MATAHARI

# Critical pathway analysis of new TB diagnostic tools in Africa

## *Insights from 4 countries & continental regulatory stakeholders*

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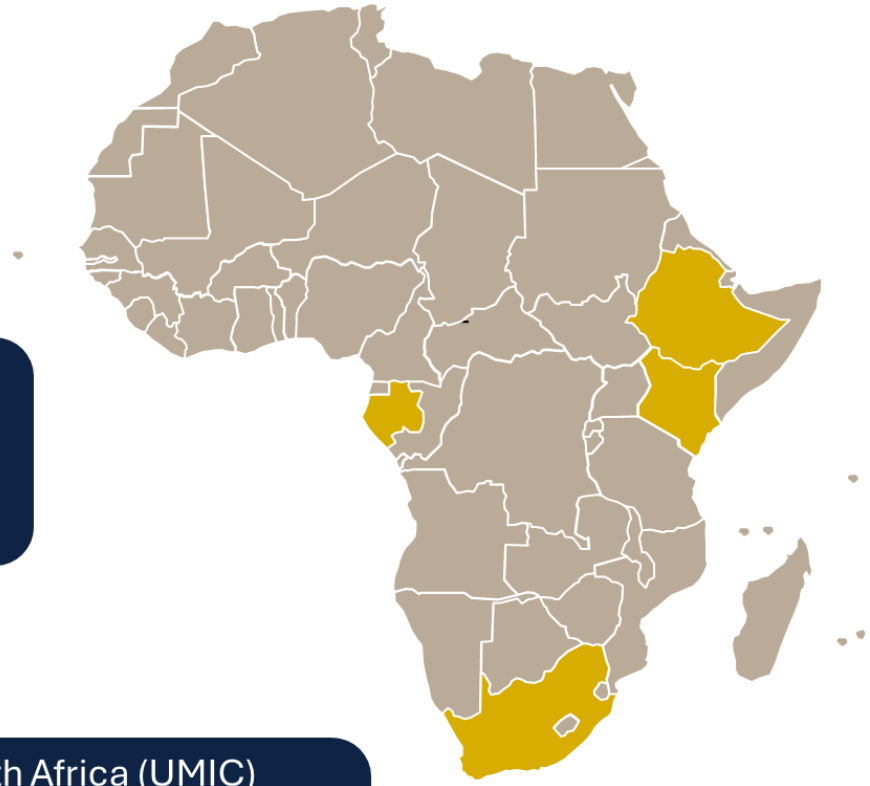
Photo credit: pexels.com

# New TB Dx Critical Path Analysis project



## Ethiopia (LIC)

Population: 129 M
TB incidence: 146 /100 000
**% mWRDs: 30 %**
TB funding (2023): 78 % international

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# New TB Dx Critical Path Analysis project

**Objective:**

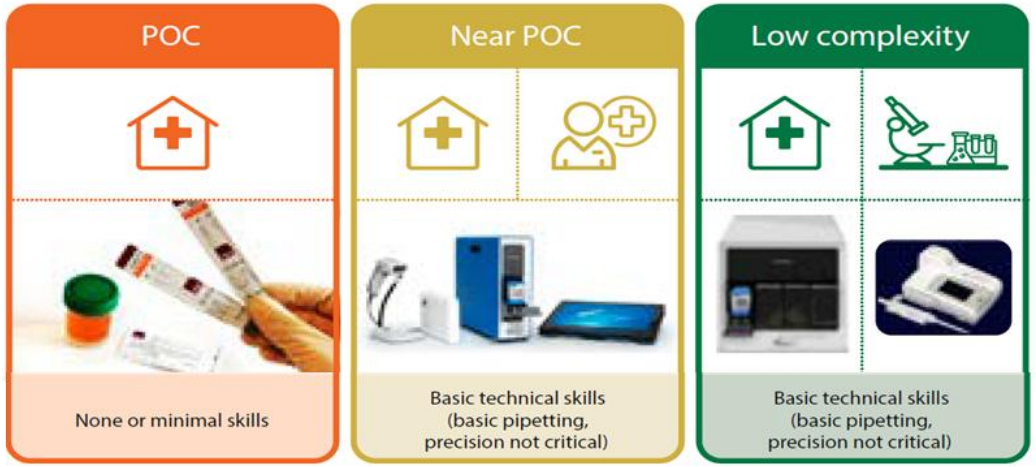
- to identify **relevant context** and **obstacles** to the introduction to the market of novel diagnostics for TB

**Anticipated results:**

- **Consolidated** and **usable information** and recommendations for manufacturers, technical agencies and donors to **accelerate the initial introduction and early uptake** of new TB diagnostics

**Products of interest:**

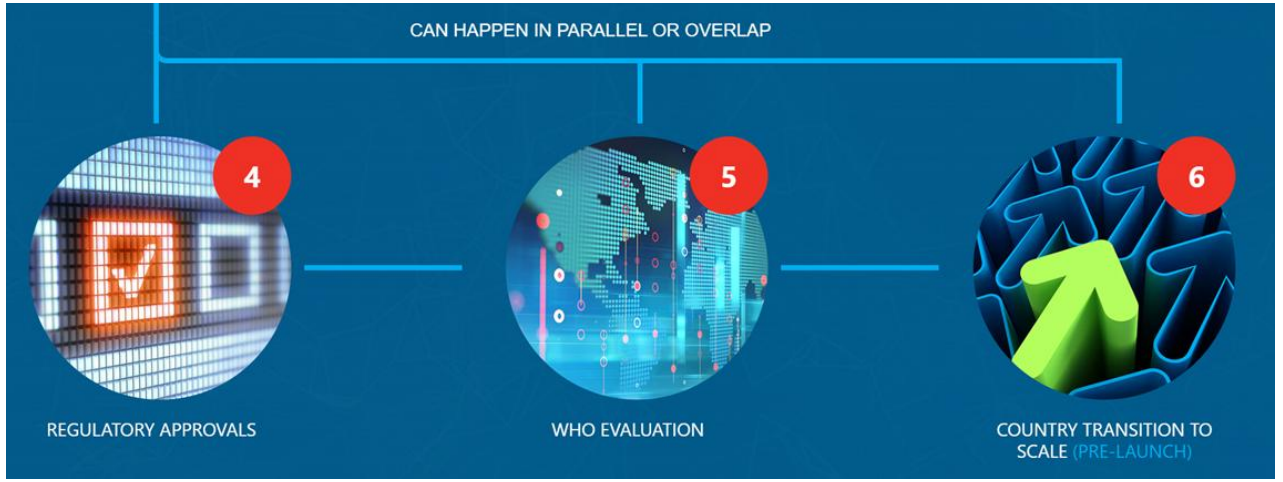
- Sputum/swab based near POC molecular tests
- Next generation high sensitvity lateral flow assay (irrespective of HIV status)
- Imported products



