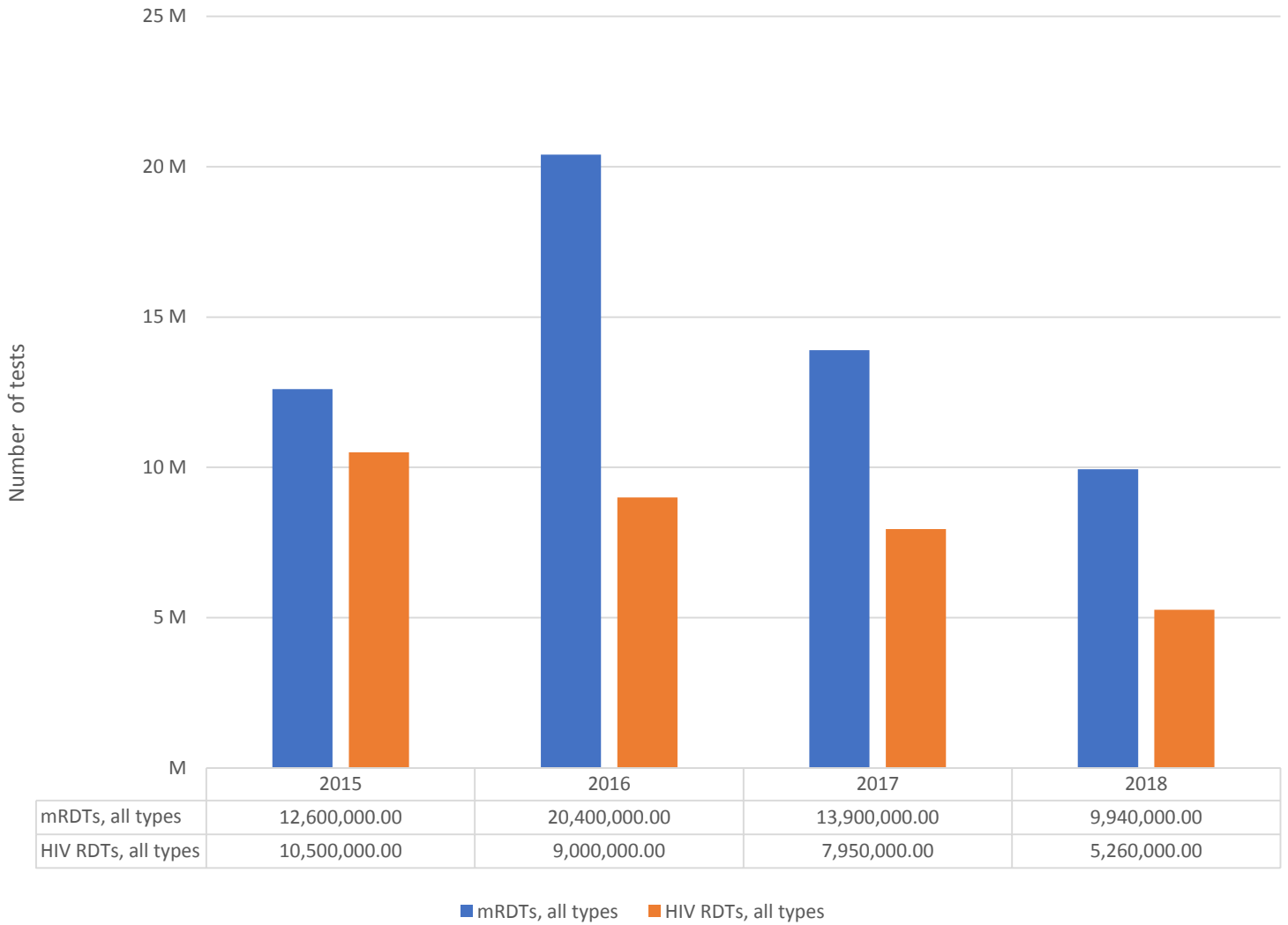
Content

1. UNICEF HIV and mRDTs Procurement Update 2015 - 2018

2. UNICEF Procurement Strategy for HIV and mRDTs in 2019-2021

3. UNICEF Procurement Approach: UN Joint Tender 2018

1.1 UNICEF HIV and mRDTs Procurement Volumes, 2015 – 2018 (as of Nov 2018)



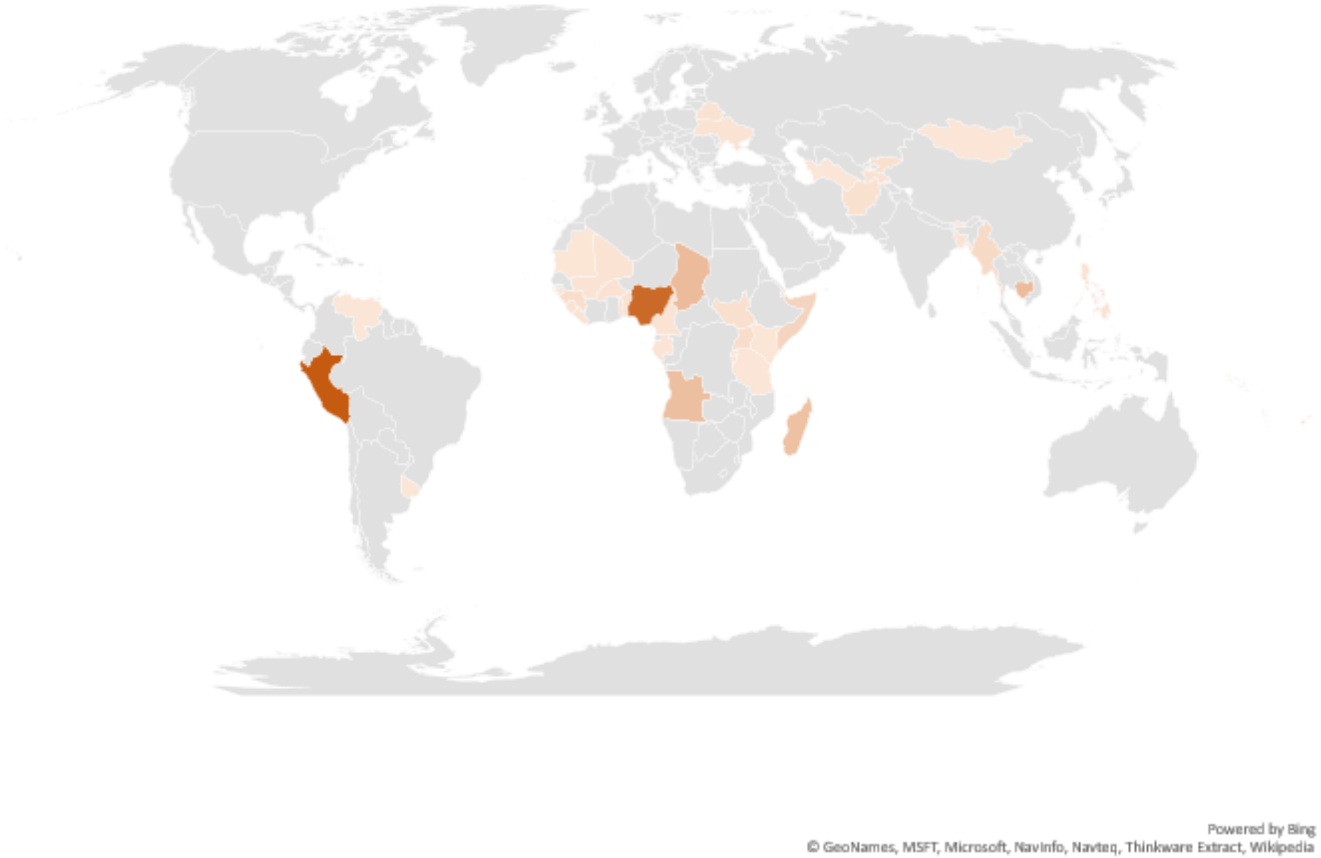
	2015	2016	2017	2018
mRDTs, all types	12,600,000.00	20,400,000.00	13,900,000.00	9,940,000.00
HIV RDTs, all types	10,500,000.00	9,000,000.00	7,950,000.00	5,260,000.00

