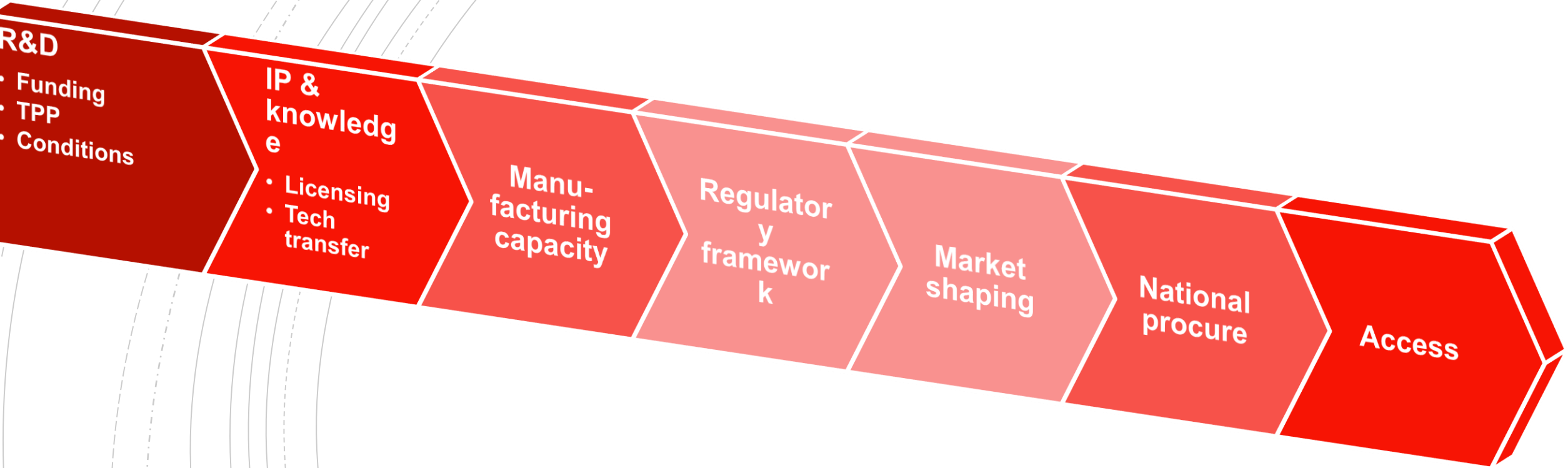
O'NEILL INSTITUTE FOR NATIONAL & GLOBAL HEALTH LAW
GEORGETOWN LAW

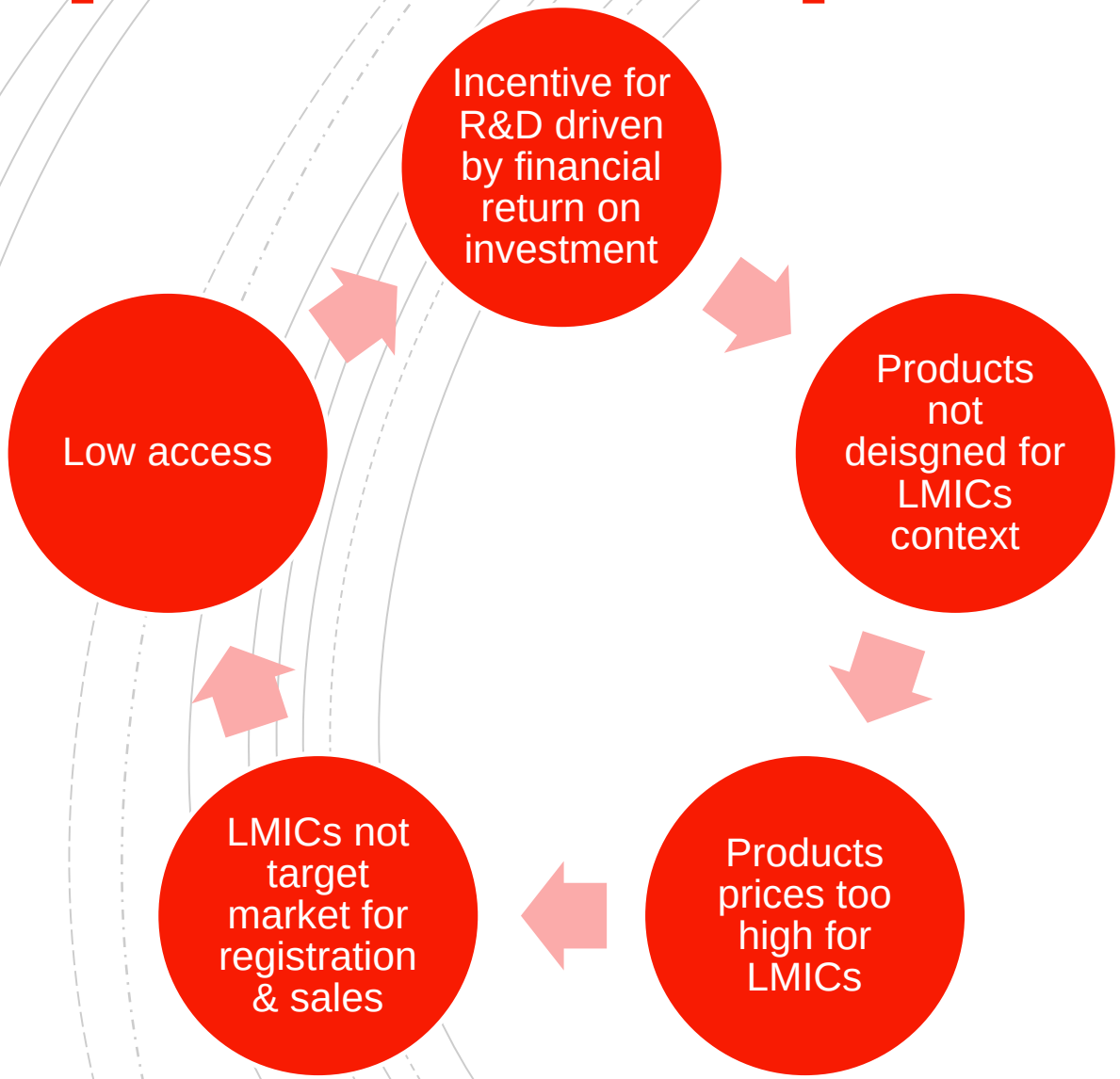
Global health policies to promote local manufacturing

Sharonann Lynch, Georgetown University

18 August 2021


R&D
• Funding
• TPP
• Conditions
IP & knowledge
• Licensing
• Tech transfer
Manu-facturing capacity
Regulatory framework
Market shaping
National procure
Access

Upstream start of the problem



Disease-specific diagnostics development, commercial developers chase donor funding or lucrative markets

- Benchtop of single-disease instruments, or in the best of cases, disease-specific cartridges and reagents
- Proprietary closed machines
- Less consideration for value chain
- Lack of interoperability & open access diagnostic platforms that allow for cartridge and reagents suppliers outside of closed proprietary systems
- Lack of follow-on innovation from additional developers for neglected diseases and populations by developing tests using existing platforms
- Less incentive for multi-disease testing
- Potentially less incentive for less invasive sampling

.... New pandemic preparedness initiatives with surveillance focus risks devaluing overall diagnostics needs

We need to re-think diagnostics

Open science

- Committing to sharing knowledge and technology transfer, especially with LMIC entities, for the purposes of supporting 'follow-on' research, adaptation, and manufacturing
- Contributing to the commons, including the scientific knowledge base, including knowledge hubs that help inform the development of diagnostics
- Publishing data and articles in open access peer-review publications and portals
- Transparency of pre-clinical and clinical trial information
- Committing to inclusive research that takes account of different racial, ethnic, and contexts/considerations, including the needs of vulnerable populations in unstable settings and those who are immune-compromised