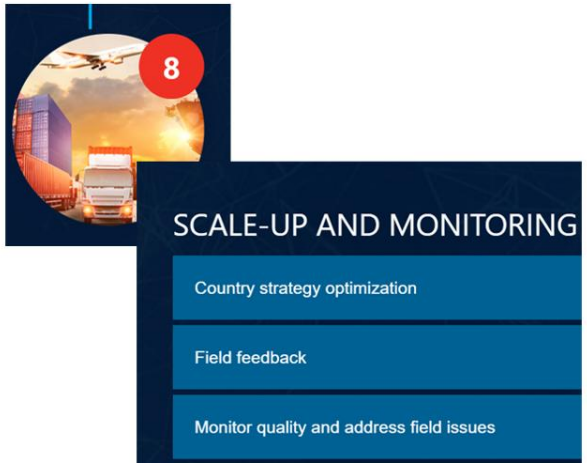
# Critical pathway analysis: approach

tbdxpathway.org
https://www.tbdxpathway.org

**Regulatory approval**
Global & country levels




**In country adoption & scale up**


# Critical pathway: analytical framework

## Structure

- 48 questions
- 9 thematic areas
  - *TB Diagnostic regulatory approval (Global/regional)*
  - *TB Diagnostic regulatory approval (in country)*
  - *Validation by NTP or MOH*
  - *Product Use Case*
  - *Demand Creation*
  - *Health System and Implementation Needs*
  - *Health Insurance and Pricing*
  - *Supply Chain and Procurement*
  - *Integration*

## Piloting

Stop TB Partnership

TAG Treatment Action Group

Diagnostics Equity Consortium
Accessible & Affordable Diagnostics for All

ACCESS CAMPAIGN
MEDECINS SANS FRONTIERES

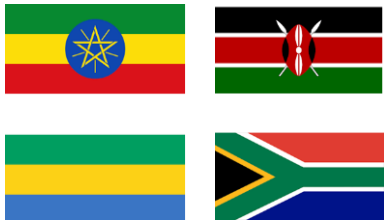
## Data collection

**A** **Desk review**

- *Stakeholders*
- *Steps & processes*
- *Inter-dependencies*
- *Timelines*

**B** **Virtual & face to face engagements**

# Critical pathway analysis: overview



**1. Country engagement (Sep-Nov 24)**

**2. Data collection & desk review (Nov 24-March 25)**

**3. Country workshops (Dec 24-April 25)**

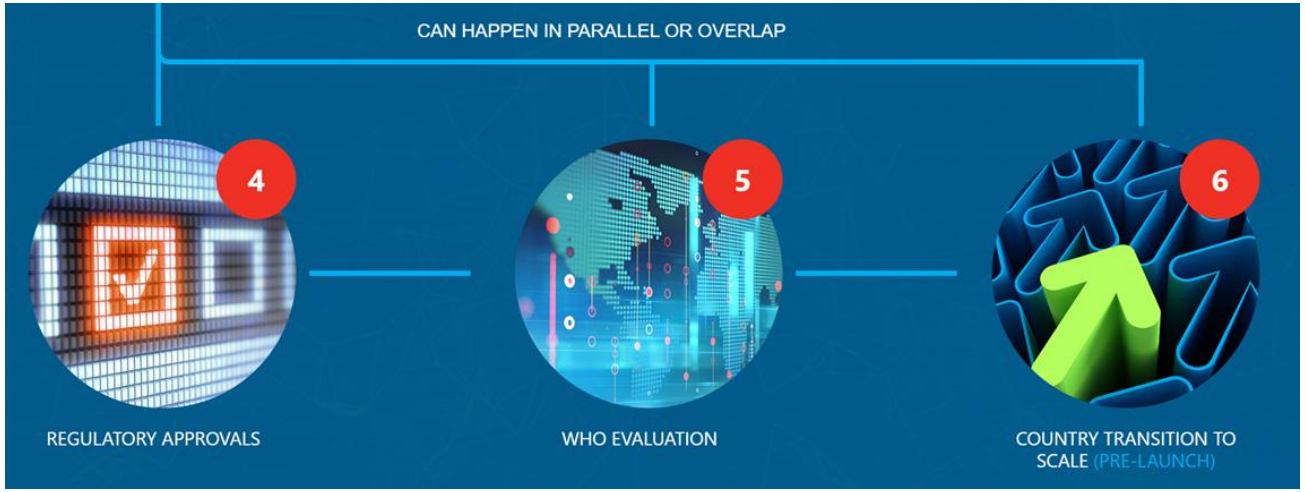
**4. Final reports (April-June 25)**

**Stakeholders mapping**
(MoH, NTP, NRL, NRA, Private sector, CSOs, partners)

Repository:
103 documents
7,317 pages of information


**Roadmap(s)**

# Regulatory considerations and early uptake




"How to **expedite the review and approval** of new TB diagnostic tools and technologies to facilitate quicker market entry & uptake in national policy while **maintaining** safety & quality **standards** ?"

# Overview: Regulatory approval of Medical devices & IVDs

| | Ethiopia | Gabon | Kenya | South Africa |
|---|---|---|---|---|
| **1.Regulatory stakeholders** | | | | |
| NRA | EFDA | ANMAPS | PPB | SAHPRA |
| WHO GBT | no | no | no | **Level 3 (vaccines)** |
| AMA treaty ratification | **yes** | **yes** | **yes** | no |
| **2.Application for market approval & registration** | | | | |
| Guiding documents | • *EFDA Guidelines for IVD Registration Requirements (2020)*<br>• *EFDA General Guidelines for Medical devices Marketing Authorization (2022)* | • *Règlement No. 5/13-UEAC-OCEAC-CM-SE-2 (2013)* | • *Guidelines for the registration of medical devices including IVDs (2022)* | • *Medicines and Related Substances Act, 1965 (Act 101 of 1965)*<br>• *Regulations Relating to Medical Devices and In-Vitro Diagnostic Medical Devices (IVDs) (2016)*<br>• **SAHPRA MD registration feasibility study** |
| Online access to guidelines/ | Yes | Partial | Yes | Yes |
| Application portal | eRIS | / | PRIMS | eCTD * |
| Language | English/Amharic | French | English | English |

** Not yet operttonal for medical devices and IVDs

# Overview: Regulatory approval of Medical devices & IVDs

| | Ethiopia | Gabon | Kenya | South Africa |
|---|---|---|---|---|
| **3. Reliance/ collaborative pathways** | | | | |
| Recognized Regulatory Authorities (RRA) | GHTF*<br>South Korea<br>Singapore<br>UK<br>WHO PQ | GHTF*<br>RRA agreement<br>WHO PQ | GHTF*<br>RRA agreement<br>WHO PQ<br>WLA | GHTF*<br>Brazil<br>RRA agreement<br>WHO PQ |
| Regional harmonization | Regional economic communities (EAC MRH, IGAD..) | CEMAC<br>Common Pharmaceutical Policy | Regional economic communities (EAC MRH, IGAD..) | SADC<br>Zazibona collaborative registration |
| **4. Approval timelines** | | | | |
| Regular review | 3-6 months | 6 months | 3-24 months | 3-12 months |
| Collaborative registration | 90 days | Not specified | 90 days | 90 days |
| Expedited review | 10 days | Not specified | 15 days | 90 days or less |
| **5. Marketing authorization** | | | | |
| Validity | 5 years (renewable) | 5 years (renewable) | | 5 years (renewable) |
| **6. In country evaluation** | | | | |
| | EPHI (not systematic) | / | KMLTTB validation | NHLS Health Technology Assessment (HTA) unit<br>Private sector assessment |

