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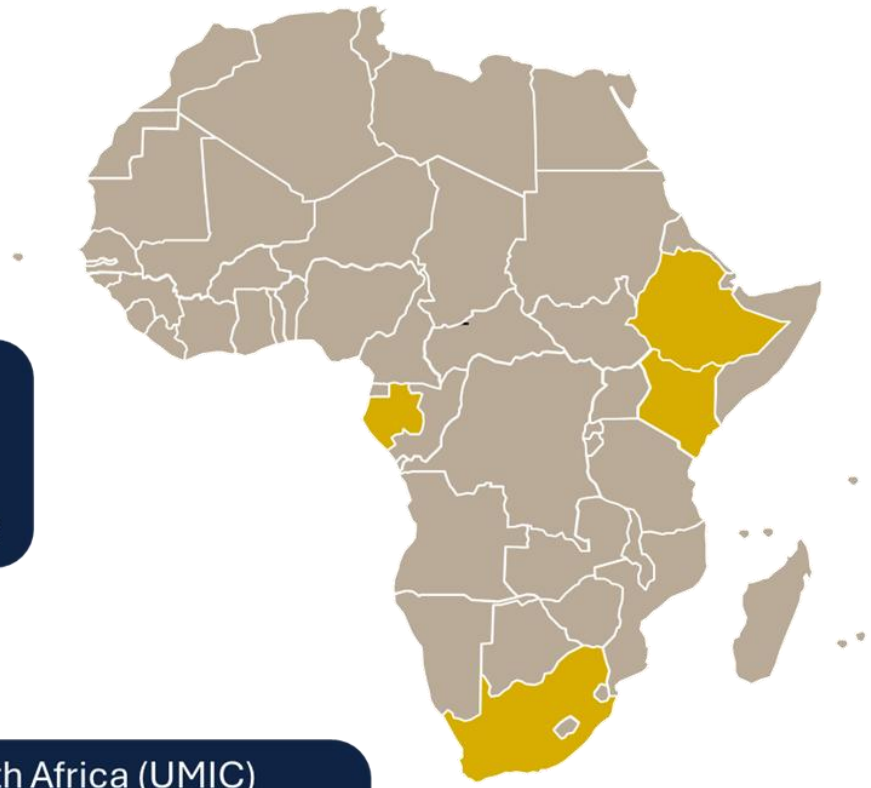
Critical pathway analysis of new TB diagnostic tools in Africa

Insights from 4 countries
& continental regulatory stakeholders

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

Gabon (UMIC)

Population: 2.5 M
TB incidence: 500 /100 000
% mWRDs: 67%
TB funding (2023): 53 % international

Kenya (LMIC)

Population: 55 M
TB incidence: 223 /100 000
% mWRDs: 54 %
TB funding (2023): 90 % international

South Africa (UMIC)

Population: 63 M
TB incidence: 427 /100 000
% mWRDs: 83 %
TB funding (2023): 32 % international

New TB Dx Critical Path Analysis project

Objective:

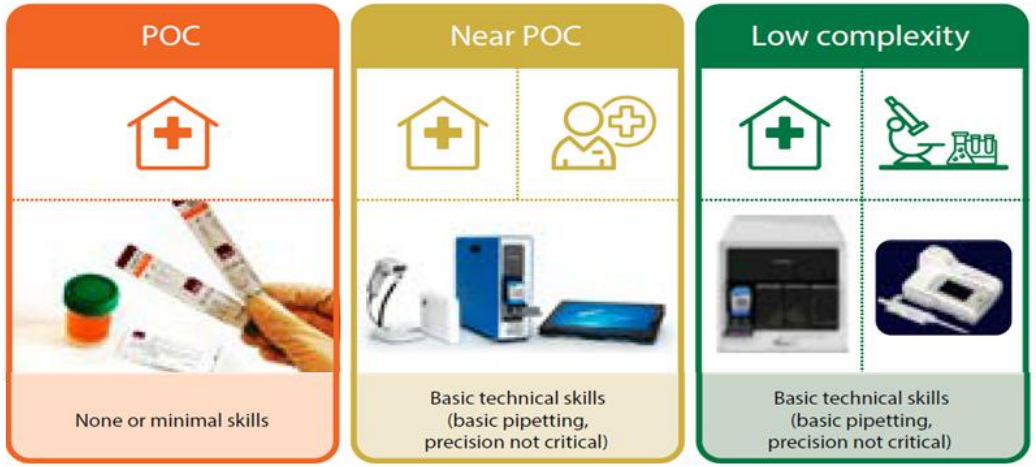
- to identify **relevant context** and **obstacles** to the introduction to the market of novel diagnostics for TB