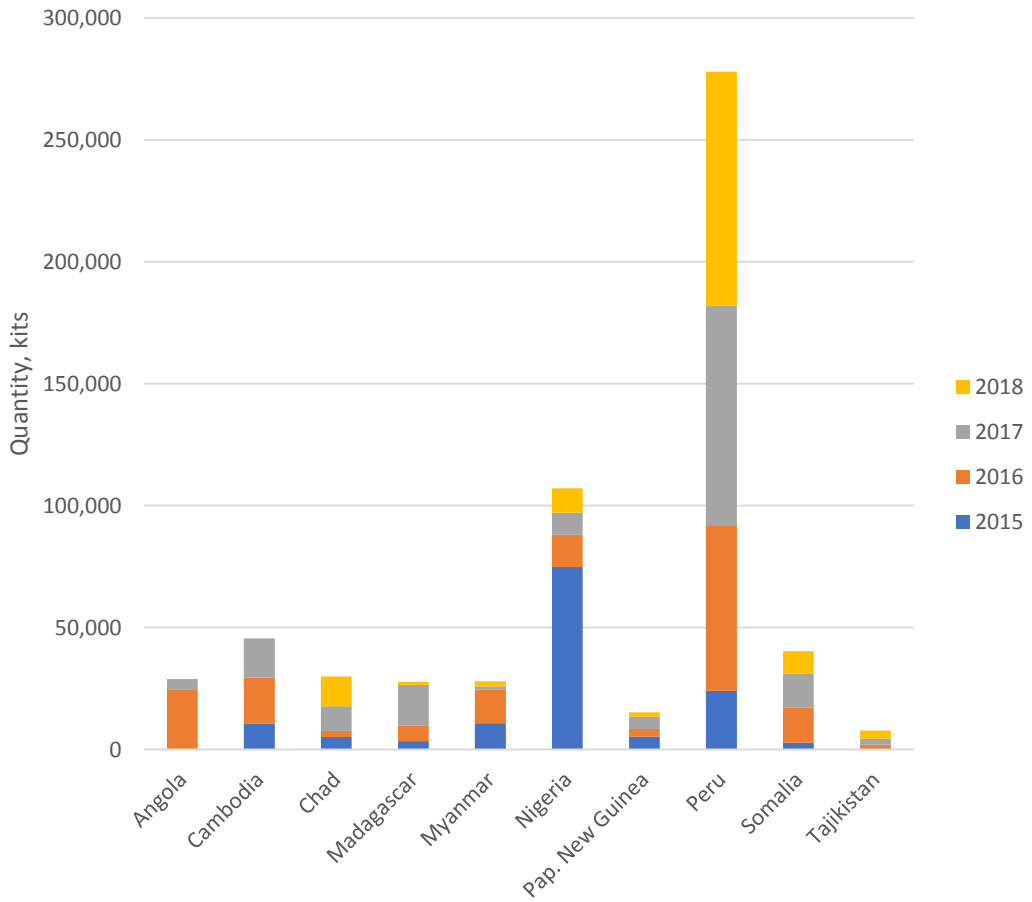
WAP 2018 $1.10

WAP 2018 $0.49

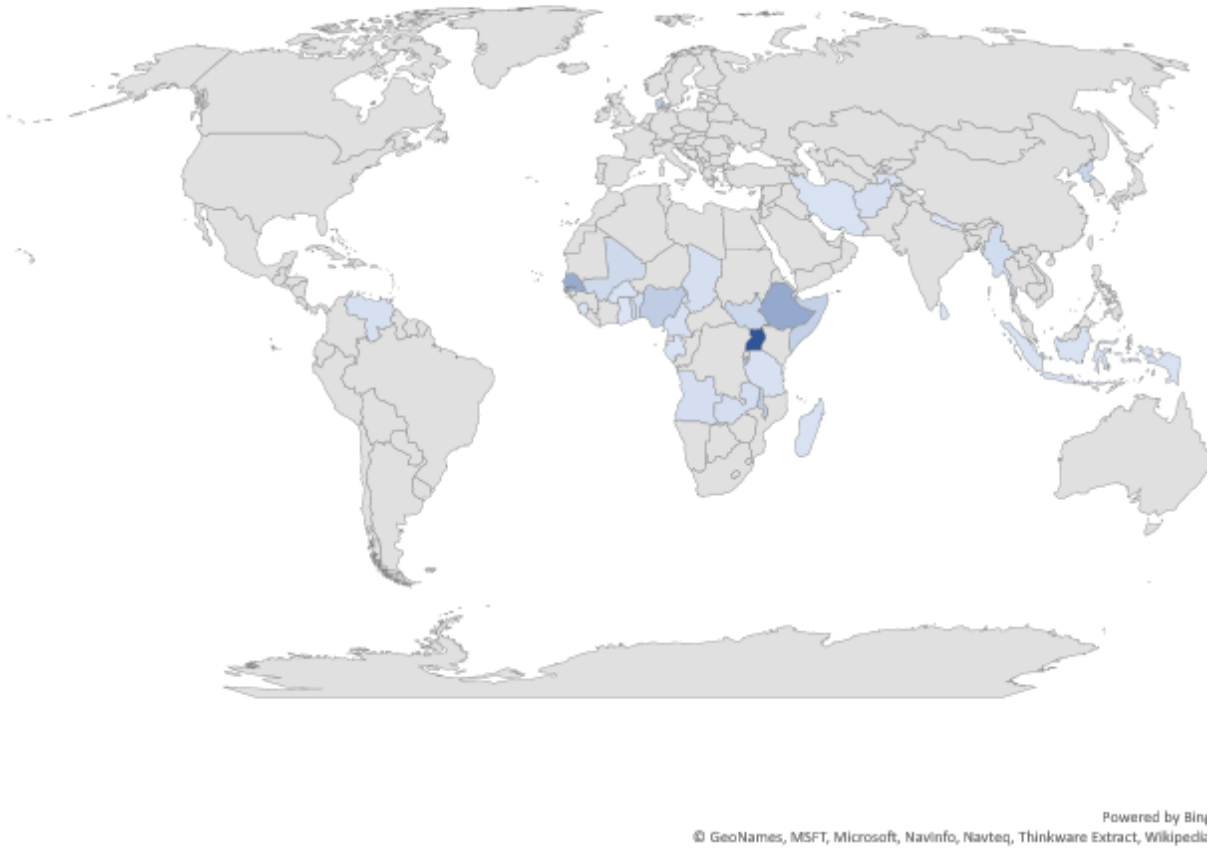
*The weighted average price (WAP) is the ratio of the value procured to total volume over a year. It represents a range of different mRDT/ HIV RDT product range

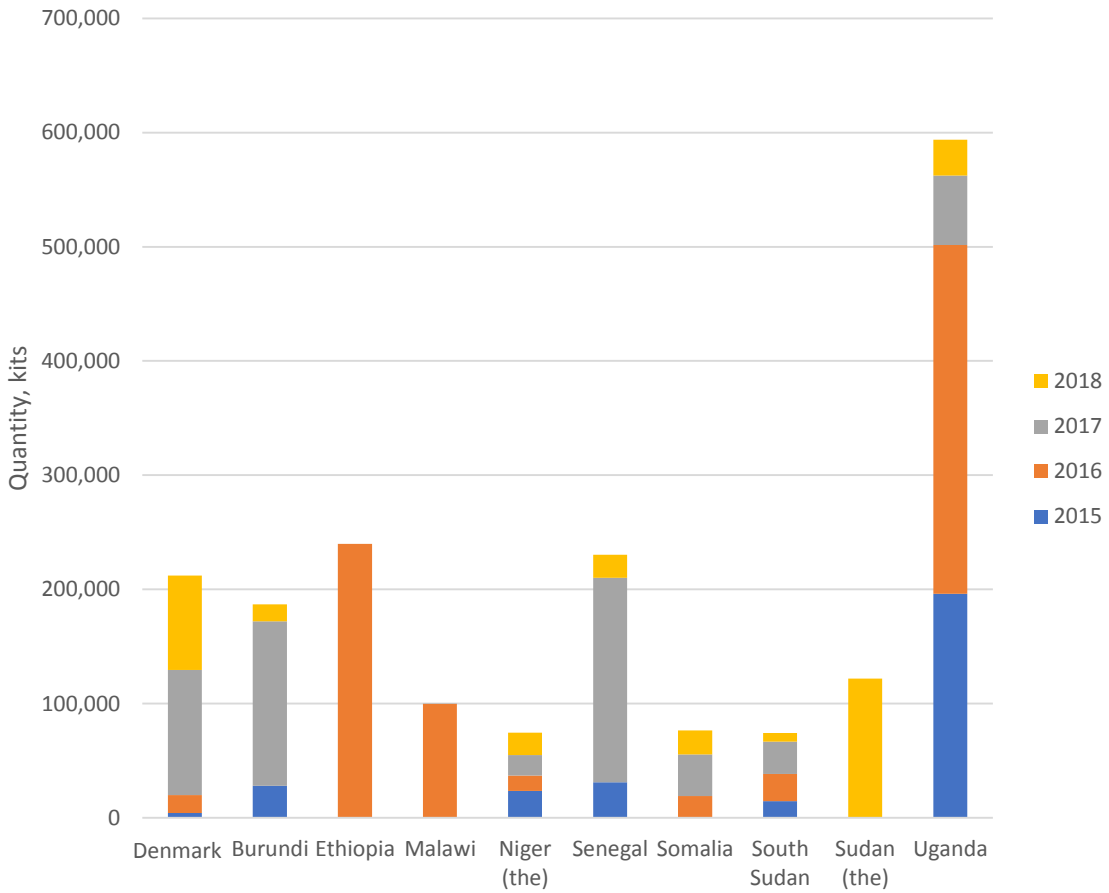
1.2 UNICEF HIV RDTs Procurement by Receiving Country, 2015 – 2018 (as of Nov 2018)





1.3 UNICEF mRDTs Procurement by Receiving Country, 2015 – 2018 (as of Nov 2018)





2.1 UNICEF Procurement Strategy for HIV and mRDTs in **2019-2021**

UNICEF PROCUREMENT STRATEGY FOR SEROLOGICAL ASSAYS FOR HIV, MALARIA, HEPATITIS B AND HEPATITIS C

OBJECTIVES

1. To secure a wide choice of quality assured serological assays for HIV, malaria, hepatitis B and C

2. To secure sustainable, affordable and equitable prices for serological assays for HIV, malaria, hepatitis B and C

3. To influence demand adaptability in HIV and malaria diagnostics market through a demonstrated cost modelling to lower perceived barriers associated with product interchangeability

4. To promote transparency and long-term competition in HIV, malaria and hepatitis diagnostics market

5. To secure access to newly innovative diagnostic products including self-testing and multiplexing RDTs

INDICATORS

1.1. The number of serology assays for HIV and malaria are available for public procurement increased compared to 2017 and the pool of the respective suppliers active in public sector is kept wide and diverse

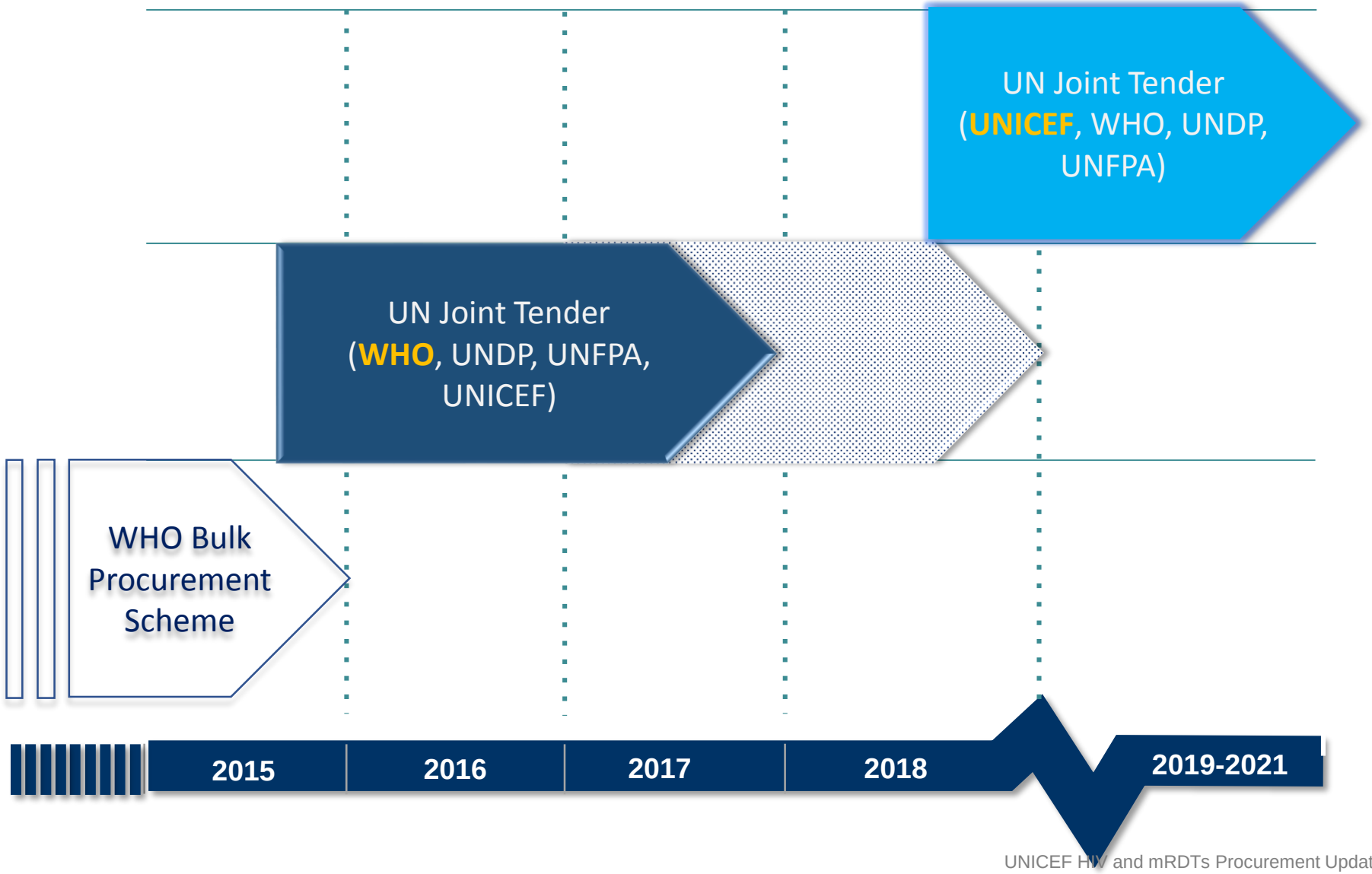
2.1. 2017 WAP for HIV RDTs is reduced;
2.2. 2017 WAP for mRDTs is maintained

3.1 Larger market shares in HIV RDTs and mRDTs are achieved by one or more smaller suppliers

4.1 UNICEF prices for serology assays for HIV and malaria are publicly available;
4.2 UNICEF updated market and product information analysis with regards to HIV RDTs and mRDTs markets is publicly available;
4.3 An aggregated forecast for HIV RDTs and mRDTs across procuring UN agencies is available

5.1 At least 2 HIVST products eligible for UNICEF procurement are available;
5.2 At least 2 multiplexing RDTs that target HIV and at least one more infection eligible for UNICEF procurement are available;
5.3 At least 1 G6PD RDTs eligible for UNICEF procurement are available

3.1 UNICEF Procurement Approach: UN Joint Tender 2018



3.2 UNICEF Procurement Approach: UN Joint Tender 2018

TENDER SCOPE aligned with WHO PQ

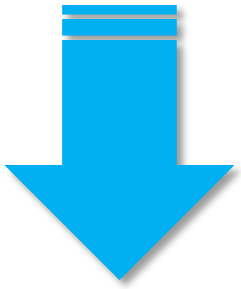
- HIV Serology: RDTs, EIA/ELISA, supplemental
- HIVST
- HIV virology (except for POC and near-POC)
- CD4

- mRDTs

- HBV assays: RDTs, EIA/ELISA, supplemental
- HCV assays: RDTs, EIA/ELISA, supplemental