* Global harmonization task force founding countries: Australia, Canada, EU, Japan, US

# Cross-cutting observations: regulatory approval

- Regulatory systems in Africa mostly rely on WHO processes (recommendation/PQ)
- Mechanisms in place for expedited review, e.g: Ethiopia has a potential timeline of 10 days for:
  - **public health emergencies**
  - **unmet medical needs**
  - **investigational products**

## From the regulator lens

- WHO endorsement/PQ **enabler** for faster timelines (all)
- National processes for review & approval (i.e.: expert committees) also available

## From the NTP/programmatic lens

- WHO endorsement/PQ is a **prerequisite** (all)
- Required for access to funding (ie: Global Fund list of eligible TB Dx) and TA (ie: WHO, USAID etc)
- Provides necessary operational guidelines for (programmatic) implementation

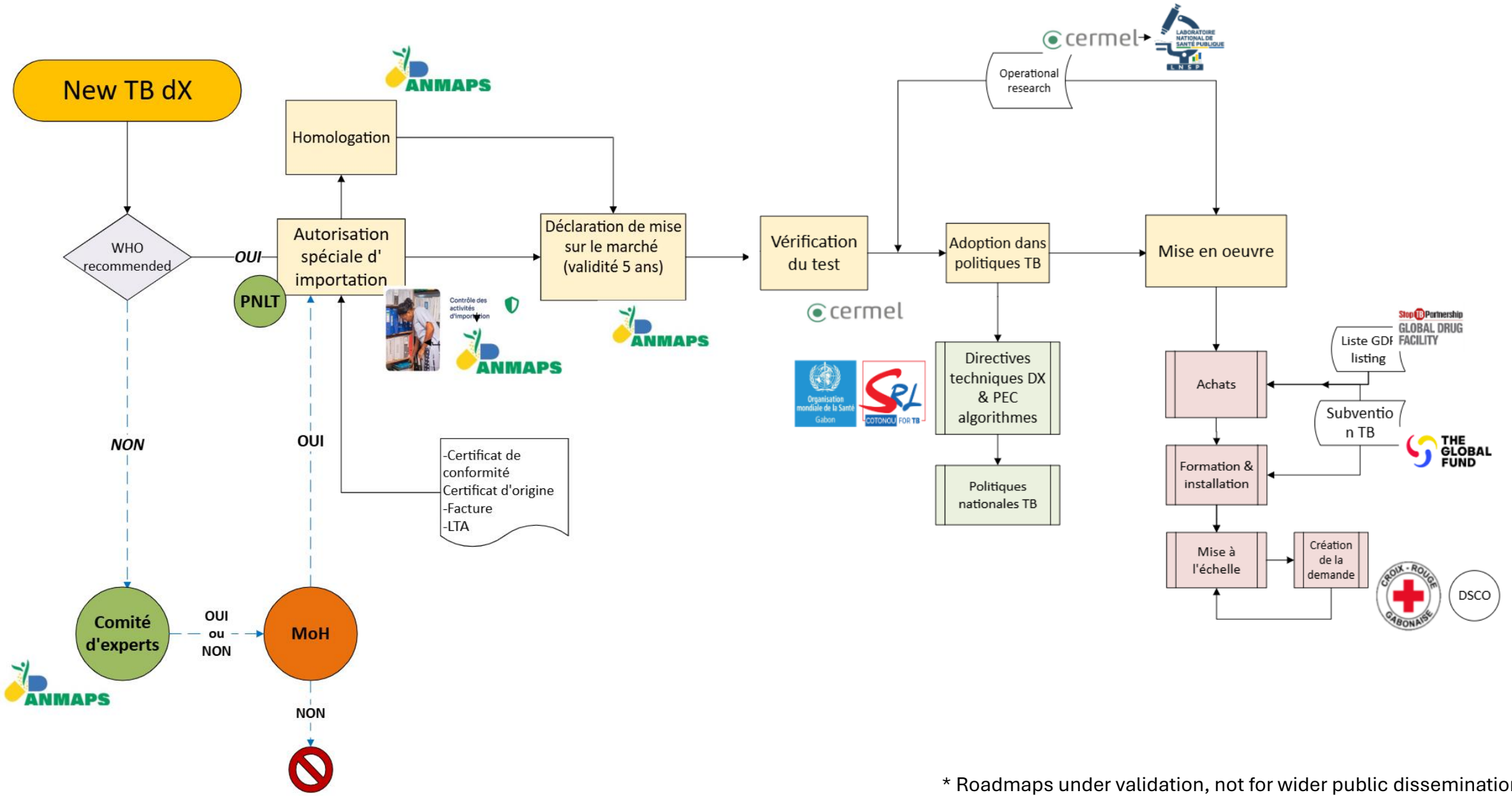
## From the private sector lens

- Comply with regulatory requirements

but

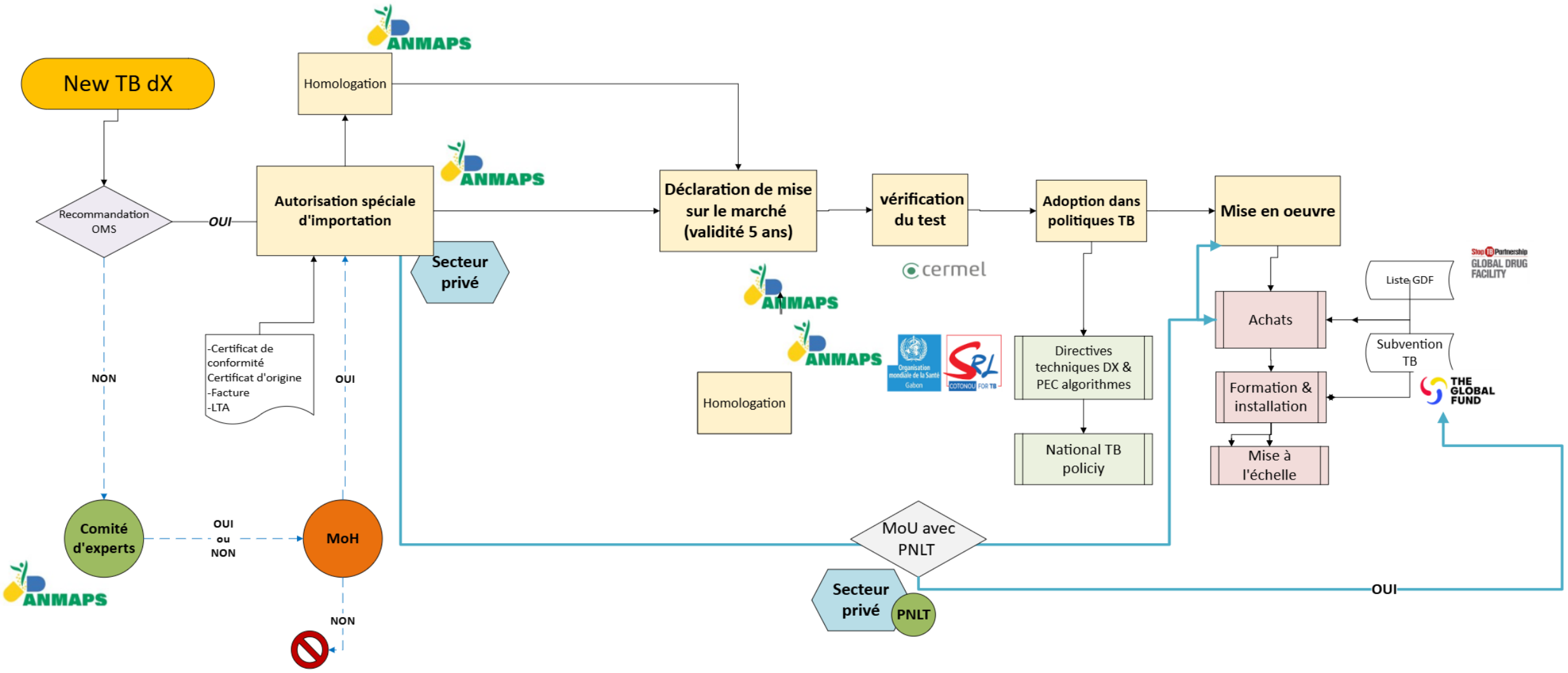
- Not always bound by availability of NTP policy and guidelines for implementation (ie: Gabon, South Africa)