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

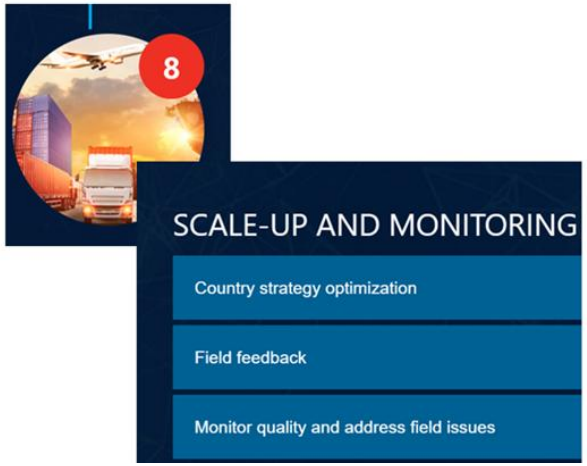


Critical pathway analysis: approach

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
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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)

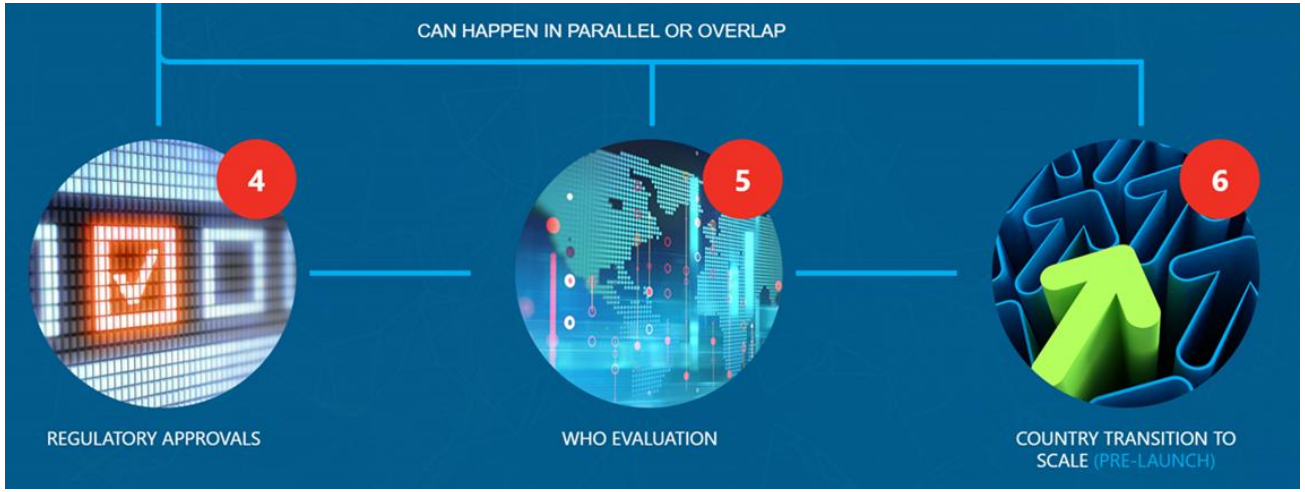
Stakeholders mapping

(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)* · *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)* · *Regulations Relating to Medical Devices and In-Vitro Diagnostic Medical Devices (IVDs) (2016)* · 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 operational 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* South Korea Singapore UK WHO PQ	GHTF* RRA agreement WHO PQ	GHTF* RRA agreement WHO PQ WLA	GHTF* Brazil RRA agreement WHO PQ
Regional harmonization	Regional economic communities (EAC MRH, IGAD..)	CEMAC Common Pharmaceutical Policy	Regional economic communities (EAC MRH, IGAD..)	SADC 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)	5 years (renewable)
6. In country evaluation				
	EPHI (not systematic)	/	KMLTTB validation	NHLS Health Technology Assessment (HTA) unit 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 (including TB)**
  - **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