IMPORTANT IMPLEMENTATION ELEMENTS

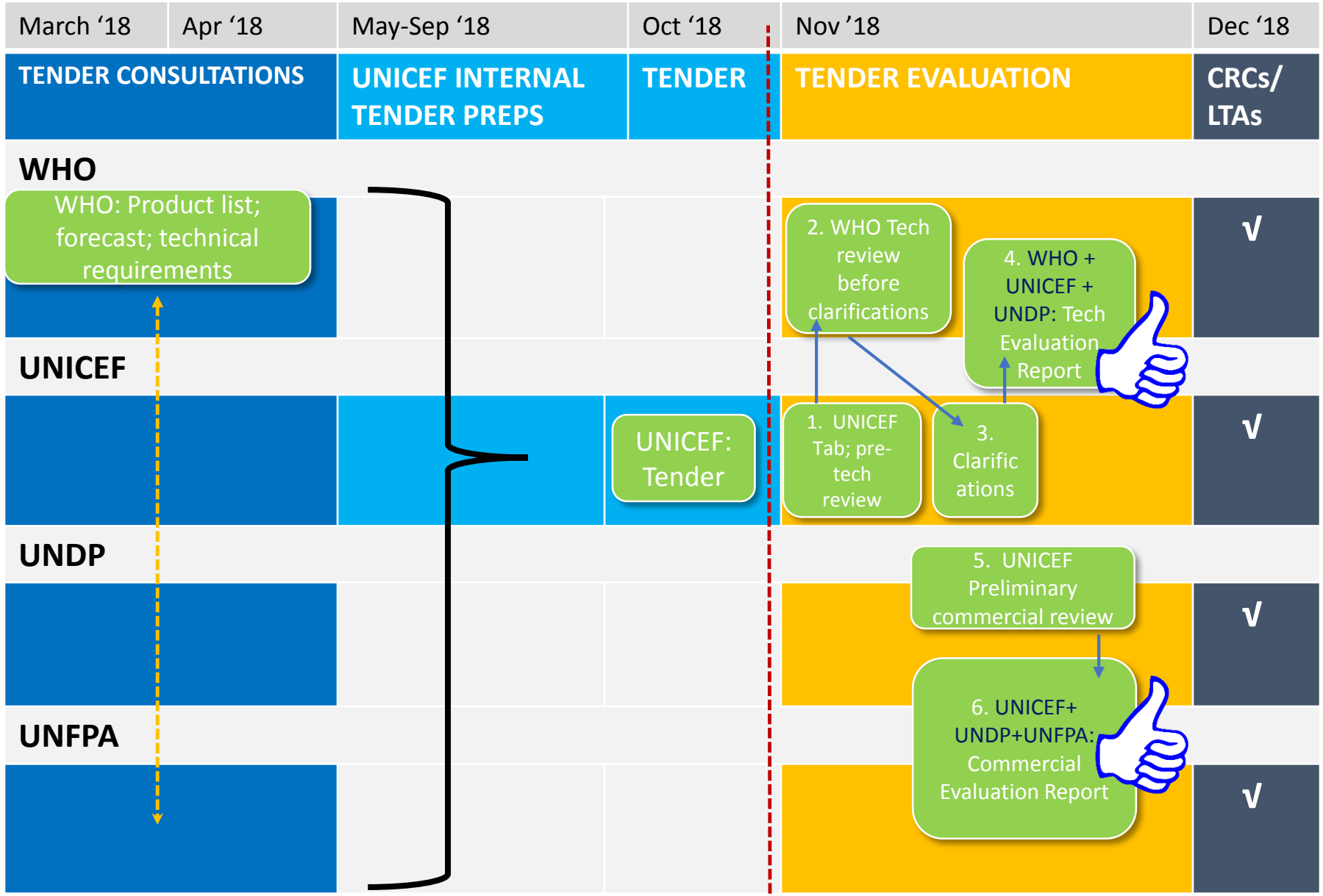
1. Participating UN agencies will be reviewing updated WHO List of Prequalified IVDs on a regular basis (next review is Q1 2019)



2. A mini-tender is to be issued for the newly added products as well as for the products nearing WHO PQ (WHO judgement and recommendation)

The tender will result in multiple time-bound, 36 + 24 months, LTAs with all suppliers that meet technical, QA and commercial requirements, have sufficient production capacity and sound financial status proving long term security

3.3 UNICEF Procurement Approach: UN Joint Tender 2018 Timeline



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for every child

Thank You

Rapid Diagnostic Tests Supplier & Partner Consultative Meeting

Global Fund RDT Strategy

11 December 2018
Seattle, Washington – USA
The Sourcing Team

The Global Fund

Disclaimer

The Global Fund Procurement Strategy on RDTs is currently under development and will be finalized in the forthcoming months.

This document presents the Global Fund's current intention which is subject to change.

The data and information herein are provided for illustrative purposes and derived from a limited and preliminary analysis of the Global Fund.

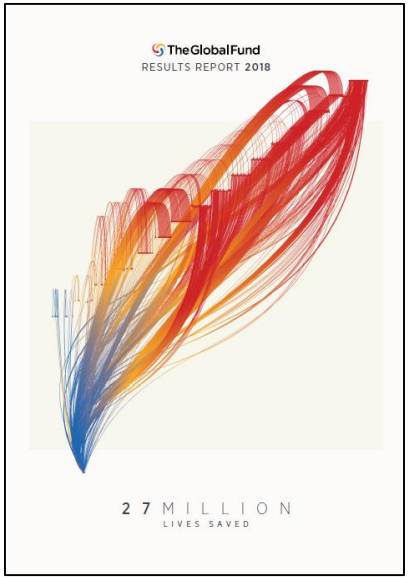
The present document shall not be considered as the Global Fund's representation or commitment of any kind.

Agenda

- Global Fund: Introduction, Market Shaping Strategy and Strategic Sourcing
- PPM RDT Spend Analysis
- Global Fund Quality Assurance Policy
- Global Fund RDTs Procurement Strategy: 2019 – 2021

The Global Fund

A 21st-century partnership organization to accelerate the end of HIV, tuberculosis and malaria as epidemics



Founded in 2002, the Global Fund is the **leading contributor of resources in the fight against AIDS, tuberculosis and malaria.** It **mobilizes and invests nearly US$4 billion a year** to support countries and communities most in need. It has an active portfolio of **over 430 active grants in over 100 countries**, implemented by local experts.

The Global Fund spends **close to US$2 billion per year** on **medicines, diagnostics and prevention tools** like insecticide-treated nets. Making efficient use of these financial resources to ensure that critical health commodities reach those in need is core to the Global Fund's mission.

The Global Fund Results Report 2018: https://www.theglobalfund.org/en/impact/

The USD 4 billion per year spent by the Global Fund is critical in the fight

HIV/AIDS

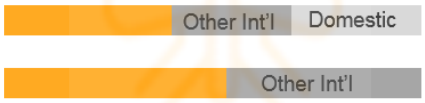
Global Fund accounts for **8%** of global HIV funding and **20%** of international financing

Tuberculosis

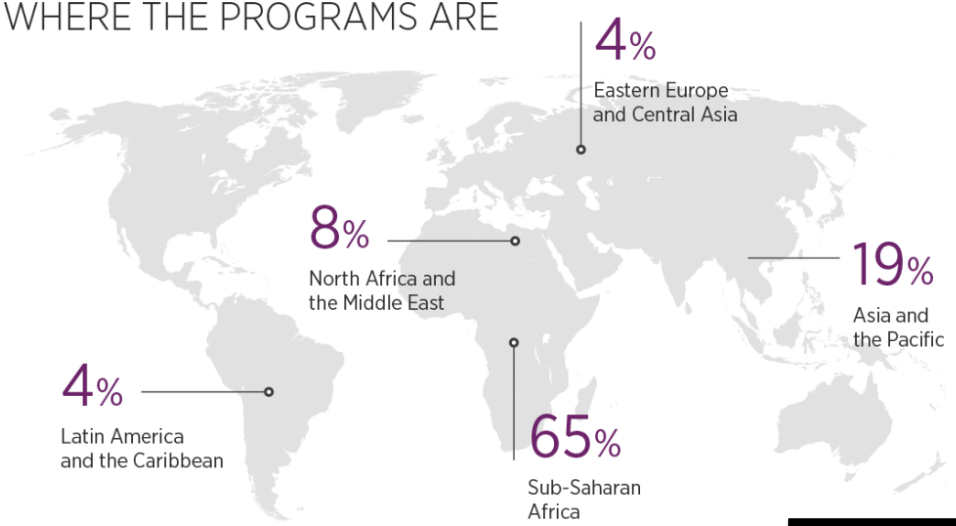
Global Fund accounts for **10%** of global TB funding and **69%** of international financing

Malaria

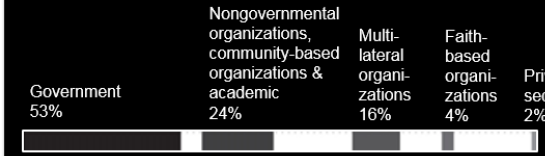
Global Fund accounts for **40%** of global Malaria funding and **57%** of international financing



WHERE THE PROGRAMS ARE

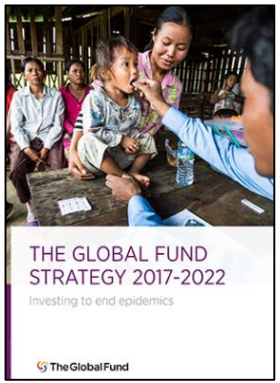


Breakdown of Global Fund Portfolio by Type of Implementer (Active Grants)

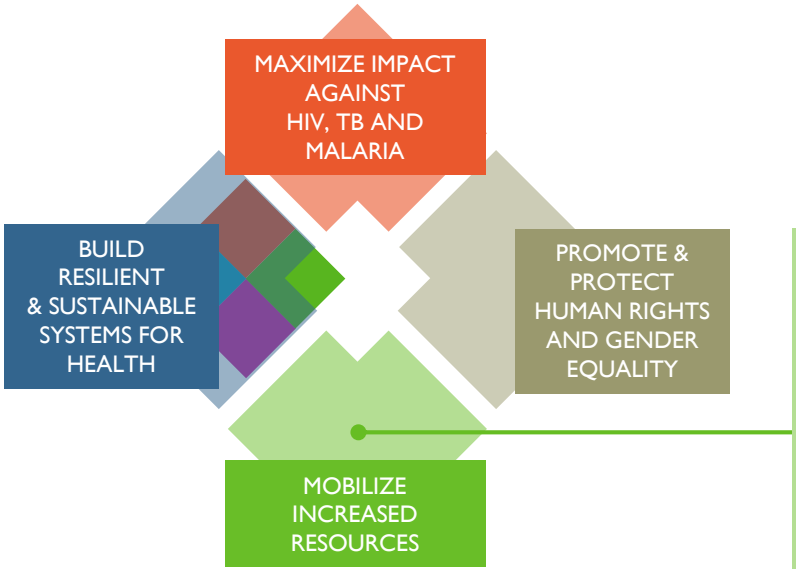


Funding sources [2016 data for HIV/Malaria, 2018 for TB]: OECD DAC-CRS; UNAIDS FactSheet World AIDS Day 2017, UNAIDS; Global Tuberculosis Report 2018, WHO; World Malaria Report 2017, WHO *GF share of international funding:* Global Fund 2017 Results Report. Figures are global and are not solely for countries where Global Fund resources are disbursed.