# Illustration: entry via the public sector




* Roadmaps under validation, not for wider public dissemination

# Illustration: entry via the private sector

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# Cross-cutting observations: uptake into policy

- Aspiration: “studies in support of the intended use should consider the intended user and the intended setting of use” (EFDA, Ethiopia)  but not a strict requirement from NRA.
- ISO 15189 compliant test verification is performed (all).

**Prior to approval (global)**

- CoE as evidence generators for multicentric **performance evaluation studies** (South Africa, Ethiopia)
- Inform WHO technical advisory group (TAG) and guidelines development group (GDG)

**After approval (national)**

- Evidence generation on **performance, operational characteristics, acceptability, cost effectiveness** through pragmatic trials, operational/implementation research e.g:
  - HTA unit (South Africa)
  - Research Institutes/academia (all)
  - Donors funded pilot introduction (USAID, EDCTP..)
  - Regional initiatives such as Global Fund TB Supranational Reference Laboratory Network in Western and Central Africa).
- Timelines variable, protocol not systematically available .

***Local evidence accelerates uptake into national policy and informs programmatic deployment, scale up and integration strategies***

# Cross-cutting observations: import and procurement

- Local representative and additional documentation required: certificate of conformity, quality assurance dossier (all)
- Marketing authorization required for import but special import mechanism in place if e.g. letter of support from MoH/NTP e.g. for research purpose, public health emergency… (e.g : Ethiopia, Gabon)
- Access to foreign currency for procurement may be a barrier (e.g: Ethiopia)
- Multi-disease testing functionalities is an enabler (e.g. Gabon & outbreak prone diseases)

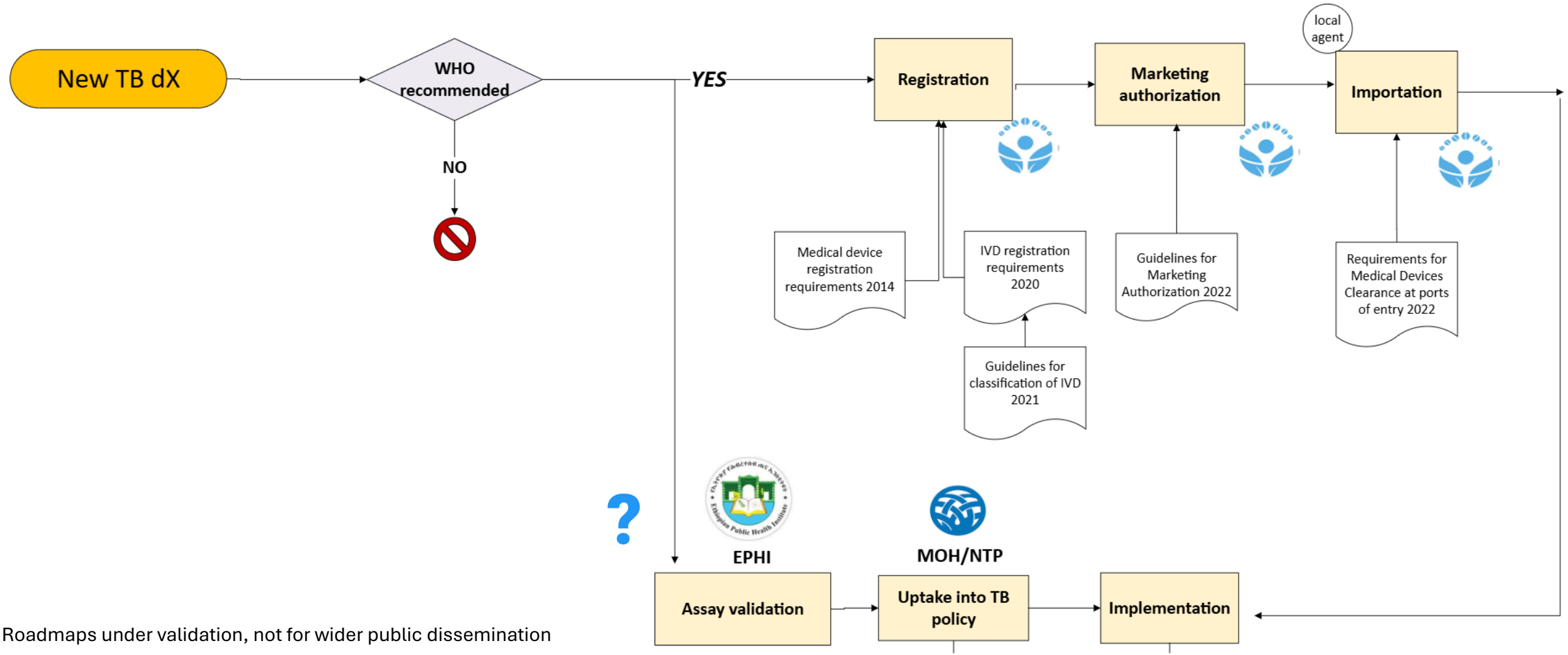
**From the donors' perspective**

- WHO PQ /recommendation is required for access to external funding, and procurement via pooled mechanisms /subsidized pricing (ie: Global Fund list of eligible Dx, GDF catalog)
- Exception: interim processes such as Global Fund Expert Review Panel Process for Diagnostic Products (ERPD)

**From a continental perspective**

- Pooled mechanisms implemented during COVID-19 (e.g: African Union AMSP)
- Operationalization of SADC Strategy for Pooled Procurement of Essential Medicines and Health Commodities underway
- Aim to foster self reliance and promote local manufacturing (context of *limited external funding*)