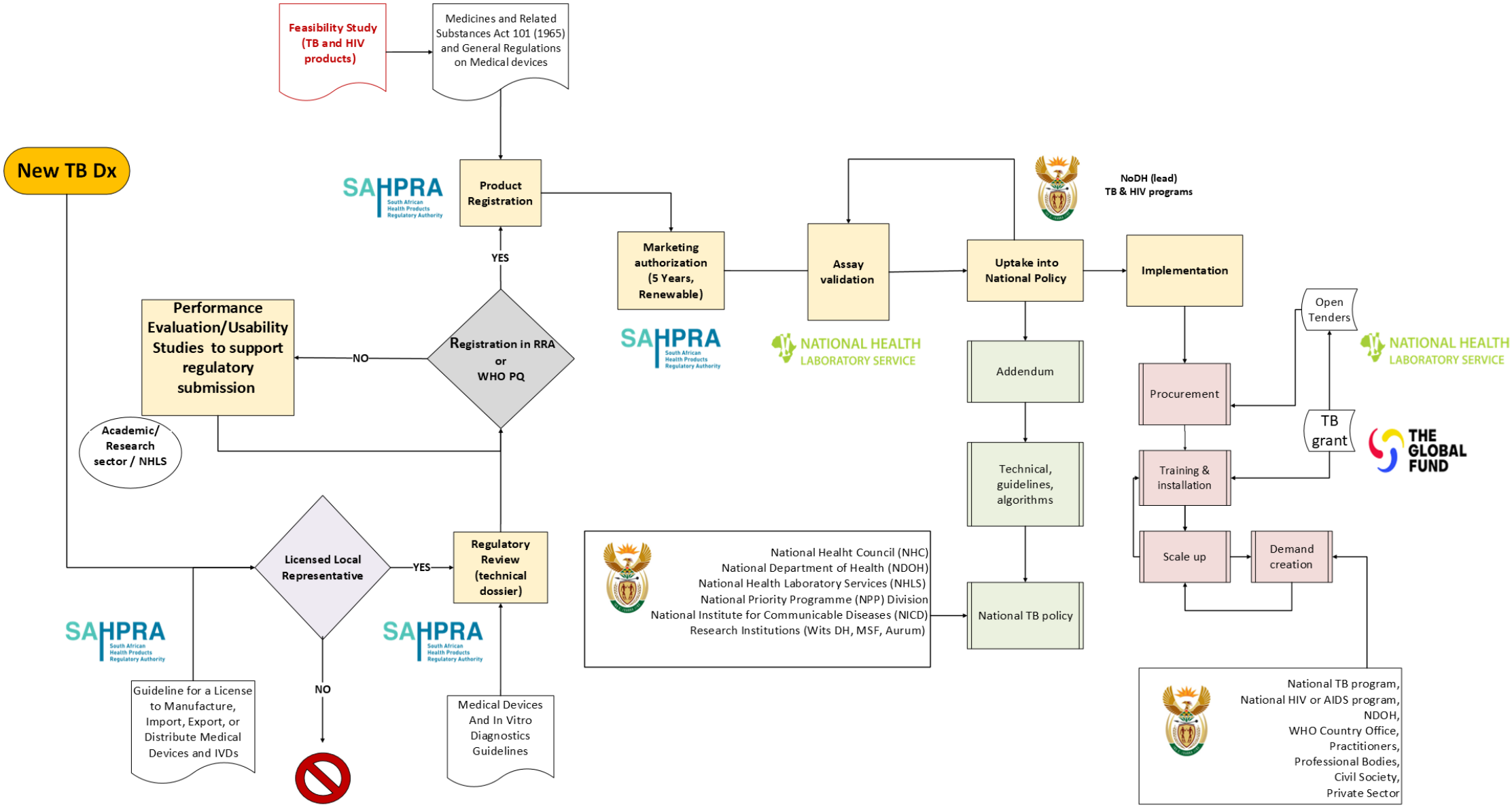
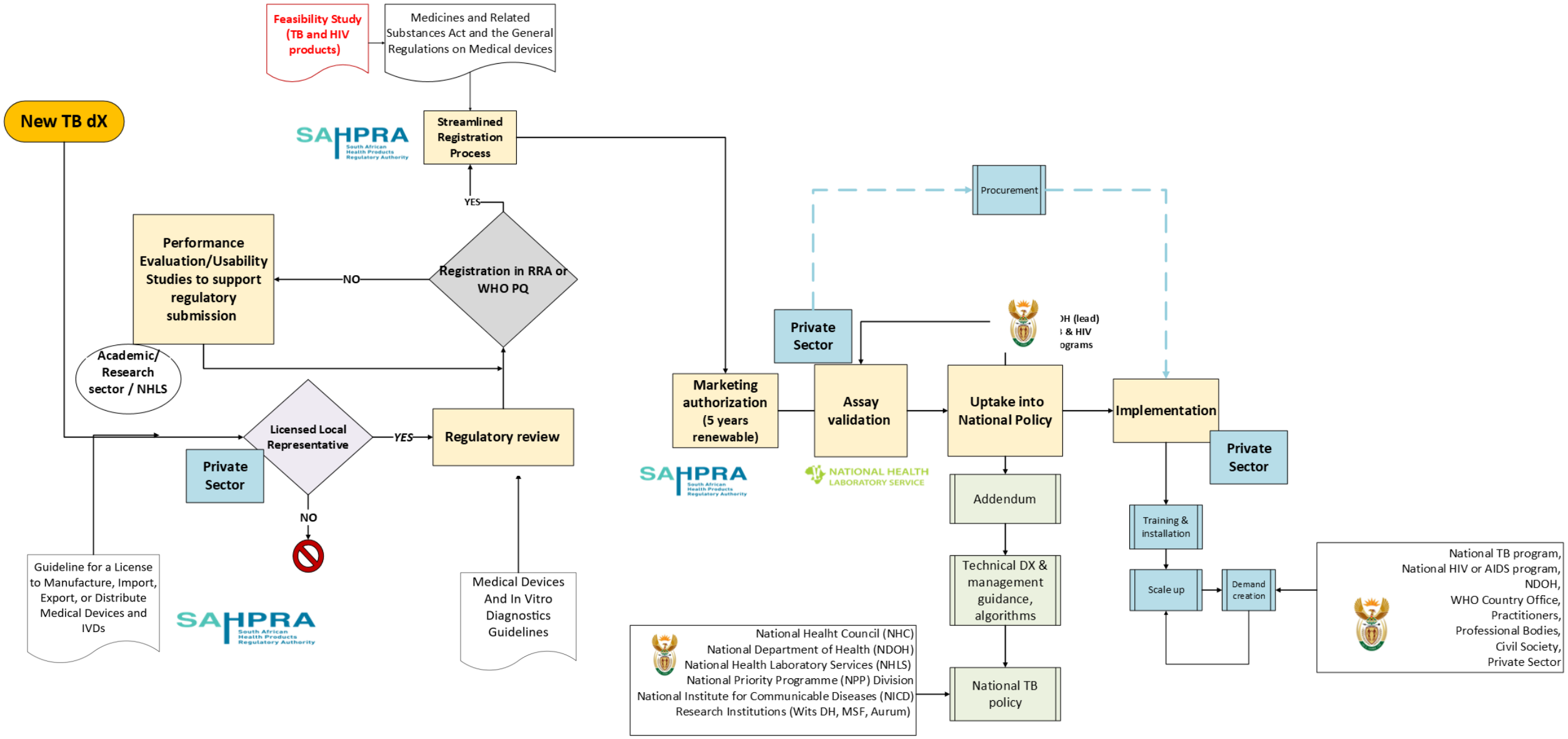