The Global Fund's Market Shaping Strategy is core to the Global Fund's 2017-2022 strategy: *Investing to End Epidemics*



Global Fund Strategy 2017-2022



STRATEGIC ENABLERS: Innovate and differentiate along the development continuum + Support mutually accountable partnerships

- c Implement and partner on market shaping efforts that increase access to affordable, quality-assured key medicines and technologies
- d Support efforts to stimulate innovation and facilitate the rapid introduction and scale-up of cost-effective health technologies and implementation models

Global Fund Strategy 2017-2020: https://www.theglobalfund.org/en/strategy/ ***Market Shaping Strategy:*** https://www.theglobalfund.org/en/sourcing-management/market-shaping-strategy/

The Global Fund has proactively shaped markets to improve health outcomes since 2004

2004 — With WHO, recipients transitioned to ACTs from suboptimal therapies

2007 — Board approves first Market Shaping Strategy, including Price & Quality Reporting and Voluntary Pooled Procurement

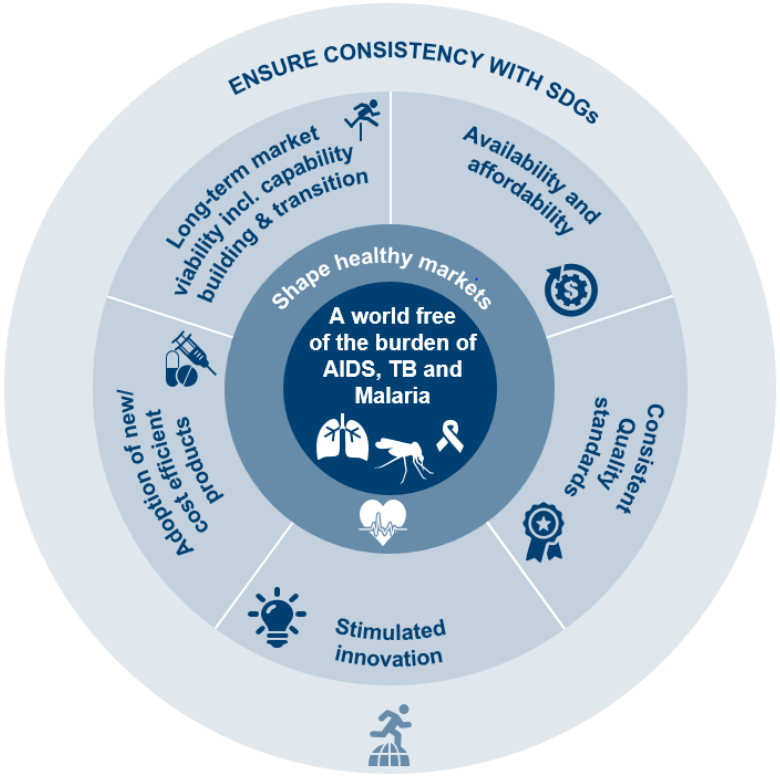
2011 — Market Shaping Strategy is approved by Board, with focus on pooling procurement, value for money, capacity building and ARVs

2013 — Operational initiatives through Procurement for Impact strengthen market shaping tools

2015

Changing market dynamics, context, and new Global Fund strategy prompted revision of Market Shaping Strategy

The Global Fund's Market Shaping Strategy extends beyond its direct spend to help ensure healthy markets and value for money



Mission of the Global Fund's Market Shaping Strategy:
Leverage its position to facilitate healthier global markets for health products – today and in the future

Healthy markets have 6 characteristics

Dimensions	Definitions
Innovation	There is a **robust pipeline of new products** intended to improve efficacy, reduce cost, or better meet the needs of end users, providers or the supply chain
Availability	**Adequate and sustainable supply exists to meet global needs** with new products being rapidly introduced and available.
Demand and adoption	Countries, programs, providers and end-users rapidly introduce and adopt the **most cost-effective products.**
Quality	Medicines and technologies are available at an **internationally-recognized standard of quality**
Affordability	**Medicines and technologies are offered at the lowest possible price that is sustainable** for suppliers and does not impose an unreasonable financial burden on buyers or other payers
Delivery	Supply chain systems (including quantification, procurement, storage, and distribution) **function effectively to ensure that products reach end users in a reliable** and timely way

https://www.theglobalfund.org/en/sourcing-management/market-shaping-strategy/

Source: Market Shaping Strategy, Annex 1 to GF/B4/17- Revision 1

Responsible procurement features in the Global Fund's market shaping work

Dimensions	Description
Economy	▪ Provide additional economic benefits to in-country community ▪ Empower community by sharing knowledge
Ecology	▪ Mitigate effect on environment along the end-to-end supply chain ▪ Use knowledge and skills to contribute to a constant rise in eco-efficiency
Society	▪ Promote fundamental human rights, e.g., – Advocate for decent labor conditions – Promote children rights ▪ Promote workers' health and safety
Business practices	▪ Promote best business practices among suppliers and other buyers

Principles for building holistic standards

- Build on existing guidelines
- Provide practical guidance
- Include phased approach
- Focus on procurement
- Align with GF objectives

See https://www.theglobalfund.org/en/sourcing-management/market-shaping-strategy/

The Global Fund uses a set of tools to shape markets

Price & Quality Reporting

- Public database with transaction-level data on Global Fund-financed procurements of core health products, after delivery

Quality Assurance policies

- Policies to assure quality of pharmaceutical and diagnostic products financed by the Global Fund

Pooled Procurement Mechanism / wambo.org

- Mechanism to pool procurement of health products. Can be leveraged toward market shaping objectives, reduces grant implementation risks

Revolving fund

- Small revolving fund that provides working capital to scale up new products

PSM policies

- Legal obligations and best practices that recipients should apply in procuring Global Fund-financed products

Guidance from Health Product Managers

- Country Team members responsible for PSM topics throughout grant-making and implementation

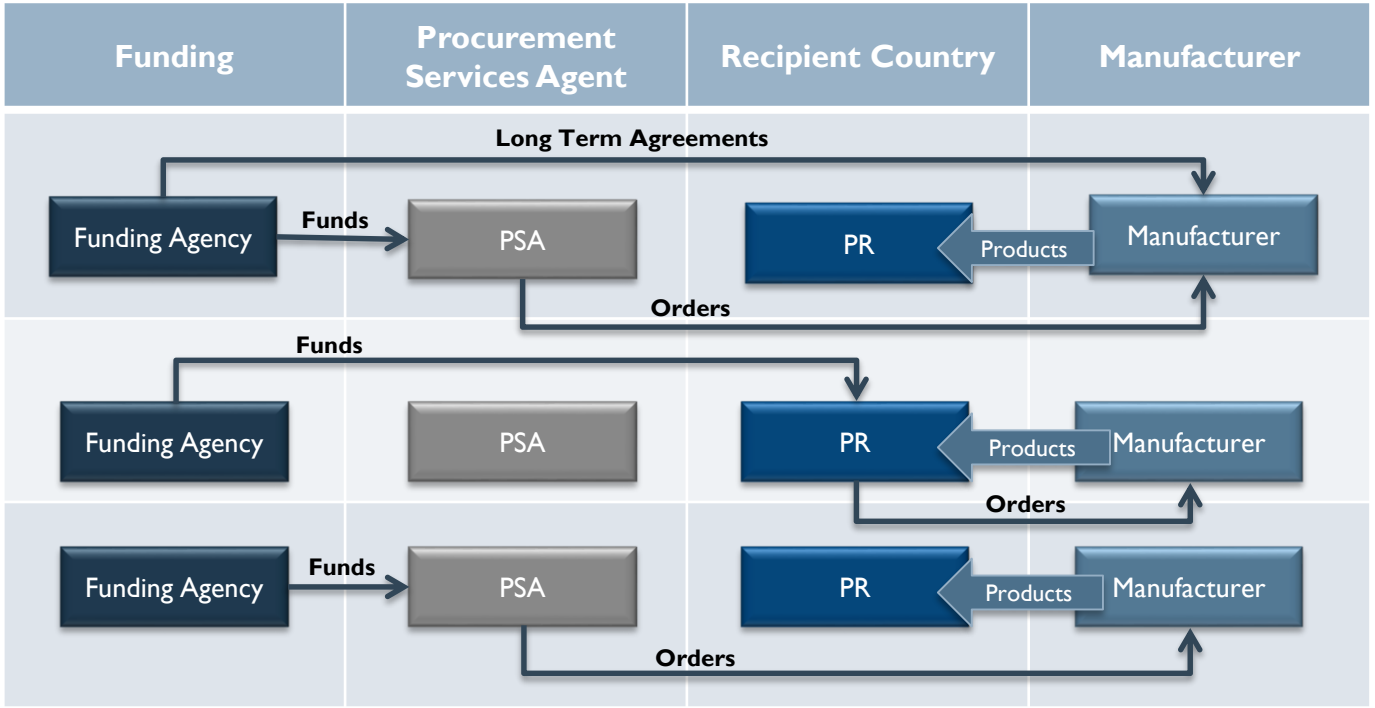
The Pooled Procurement Mechanism is the largest of the Global Fund's procurement channels, representing just over half of the Global Fund health product spend, depending on the category

~55% of Global Fund health product spend

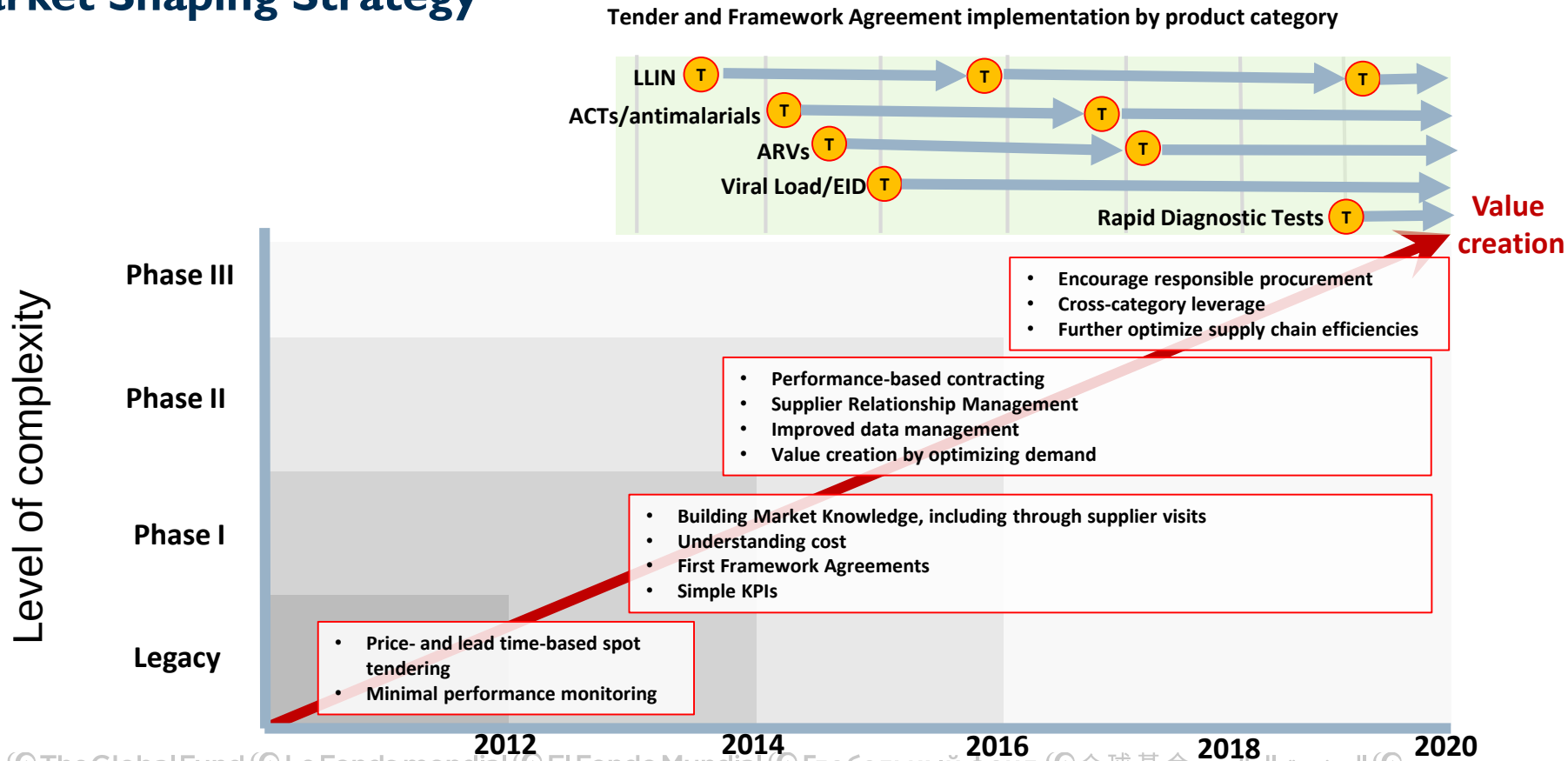
Pooled Procurement Mechanism (PPM)

National Procurement Mechanisms

Other Procurement Agents; Global Drug Facility (TB)



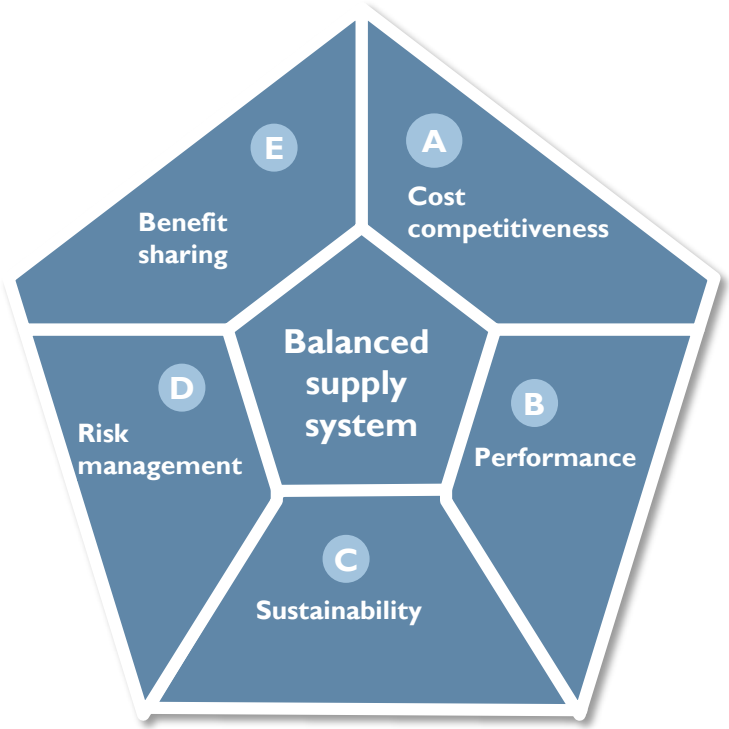
Implementation of PPM has evolved over time to better deliver on the Market Shaping Strategy