# Illustration: accelerated uptake with evidence generation

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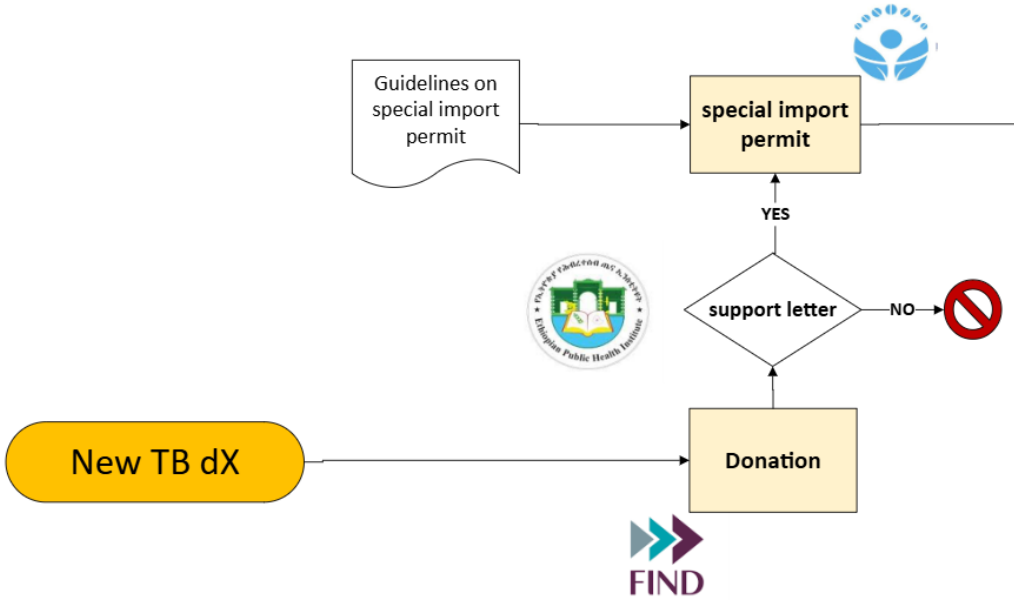
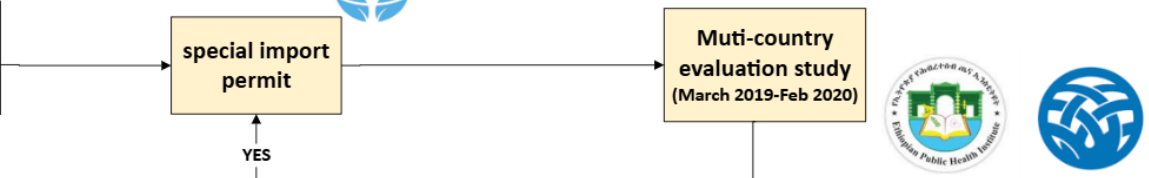
# Cross-cutting observations: accelerated uptake with evidence generation

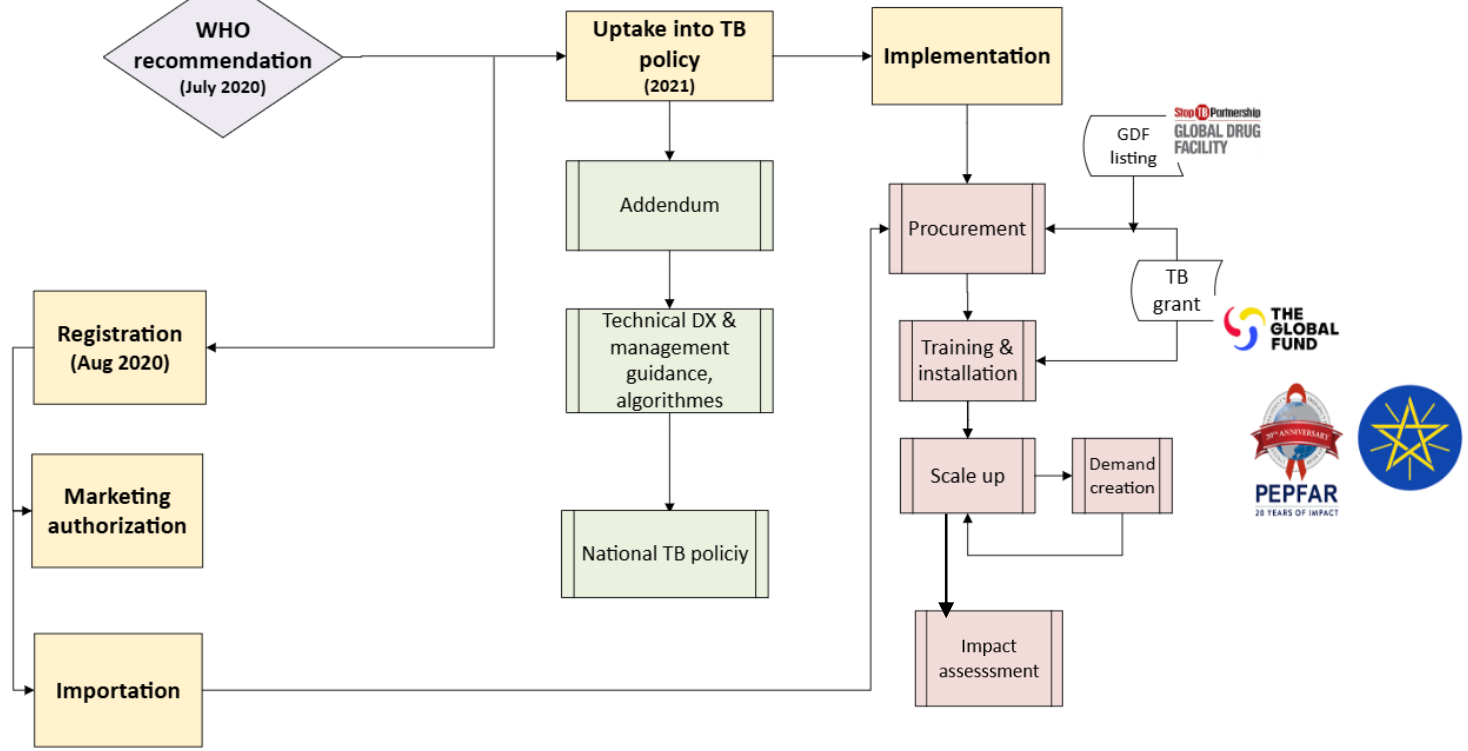



**EPHI as evidence generator for Truenat**

- WHO recommended July 2020
- EFDA approval Aug 2020
- Policy uptake 2021

| TIMELINE | ACTIVITY | STAKEHOLDERS IN CHARGE |
|---|---|---|
| **6 months** | Uptake into national policy | NTLP, NTRL |
| **1 month** | TWG initiation | NTLP, NTRL & HIV program |
| **1 year** | Updating technical guidelines, algorithms, SOP, job aids, training material, checklist | NTLP, NTRL, Regional health bureaux, Regional Reference laboratories, HIV team, partners |
| **2 months** | Training of trainers | NTLP, NTRL, National capacity Building Directorate, partners |
| **2 months** | Basic training of end users and sensitization workshop (sub national cascade) | Regional health bureaux & Regional referral laboratories (for laboratory staffs under their region) in collaboration with the NTRL & partners |