Illustration: entry via the private sector



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

General roadmap for introduction of new TB tools in Ethiopia

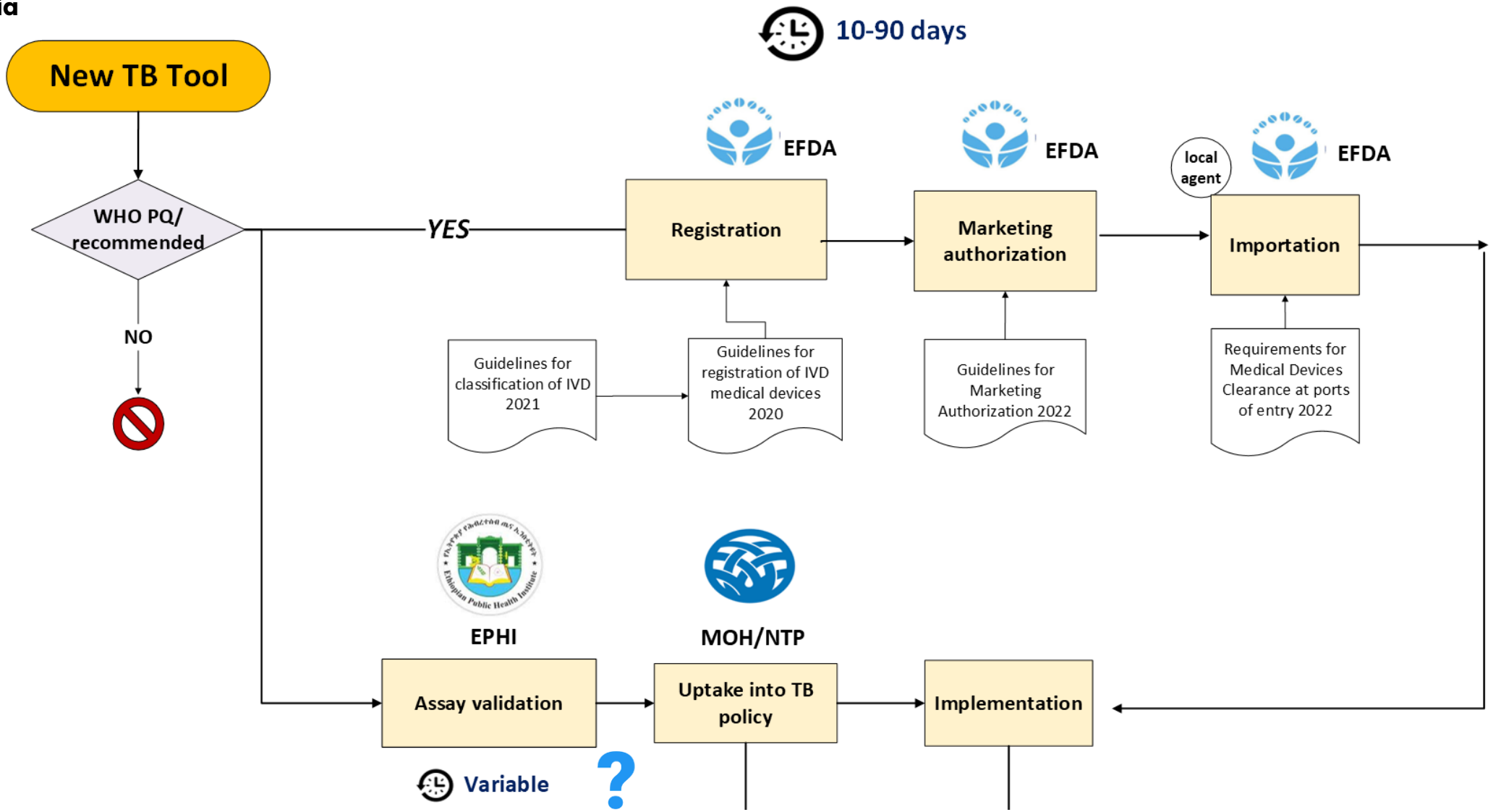