The Global Fund's Sourcing Team manages health products through PPM along 5 key dimensions

Pooled Demand	Registering Principal Recipients into the mechanism creates the **opportunity to pool volumes of large and small volume countries**
Product Category Strategies	**Design**, **issue** and **manage sourcing strategy, including competitive tenders,** to support category-specific market shaping objectives
Supplier Relationship Management	Manage the implementation of long term agreements **including the allocation and performance management of suppliers**
Demand Management	Optimize resources to manage Principal Recipient demand along three dimensions: **volume, time and specification**
Transaction Management	Execute PPM orders from requests to deliveries **via wambo.org**, a **Principal Recipient-facing portal** that increases visibility of ordering operations with full visibility and a transparent and auditable process

Global Fund's balanced supply system embedded in its strategic sourcing work is based on 5 elements



A

- Providing quality assured products **at the lowest possible affordable and sustainable price** to reach the maximum number of patients
- **Reducing price volatility** and eliminating predatory pricing
- Operationalizing **value creation levers**

B

- Supplying product **timely and in full**
- Incentivizing the **introduction of new regimen and better formulations**

C

- **Supporting existing and new suppliers** to ensure **sufficient supply of all the needed products and mitigate geographic supply risks**
- Investing in suppliers with **responsible and sustainable practices**

D

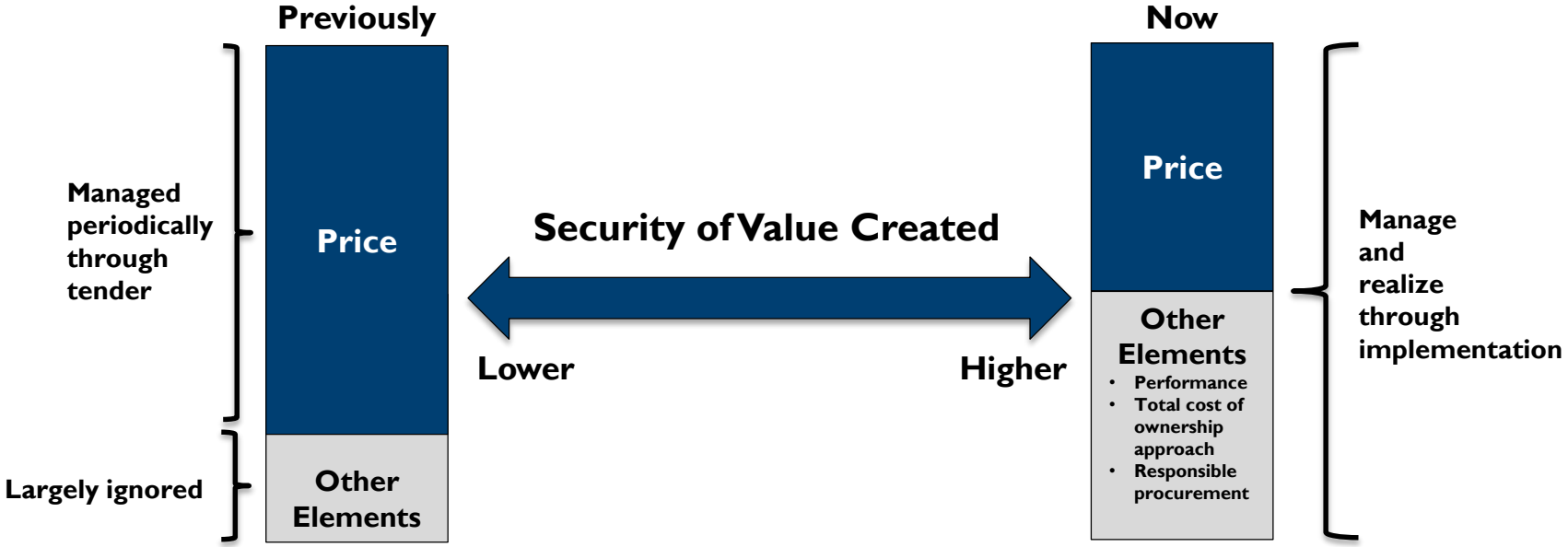
- Maintaining **well-diversified supplier base**
- Meeting the **Global Fund and national quality** requirements
- Mitigating **implementation risks** including quality & supply security risks

E

- Publishing **reference prices**
- **Building capabilities** and implementing rapid supply mechanisms
- **Providing access** to PPM contract terms for other buyers
- Further incentivizing **broad national registration footprint**
- Leveraging volumes to **improve access to other products**

Moving from spot tenders to long term agreements with supplier relationship management permits PPM to deliver better value

- Previous approaches focused on the price value lever
- Value creation has been extended and can be further extended across a range of levers
- The importance of this will increase in importance as cost is optimized



Agenda

- Global Fund: Introduction, Market Shaping Strategy and Strategic Sourcing
- PPM RDT Spend Analysis
- Global Fund Quality Assurance Policy
- Global Fund RDTs Procurement Strategy: 2019 – 2021

Highlights: PPM Observations on RDTs

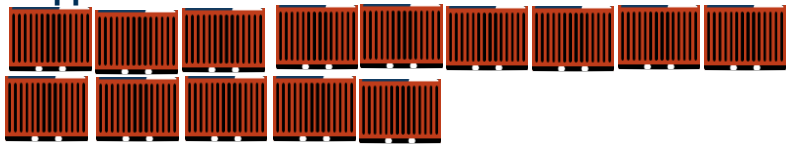
- National policy, guidelines and procedures guide product selection
- Global Fund Quality Assurance Policy determines product eligibility
  - ❑ HIV and other diagnostics based on WHO PQ, CE Mark, GHTF as defined in GF QA Policy
  - ❑ Malaria RDTs based on WHO PQ
- Industry maturity varies across production processes – production cost efficiencies can be achieved
- Lengthy timeline from R&D to market deployment
- Market volatility due to lack of demand visibility for suppliers
- Supply risk/security: market dominated by few suppliers
- Large price variability across spot tenders
- HIV RDT pricing remains unchanged – does not respond to volumes procured
- Product interchangeability is a challenge due to limited re-validation of national guidelines, leading to requests for "single source" procurement resulting in limited competition
- Product shelf life varies across suppliers and product packaging is not standardized (further information, next slide)

Source: Team analysis of PPM spend

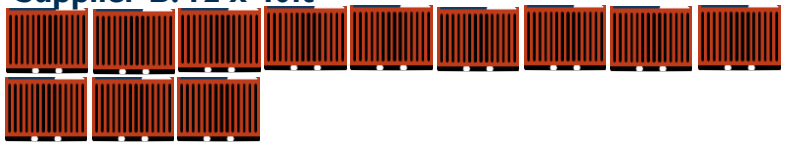
Further market observations – Product packaging and Product shelf life

Product packaging and implications

Supplier A: 14 x 40ft



Supplier B: 12 x 40ft



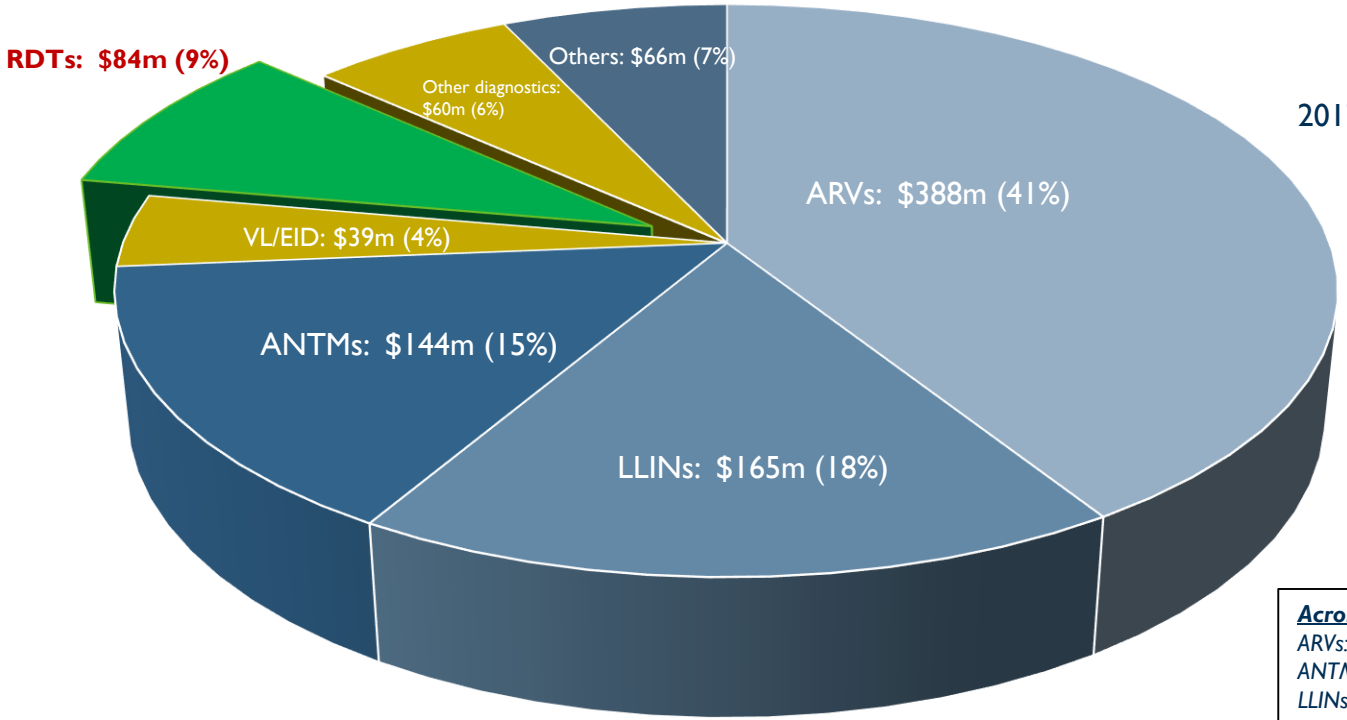
Supplier C: 7 x 40ft

Product shelf life and constraints

- For test kits with accessories, product shelf life is based on the shortest dated item in the kit – resulting in significantly shorter expiry dates different from shelf life published in the List of HIV Diagnostics.
- Due to short-shelf life at time of pick up, products are shipped by air.
- Ocean freight is the preferred mode of transit to unlock freight efficiency and reduce environmental footprint (less carbon emissions) compared to air freight.