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# Time to uptake (historical data)

Xpert MTB RIF for replacement of Microscopy in high-risk groups

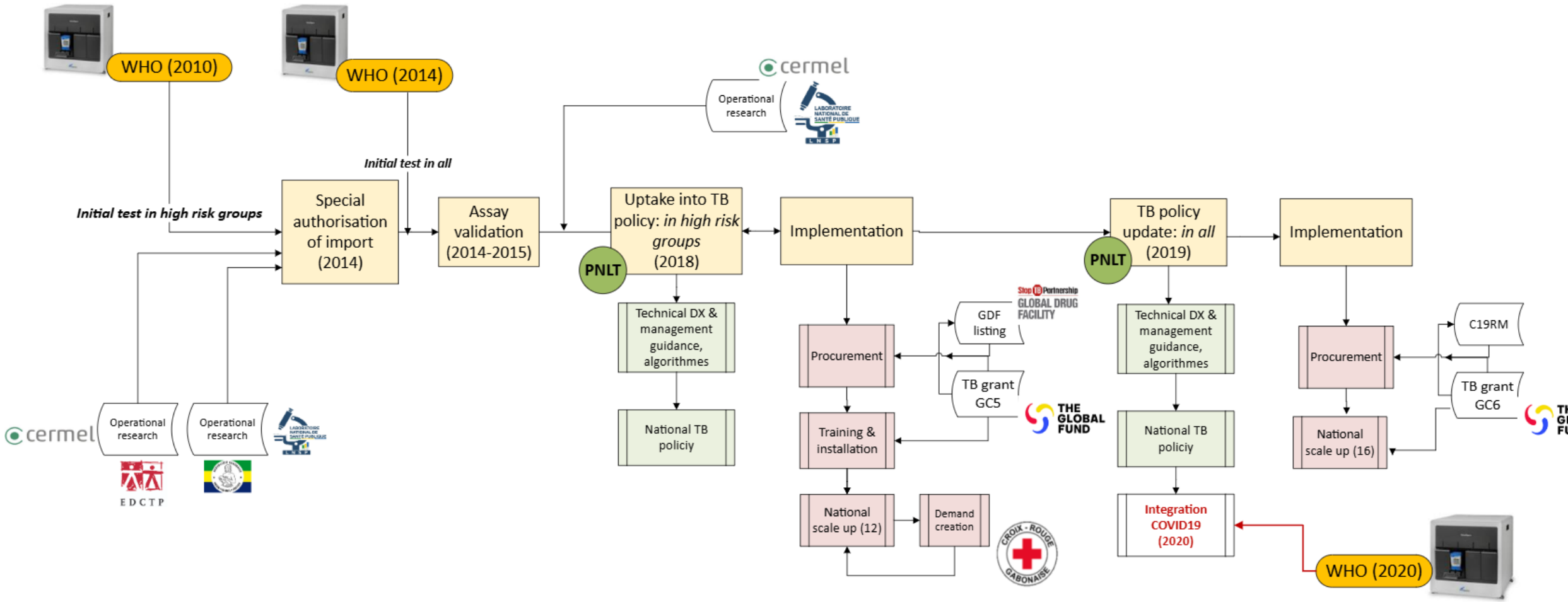
| | Ethiopia | Gabon | Kenya | South Africa |
|---|---|---|---|---|
| | | | | |
| WHO recommendation | / | 2010 | 2010 | 2010 |
| Registration | / | 2014 (SAI) | 2018/2020 | 2010 (HTA validation) |
| Uptake into policy | / | 2018 | 2016 | 2011 |
| **Time to adoption** | / | **8 years** | **6 years *** | **1 year** |

Truenat as initial test (mWRD) for replacement of Microscopy in all

| | Ethiopia | Gabon | Kenya | South Africa |
|---|---|---|---|---|
| | | | | |
| WHO recommendation | 2020 | 2020 | 2020 | / |
| Registration | 2020 | 2023 (SAI) | 2021 | / |
| Uptake into policy | 2021 | 2024 | 2022 | / |
| **Time to adoption** | **1 year** | **4 years *** | **2 years** | **/** |

# Timelines for uptake into policy: historical data (GeneXpert)

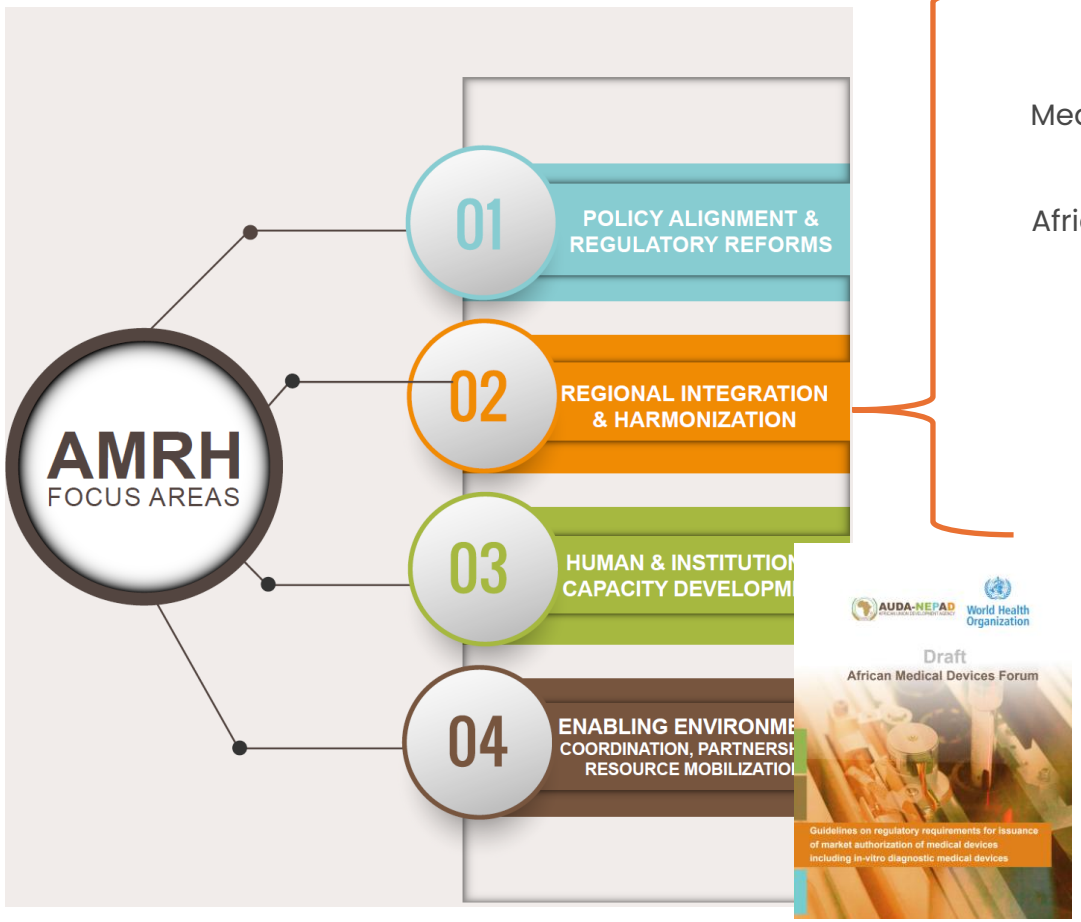
Replacement of microscopy in high risk groups: 8 years
Replacement of microscopy in all: 5 years
Integrated testing for COVID-19/TB: less than 1 year



# An opportunity: the Africa Medicine Agency


AMA | African Medicines Agency

**Marketing authorization:**
The AMA shall be responsible for evaluation and decision making with regard to selected medical products for treatment of priority diseases/conditions as determined by the African Union.