Illustration: accelerated uptake with evidence generation

General roadmap for introduction of new TB tools in Ethiopia

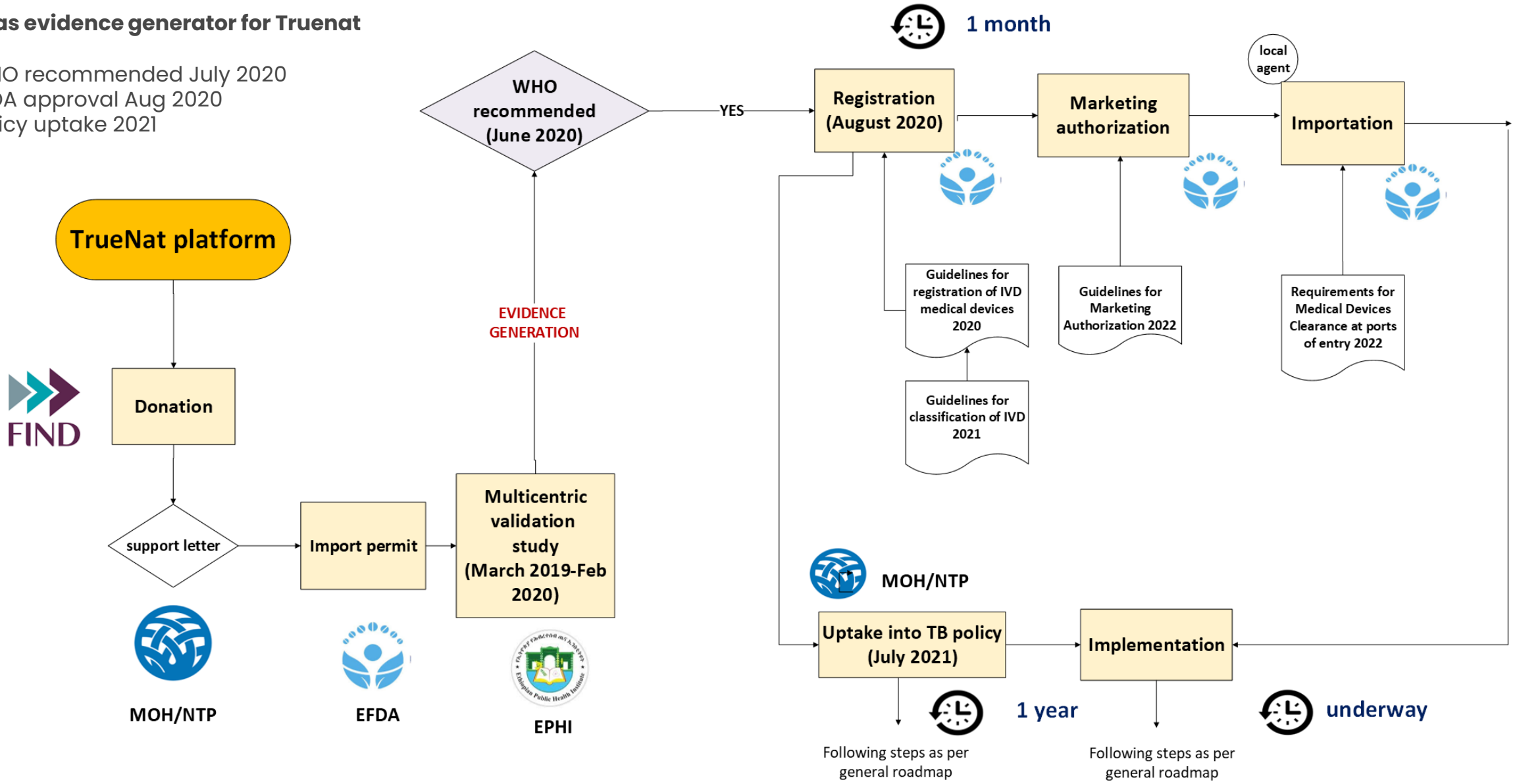
Policy uptake and early implementation: 1,5-2 years