***For illustrative purposes only. This does not represent a preference or endorsement of any sort by The Global Fund of a particular supplier product.**

RDTs represent 9% of total PPM spend and ~50% of PPM diagnostics spend



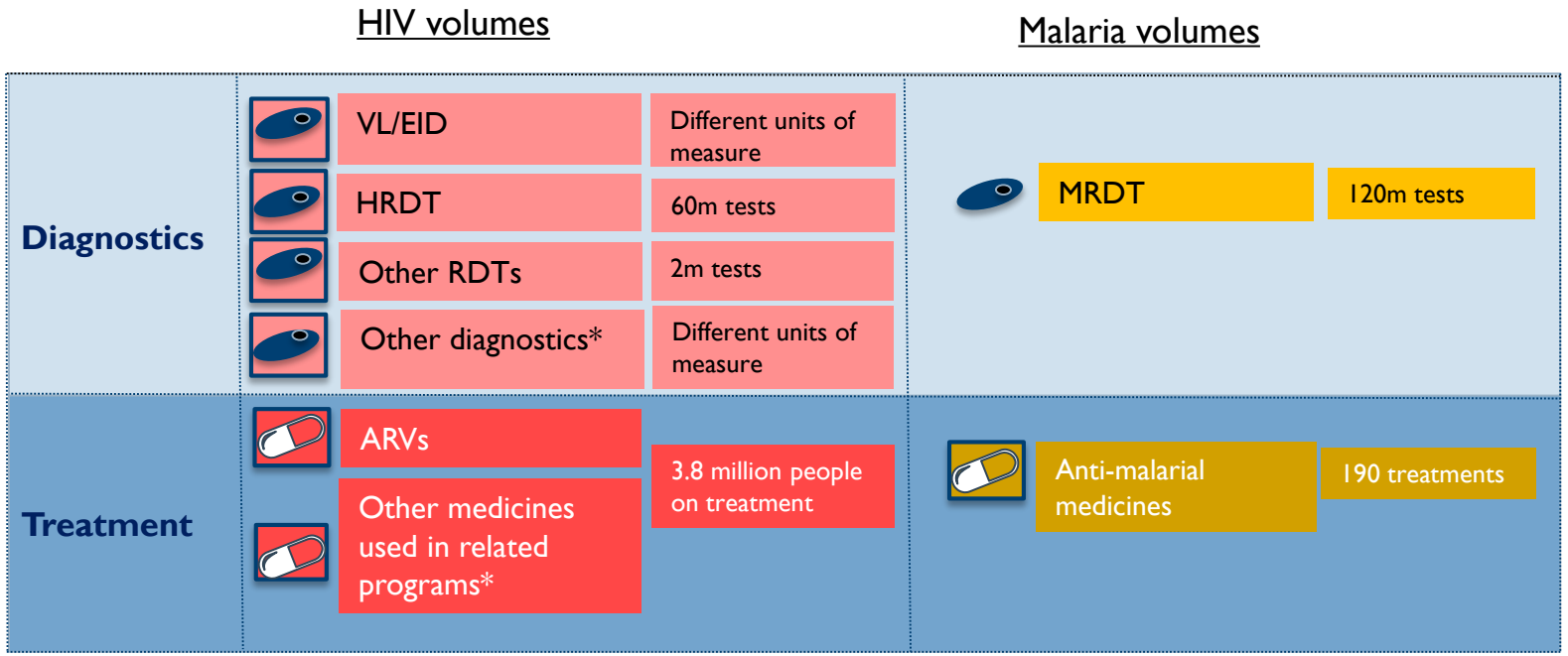
2017 Total PPM spend: $946m

Acronyms:

ARVs:	*Antiretroviral drugs*
ANTMs:	*Antimalarial medicines*
LLINs:	*Long-Lasting Insecticide treated nets*
RDTs:	*Rapid Diagnostic Tests*
VL/EID:	*Viral Load/Early infant diagnosis*
Other:	*General lab equipment & supplies*

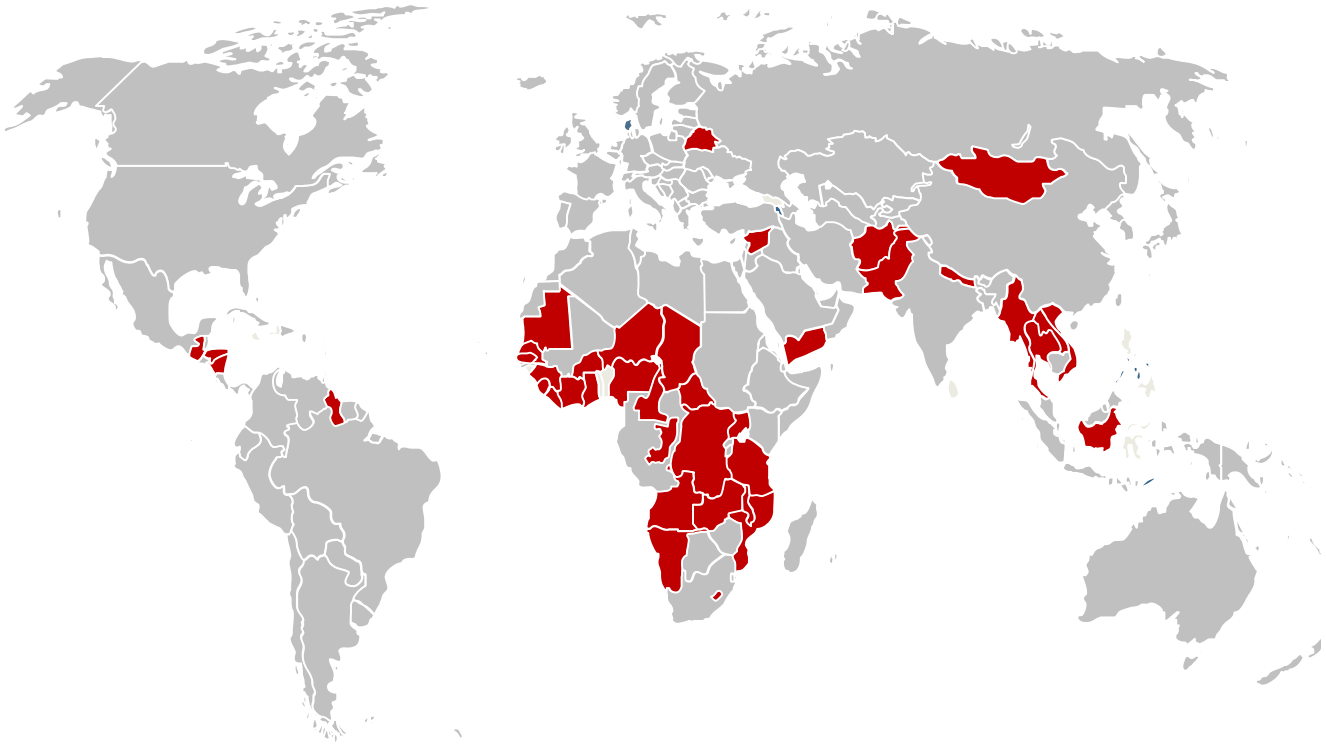
*RDTs include HRDTs, MRDTs and others
**Data source: PSA data, includes product cost, freight, logistics and other costs

Volumes for diagnosis and treatment for HIV and Malaria



Source: Team analysis of PPM spend
*2017 PPM data: spend includes insurance, freight and other costs
*includes both HIV and TB related products

PPM RDT demand is spread across 59 countries in 2016-2018

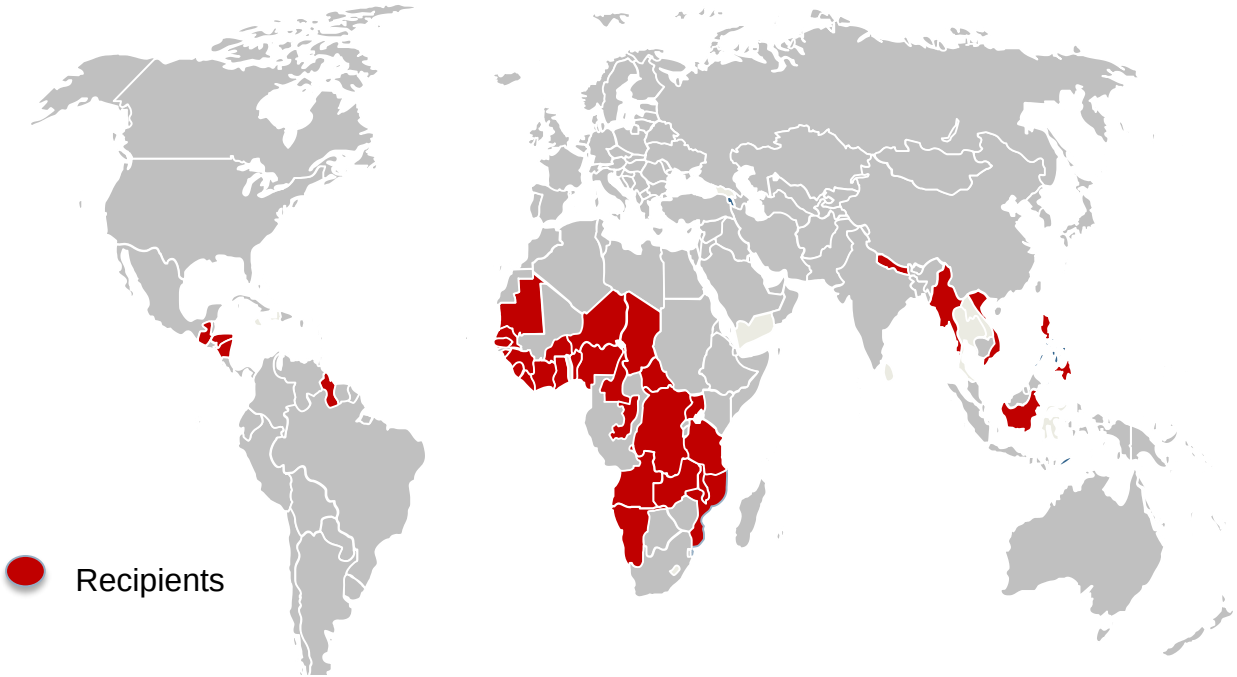


Recipients

Afghanistan, Armenia, Belarus, Benin, Burkina Faso, Burundi, Cote d'Ivoire, Cameroon, Cape Verde, Central African Republic, Chad, Comoros. Congo, Congo DRC, Fiji, Gambia, Georgia, Ghana, Guatemala, Guinea, Guyana, Haiti, Honduras, India, Indonesia, Jamaica, Laos, Lesotho, Liberia, Malawi, Mauritania, Mongolia, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Niger, Nigeria, Pakistan. Philippines, Senegal, Sierra Leone, Sri Lanka, Syrian Arab Republic, Tanzania, Thailand, Timor-Leste, Togo, Uganda, Vietnam, Yemen, Zambia, Zimbabwe

Source: Team analysis of PPM spend

MRDT country demand – 39 countries, with top 15 countries accounting for ~90% of demand



Top 15 countries
Uganda
Tanzania
Mozambique
Ghana
Congo DRC
Malawi
Burkina Faso
Cote d'Ivoire
Nigeria
Niger
Burundi
Angola
Sierra Leone
Guinea
Pakistan

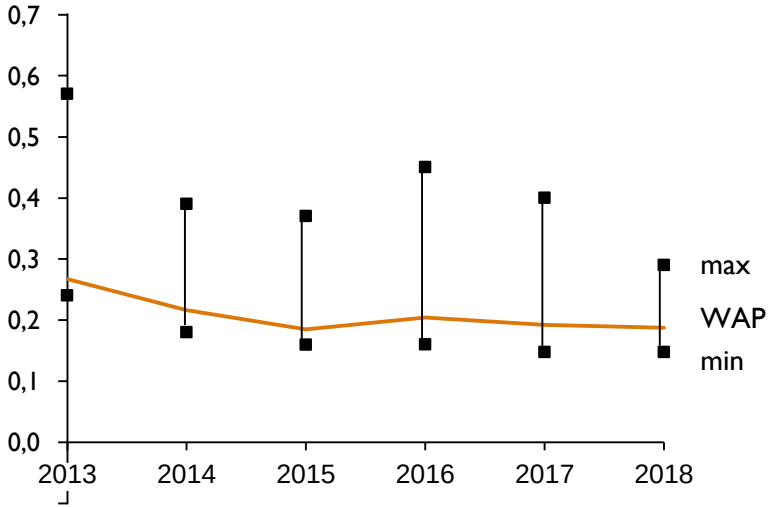
Angola, Bangladesh, Bhutan, Burkina Faso, Burundi, Cote d'Ivoire, Cameroon, Cape Verde, Central African Republic, Comoros, Congo DRC, the Gambia, Ghana, Guatemala, Guinea, Guyana, Honduras, Indonesia, Laos, Malawi, Mauritania, Mozambique, Myanmar, Nepal, Niger, Nigeria, Pakistan, Papua New Guinea, Sierra Leone, Solomon Islands, Sri Lanka, Tanzania, Timor-Leste, Togo, Uganda, Vietnam, Yemen, Zambia, Zimbabwe

Source: Team analysis of PPM spend

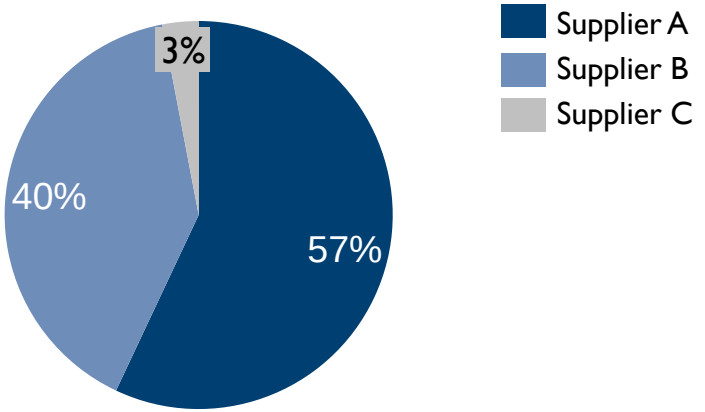
In malaria RDT market, prices vary across countries with notably higher pricing for "single source" procurement