AMRH

Medical Devices Assessment Technical Committee (**MDA-TC**)

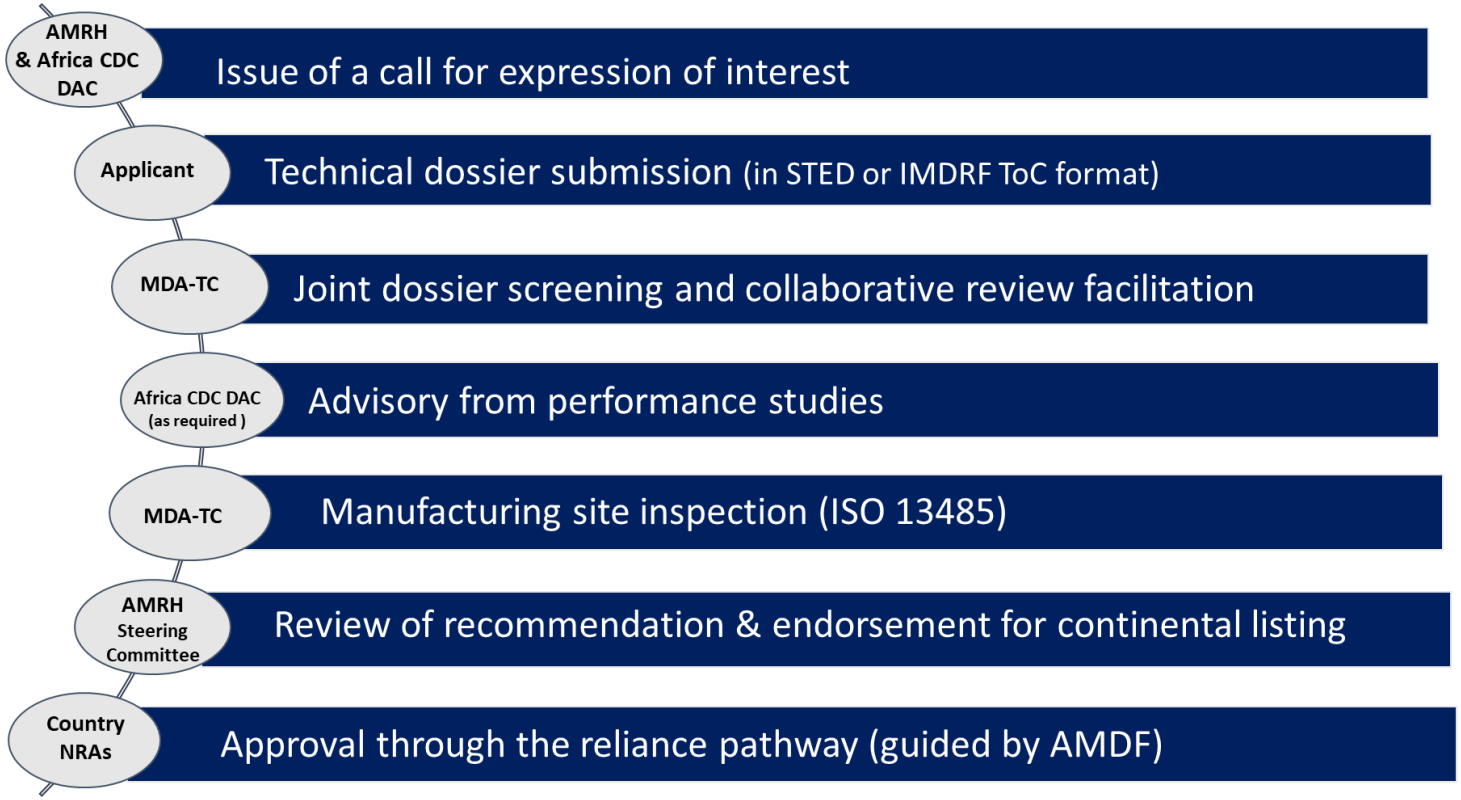
African Medical Devices Forum (**AMDF**)

AfricaCDC
Centres for Disease Control and Prevention

Diagnostic Advisory Committee (**DAC**)