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 materials, checklists	NTLP, NTRL, Regional health bureau, 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 bureau & Regional referral laboratories (for laboratory staffs under their region) in collaboration with the NTRL & partners

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



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**

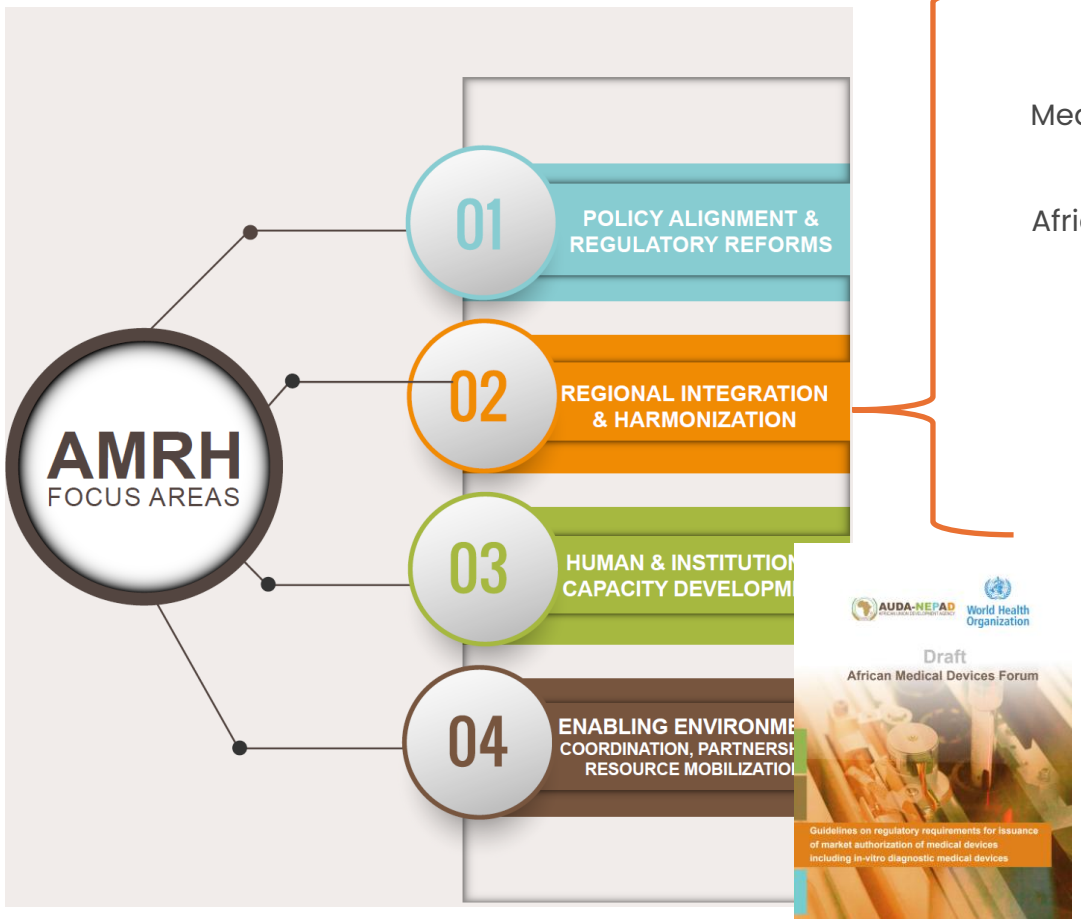
Truenat as initial test (mWRD) for replacement of Microscopy in all