- There are 4 Malaria RDT WHO-prequalified suppliers
- Market is dominated by 2 suppliers
- Higher pricing for "single source" vs. "competitive" procurement for the same product supplied to different countries

P.f. test: price per test, USD



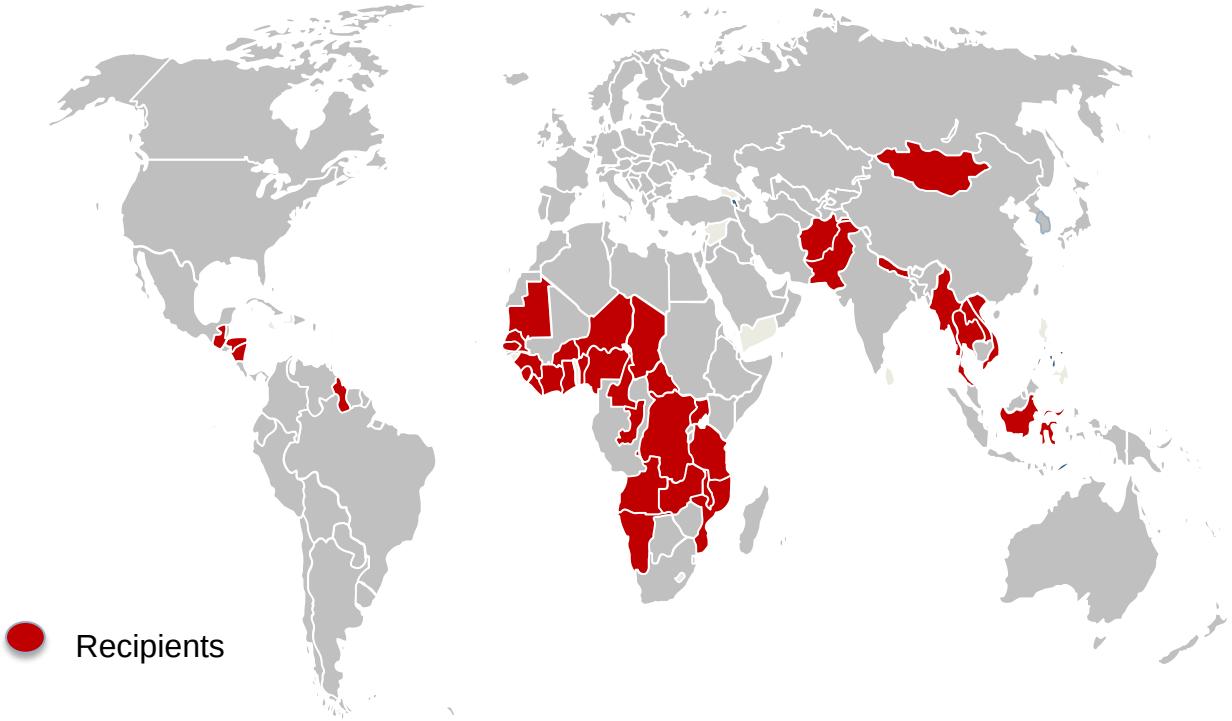
% tests per supplier (2015-2018YTD)



Source: Team analysis of PPM spend

WAP: weighted average price YTD: year to date

HRDT country demand – 53 countries, top 15 countries accounting for ~90% of demand.



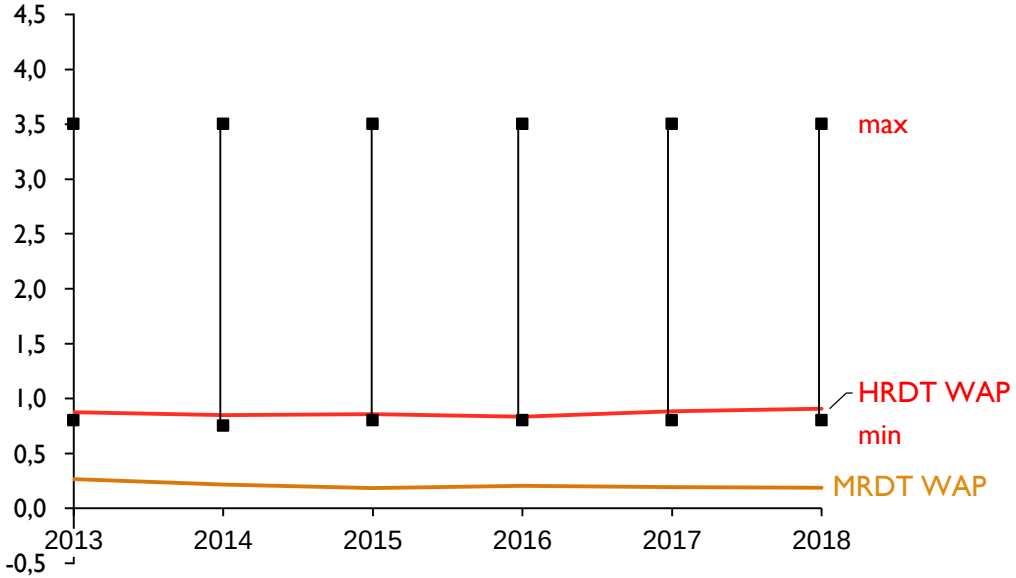
Top 15 countries
Uganda
Malawi
Tanzania
Mozambique
Nigeria
Zambia
Congo DRC
Cameroon
Ghana
Ethiopia
Cote d'Ivoire
Burkina Faso
Burundi
Nepal
Niger

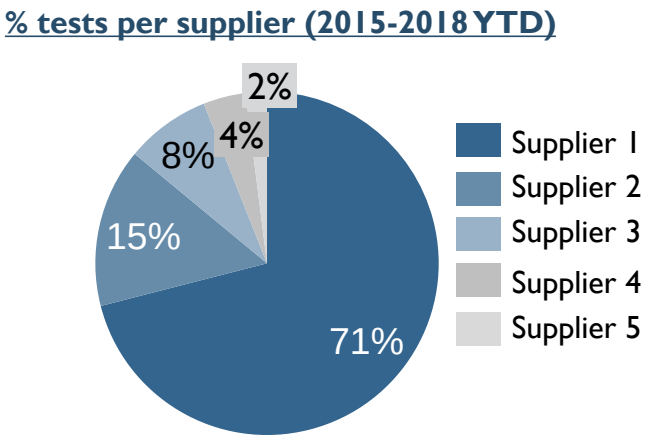
Afghanistan, Armenia, Belarus, Benin, Burkina Faso, Burundi, Cote d'Ivoire, Cameroon, Cape Verde, Central African Republic, Chad, Comoros. Congo, Congo DRC, Dominican Republic, El Salvador, Ethiopia, the Gambia, Ghana, Guatemala, Guinea, Guyana, Haiti, Honduras, Jordan, Laos, Lebanon, Lesotho, Liberia, Madagascar, Malawi, Mauritania, Mongolia, Mozambique, Myanmar, Nepal, Nicaragua, Niger, Nigeria, Pakistan. Philippines, Senegal, Sierra Leone, Sri Lanka, Tanzania, Thailand, Timor-Leste, Togo, Uganda, Vietnam, Yemen, Zambia, Zimbabwe

Source: Team analysis of PPM spend

HRDT pricing has remained static for several years

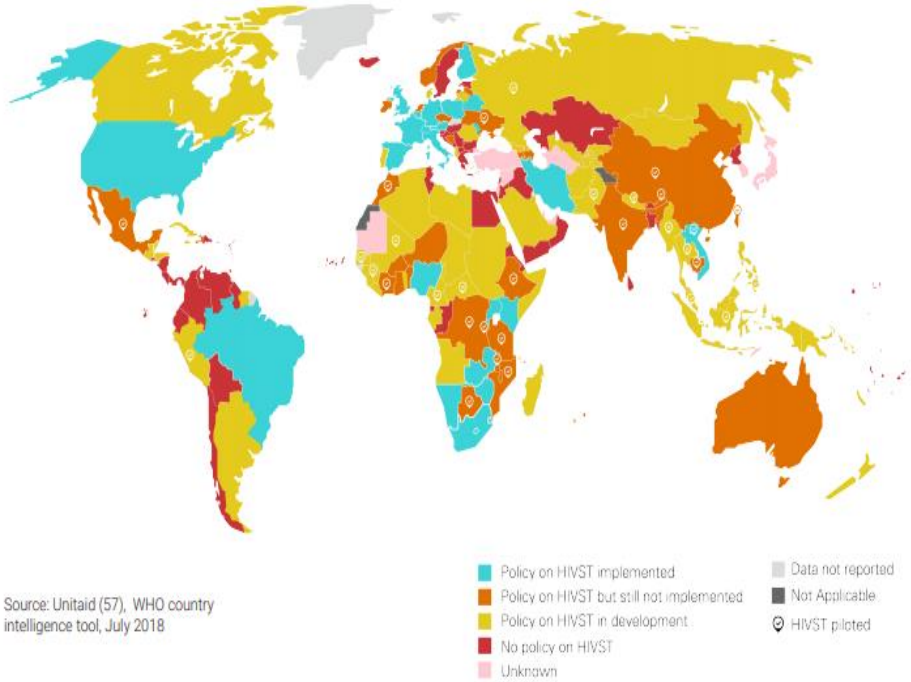
- The lowest HRDT price is 4 times as high as weighted average MRDT price despite similar production technologies.
- Large price gap between lowest and highest price depending on the brand.
- Some suppliers offer their products at different prices in various countries/regions due to special labelling requirements, in-country regulations, and cost experiences.





Source: Team analysis of PPM spend

HIV Self Testing Market (HIVST)



- **Countries:** 59 countries have supportive HIVST policies in place, 28 actively implementing, 53 under development (UNITAID, 2018).
- **Manufacturers:** 5 Global Fund QA approved sources
- **GF HIVST:** Included in grant cycle
- **HIVST Procurement:**
  - **2018:** 223k tests
  - **2019:** 300k tests
  - **PPM procurement so far:** Zambia, Malawi, Cote D'Ivoire, Zanzibar

Source: UNITAID Knowing Your Status – Then and Now; Realizing the potential of HIV Self-Testing *Fig. 12 National Policies on HIVST, July 2018 (pg. 26)*

Other diagnostics – Why a multi-disease diagnostics approach?

- Program intervention includes HIV and other diagnostics (HBV, HCV, HPV, Syphilis, VL/EID, HIV-Syphilis Combo, TB-LAM)
- Manufacturers have broad product portfolio across multiple diseases
- Opportunity to support other efforts to increase lab optimization for multi-disease testing platforms
- Key contributor to diagnosis and treatment in fighting the epidemics (WHO published guidance in 2017 highlighting considerations for use of multi-disease testing devices in integrated laboratory networks)
- Market driven by technological advances (e.g. POC a benefit in limited resource areas)

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The Global Fund updated its Quality Assurance Policy for Diagnostic Products in 2017

Products in the scope of the policy (not exhaustive)

Rapid Diagnostic Tests for malaria, HIV, TB, Hepatitis B, Hepatitis C, Syphilis, Equipment/consumables, IVD reagents, calibrators, Software, Receptacles, Microscopes & Imaging equipment

Intended use

To provide information on concerning a physiological or pathological state concerning a congenital (inherited) abnormality to determine the safety and compatibility with potential recipients to monitor therapeutic process ***Note: NOT for transfusion purposes***

I. Clinical Criteria *(Section 6)*

- Compliance with National guidelines
- Consistent with WHO Guidance

Funding request must give evidence and technical justification if needed.