**Harmonized process for joint review & listing of medical devices and IVDs**

# Continental regulatory framework for medical devices and IVDs




**2024-2025 pilot**
**joint review & emergency use listing**
**of Mpox diagnostics (molecular tests)**

https://africacdc.org/download/mpox-molecular-diagnostic-tests-rt-pcr/

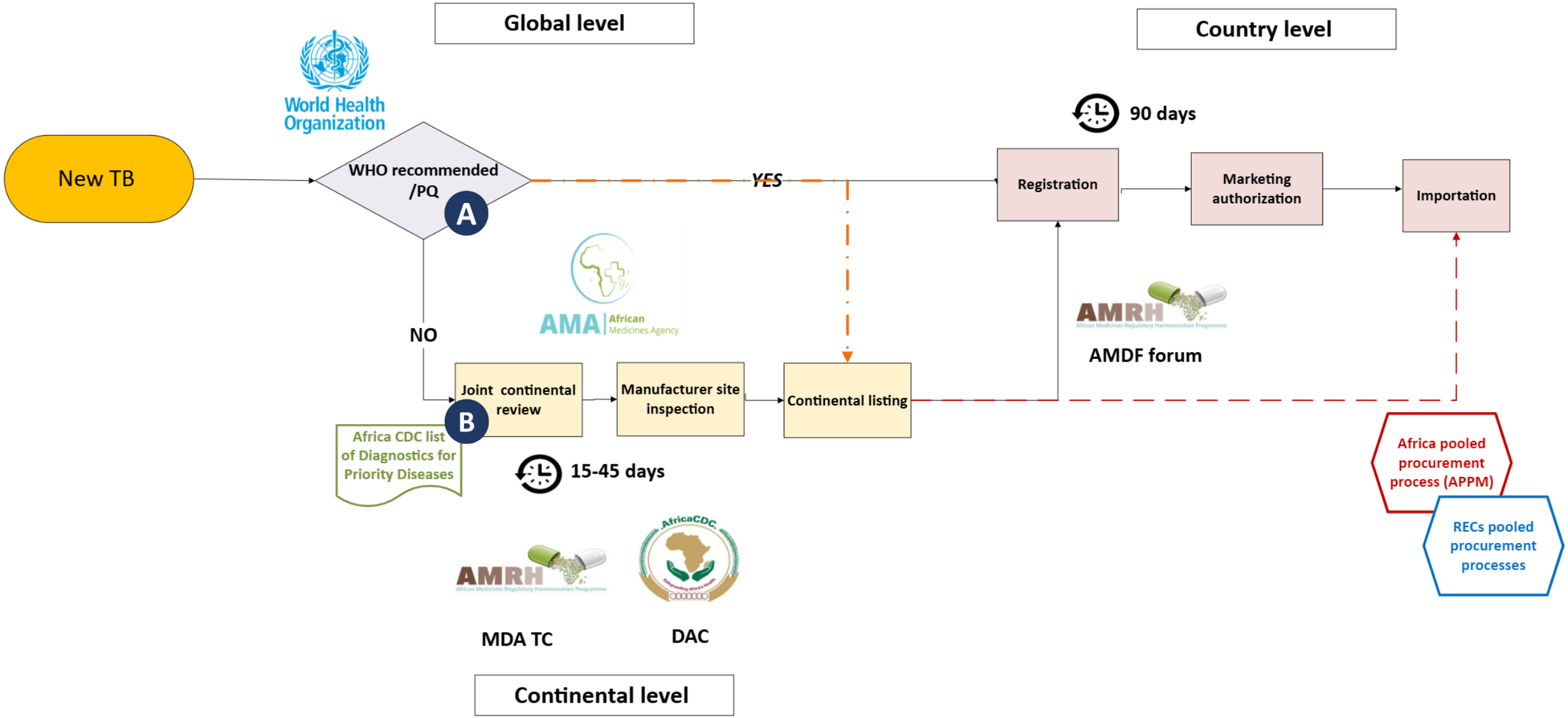
**2025-2026 pilot**
**joint review & listing**
**of medical devices and IVDs for priority diseases**

AfricaCDC
Centres for Disease Control
News Stories

Africa Lists Diagnostics for Priority Diseases

https://africacdc.org/news-item/africa-lists-diagnostics-for-priority-diseases/

# Continental listing of new TB diagnostics ?



# Moving forward….

“How to **expedite the review** and approval of new TB diagnostic tools and technologies to facilitate quicker market entry & uptake in national policy while **maintaining** safety & quality **standards** ?’’

# Recommendations

**WHO**

- Expand the roll out of the GTB+MDs benchmarking tool
- Increase awareness & outreach (for developers & manufacturers)
- Maintain collaboration with continental stakeholders

**Continental regulatory stakeholders**

- Ensure alignment & synergies with existing initiatives
- Support strengthening of NRAs capacity at country level for MD & IVDs /expand pool of assessors
- Increase awareness & outreach (for developers & manufacturers)
- Select TB as use case for the joint review and listing of priority diseases

**NRAs (country level)**

- Ensure operationalization of (regional & country) legal frameworks
- Leverage the WHO GBT + medical devices and AMDF guidance to streamline & harmonize MD & IVDs guidelines (i.e. pilot in South Africa)
- Ensure transparency of the regulatory process (e.g: up to date online repositories (regulatory guidelines, listing of authorized tests/devices, licensed distributors, etc.) for timely access)
- Improve the interface between NRAs and HTA

**Manufacturers**

- Address documentation requirements (leverage NRAs checklists) & language requirements
- Ensure availability of full technical dossier to facilitate review.
- Consider interim pathways to procurement eligibility listing, such as Global Fund ERPD open call for TB products
- Consider alternative diseases entry point (integration) with higher market attractivness
- Stay abreast of and leverage regional pooled procurement mechanisms as alternative market entry points
- Leverage capacity of academia, regional initiatives, private sector for production of (local) evidence

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# Thank you

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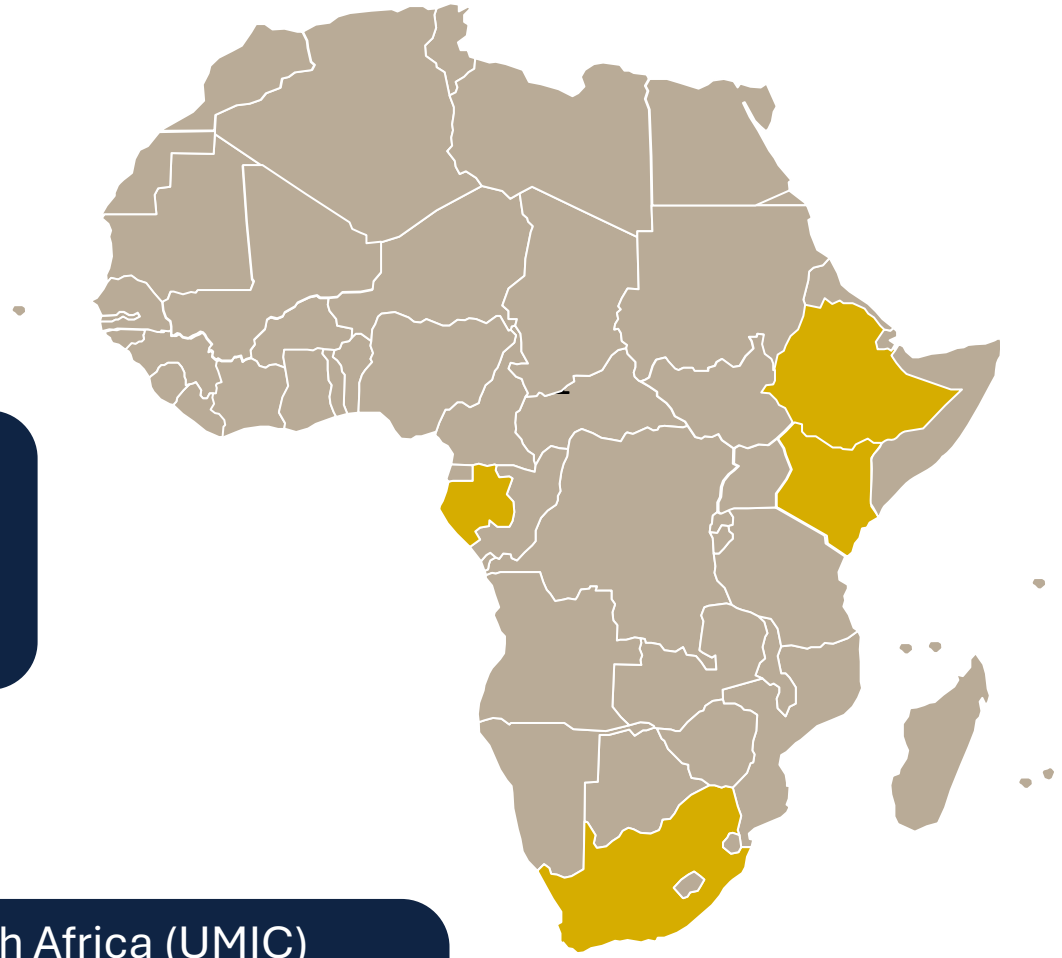
# Countries of interest



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