	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**	**/**

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**)

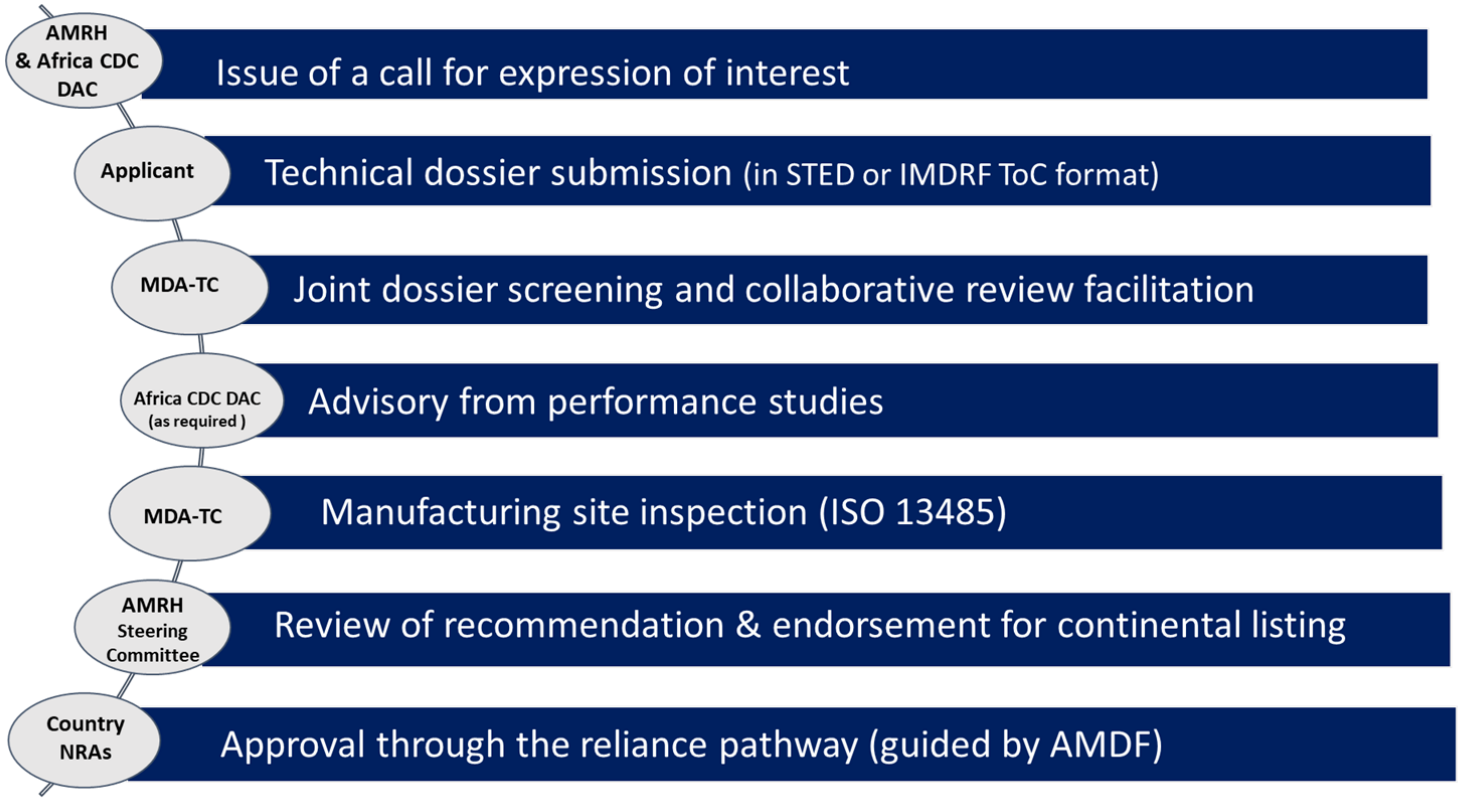
African Medical Devices Forum (**AMDF**)