III. Monitoring Quality by Global Fund Principal Recipients

- Post-Market Surveillance following WHO Guidance
- Reporting defects to Global Fund

IIa. General Quality Criteria for ALL Diagnostics Products *(Section 7)*

Manufacturing site for all products:

- Compliant with ISO 13485* for IVD and Imaging Equipment
- Compliant with ISO 9001* (all others)

** or equivalent*

IIb. Additional SPECIAL Quality Criteria for a selection of IVDs *(Section 8)*

- Prequalified by WHO PQ
- Recommended by WHO TB programme
- Authorized through stringent regulatory assessment (in high risk classification) by authorities being founding member of GHTF**
- Assessed by GF Expert Review Panel

*** not for HIV ST*

Global Fund Quality Assurance Policy: https://www.theglobalfund.org/en/sourcing-management/quality-assurance/

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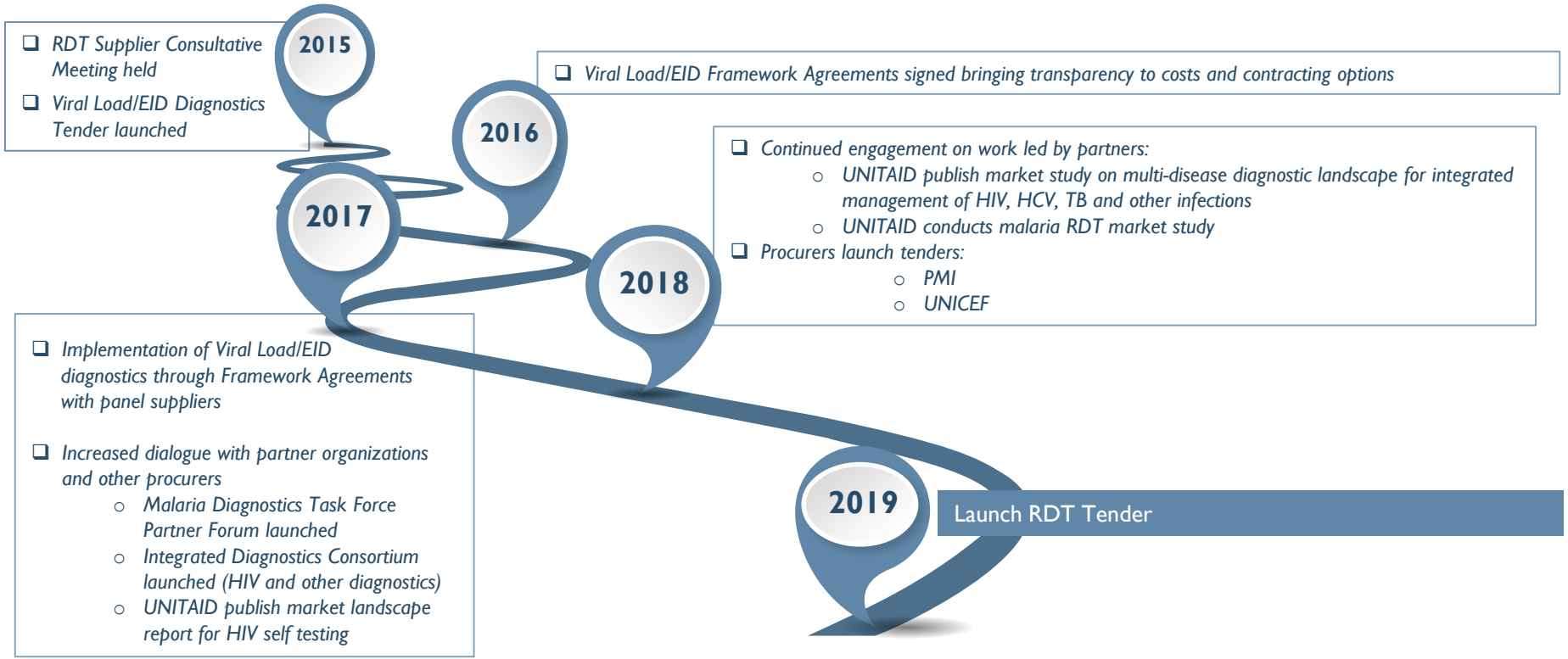
Consultation with suppliers and partners provide feedback to inform GF RDT Strategy Development



The product scope of the Global Fund RDT strategy (2019 -2021)

- Product scope
  - HIV RDTs (Screening, Confirmatory, Tie-Breaker & Self Test)
  - Malaria RDTs (Pf, Pan, Pf/Pan, Pf/Pv, Pf and Pv/Pvom, Pf, Pf/Pv)
  - Other RDTs (HBV, HCV, CrAg, HPV, Syphilis, HIV-Syphilis Combo, TB LAM)

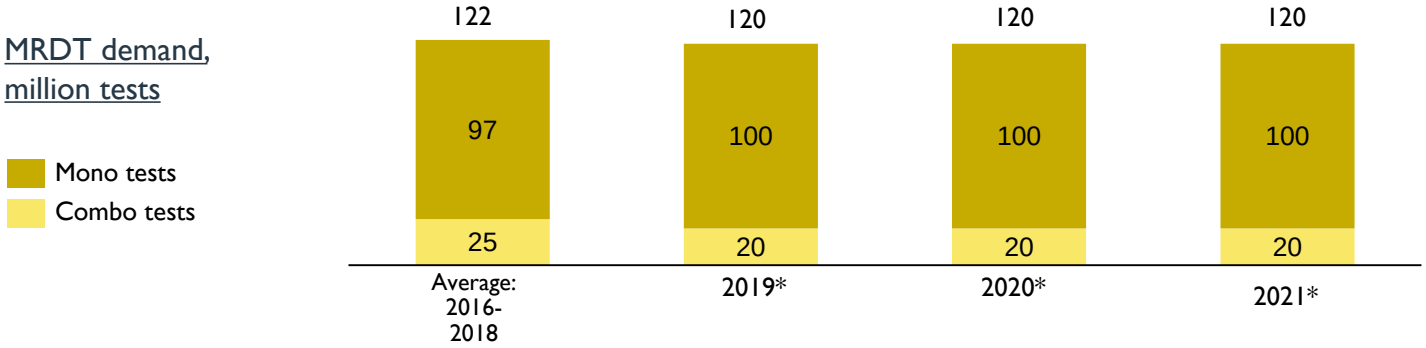
Note: Applicable machined based assays will be brought under Viral load Framework agreement in 2019.

Product scope of the Global Fund RDT Sourcing Strategy (2019 -2021)

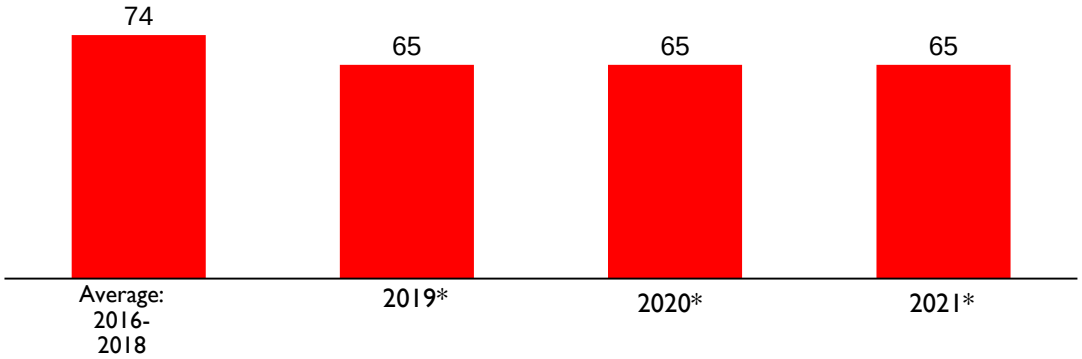
Rapid diagnostics tests			
Product set	**Tests specifications**	**Indicative volume split within product set**	**Indicative volume split across product sets**
1. HIV RDTs	▪ Screening ▪ Confirmatory ▪ Tie-breaker ▪ Self-tests	▪ 80% ▪ 13% ▪ 5% ▪ 2%	▪ 35%
2. Malaria RDTs	▪ Mono tests (p.f, pan) ▪ Combo tests (Pf/Pan, Pf/Pv)	▪ 80% ▪ 20%	▪ 64%
3. Other Diagnostic Tests	▪ Hepatitis B ▪ Hepatitis C ▪ HPV ▪ Syphilis ▪ CrAg ▪ TB LAM ▪ HIV-Syphilis Combo	Not available	▪ 2%

The Global Fund RDT procurement strategy: Indicative product volume 2019 -2021*

MRDT demand, million tests



HRDT demand, million tests



Other RDTs — Demand for other RDTs is estimated to be around 3 million tests per year

* projection

The Global Fund will offer two contractual arrangement options through the tender process for the 2019 to 2021 period*

Two options for eligible suppliers:

- **Framework Agreement**, which may include allocated volumes
- **Purchase Order Agreement**, which will not include allocated volumes

**There will be a process to consider new entrants and/or new products that become eligible for procurement after the tender submission deadline.*

Detailed objectives

(which will be reflected in the tender scope, objectives & evaluation)

Detailed Objectives	Sustainable supply	Competitive pricing & affordability	Availability & reliable delivery	Quality & regulatory
	▪ Continued supply of key diagnostics ▪ Promote responsible procurement, including good business practices, throughout the supply chain ▪ Support the introduction of new/improved products ▪ Stimulate new entrants	▪ Reduce price variability across countries ▪ Optimize product packaging design to reduce freight costs	▪ Reliable delivery performance ▪ More responsive supply ○ Shorter lead times ○ VMI to respond to stock out risks ▪ Bundling of tests (e.g. VL/EID with other virology tests (HBV, HCV, HPV,TB) to encourage lab optimization efforts for multi-disease testing platforms	▪ Mitigate risks ○ Product quality & safety ▪ Broad national registrations

The Global Fund phased approach to implement the RDT Procurement Strategy

Phase I
Establish an integrated framework for Supplier Relationship Management (2019-2021)

- Establish direct relationships with eligible supplier for all types of RDTs (e.g., Framework Agreements or Purchase Order Agreements)
- Obtain lowest sustainable price
- Encourage new entries to drive healthy competition
- Establish value-adding projects to promote continuous improvement and innovation
- Conduct regular performance management to drive value throughout the contract period

Phase II
Further leverage supplier and partner capabilities to improve cost-effectiveness (timeframe to be determined)

- Increase technical understanding and promote product interchangeability to inform best value product selection
- Promote best practices to optimize end-to-end supply chain efficiency
- Further drive value-adding projects to promote continuous improvement and innovation
- Facilitate a resilient supplier base
- Collaborative approach with suppliers and partners to enhance demand visibility and optimize production planning

Partnership work to advance the following:
- Develop policies to promote product interchangeability
- Technical support to increase in-country capacity to manage product interchangeability
- Improve demand visibility to unlock value throughout the supply chain

Principles of our approach

Tender Eligibility

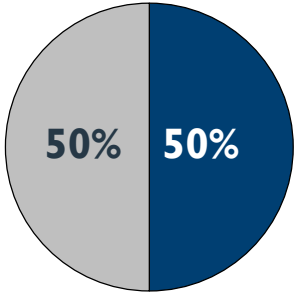
1. **Related firms*** may submit only **one** bid
2. **Global Fund Quality Assurance Policy**

Performance Principles

1. **Volume allocations** will be managed throughout implementation via a **performance-based approach**
2. **Supply security** will be a key focus area
3. **OTIF** and **Responsiveness** against promised lead times will be a factor in the performance-based approach
4. The Global Fund values **responsible procurement** and will factor this during implementation

*Related firms means affiliate, associate and subsidiary to a parent company

Both technical and commercial elements will be evaluated



2019 RDTs

Commercial factors

- ❑ Unit price
- ❑ Freight volume
- ❑ Volume discount

Technical factors

- ❑ Product coverage
- ❑ Country registration of products
- ❑ Product lead time/OTIF
- ❑ Product shelf life
- ❑ Continuous improvement and value creation projects to deliver on GF strategic objectives

Indicative approach and timeline for RDT tender

Step I: RFP issued and submissions received (March – April 2019)

Global Fund issues RFP

- RFP on Sourcing Platform, including both technical and commercial sections
- Two rounds of questions/answers prior to the tender submission deadline

Technical and commercial submissions due, including bidder presentations

Step II: Evaluation (April - June 2019)

1. Initial evaluation of bid submissions
2. Bidder presentations
3. Finalization of technical and commercial evaluation
4. Internal approvals
5. Award

Step III: Contract Negoatiation (Jun - July 2019)

- Contract finalization and signing

2019-2021 Contract Implementation

- Supplier performance measurement
- Risk assessment

Objectives for individual meetings between Global Fund and Suppliers on Wednesday, 12 December 2018

- ✓ Ensure the procurement strategy and approach is understood
- ✓ Listen to you on your views, advise any gaps and/or any concerns
- ✓ We are listening through 31 January 2019 on any further clarifications on the overall strategy

We look forward to working with you to implement this procurement strategy to ensure continued availability, affordability, and innovation of products in a sustainable market

For more information visit: https://www.theglobalfund.org/en/sourcing-management/health-products/