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/

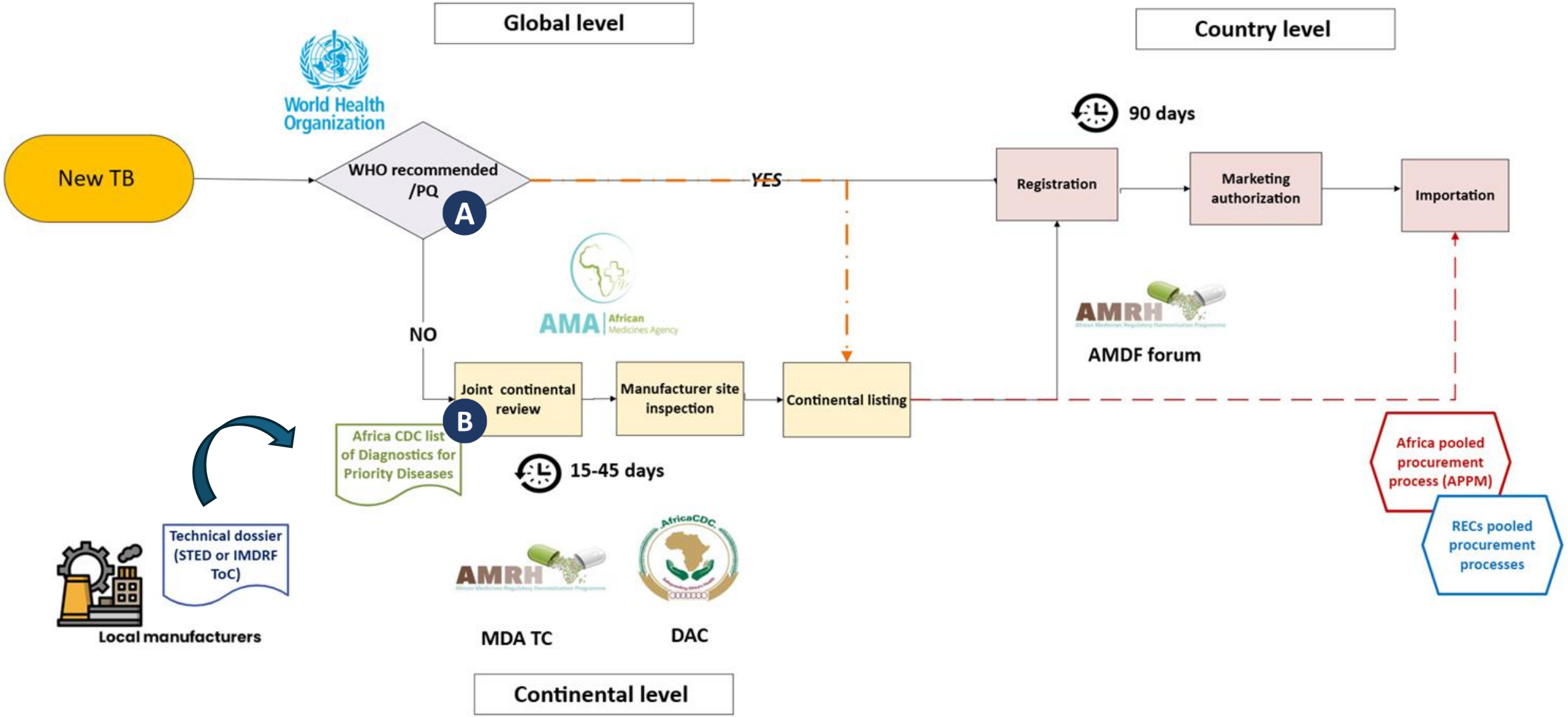
https://www.nepad.org/news/public-notice-amrh-steering-committee-approves-emergency-use-listing-of-two-mpox

https://www.sahpra.org.za/news-and-updates/sahpra-approves-mpox-test-using-african-medicines-regulatory-harmonisation-amrh-continental-eul-procedure/

2025–2026 pilot
joint review & listing
of medical devices and IVDs 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

MATAHARI

Thank you

AfricaCDC
Centres for Disease Control and Prevention

AMRH

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MINISTERE DE LA SANTE

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MINISTRY OF HEALTH-ETHIOPIA

REPUBLIC OF KENYA
MINISTRY OF HEALTH

Stop TB Partnership

TAG
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Accessible & Affordable Diagnostics for All

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