World Health Organization

SEVENTY-FOURTH WORLD HEALTH ASSEMBLY
Agenda item 13.4

A74/A/CONF./1
25 May 2021

Strengthening local production of medicines and other health technologies to improve access

Draft resolution proposed by Argentina, Australia, Brazil, Cana China, Colombia, Costa Rica, Dominican Republic, Ecuador, Eg Iceland, Indonesia, Libya, Mexico, Morocco, Norway, Paraguay, Philippines, Russian Federation, Sudan, Switzerland, Thailan Turkey, United Kingdom of Great Britain and Northern Irela United States of America, Uruguay, Member States of the African Group and Member States of the European Union

The Seventy-fourth World Health Assembly,

Momentum

OP2. Requests the Director-General:

OP2. (1) to continue to support Member States by strengthening actions related to WHA61.21 (2008), WHA66.22 (2013) and WHA67.20 (2014);

OP2. (2) to strengthen WHO's role in providing leadership and direction in promoting the strategic use of quality and sustainable local production of medicines and other health technologies by using a holistic approach and following good manufacturing practices;

OP2. (3) to raise awareness of the importance of sustainable local production of safe, effective, quality, and affordable medicines and other health technologies in improving access;

OP2. (4) to continue to support Member States upon their request in promoting quality and sustainable local production of medicines and other health technologies, including, as appropriate, by:

OP2.4. (a) providing technical support to Member States in developing and/or implementing national policies and evidence-based comprehensive strategies and plans of action for sustainable local production;

OP2.4. (b) assisting Member States to foster strategic and collaborative partnerships, including research and manufacturing;

OP2.4. (c) building capacity of Member States towards policy coherence and creating an enabling environment;

WORLD LOCAL PRODUCTION FORUM

Enhancing access to medicines and other health technologies

FIRST WORLD LOCAL PRODUCTION FORUM

Enhancing access to medicines and other health technologies

21 TO 25 JUNE 2021

13:00 to 15:30 (CEST)

Register here

ISSUE BRIEF

MÉDECINS SANS FRONTIÈRES ACCESS CAMPAIGN

LOCAL DIAGNOSTICS TO MEET LOCAL HEALTH NEEDS

Recommendations to improve local production of diagnostics in low- and middle-income countries

EXECUTIVE SUMMARY

Rupilia Martínez works in agriculture and has had malaria three times. The last time she had malaria she thought she had fully recovered, but after three days of severe illness she returned to the clinic in San Vicente, Venezuela, and was diagnosed with a relapse of the disease. Malaria RDTs are often imported from large multinational manufacturers.

The COVID-19 pandemic has uncovered what has long been appreciated in the field of diagnostics: the need to improve production and supply capacity of diagnostic tests through local research, development and manufacturing in low- and middle-income countries (LMICs).[1] Expansion and diversification of local production is particularly needed in LMICs where there is currently limited local manufacturing capacity. We cannot rely only on manufacturers primarily in high-income countries (HICs) if global needs are to be met.

As an international medical humanitarian organisation, Médecins Sans Frontières (MSF) relies on diagnostic tests daily as an entry point for appropriate clinical care in our medical projects in more than 70 countries. MSF teams have seen first-hand how insufficient access to diagnostics hinders effective medical care and can lead to worse outcomes for people's health.

In light of growing recognition of LMIC needs and accompanying efforts to increase access to diagnostics in these countries through improved local production,[2] this brief offers an analysis of local production of diagnostics in LMICs with limited capacity and makes recommendations for improvement. It is based on a desk review, mappings of select local manufacturers of diagnostics in LMICs (primarily in Africa and South America) and global health initiatives,[3] and interviews with 67 manufacturers, donors, and global health actors.

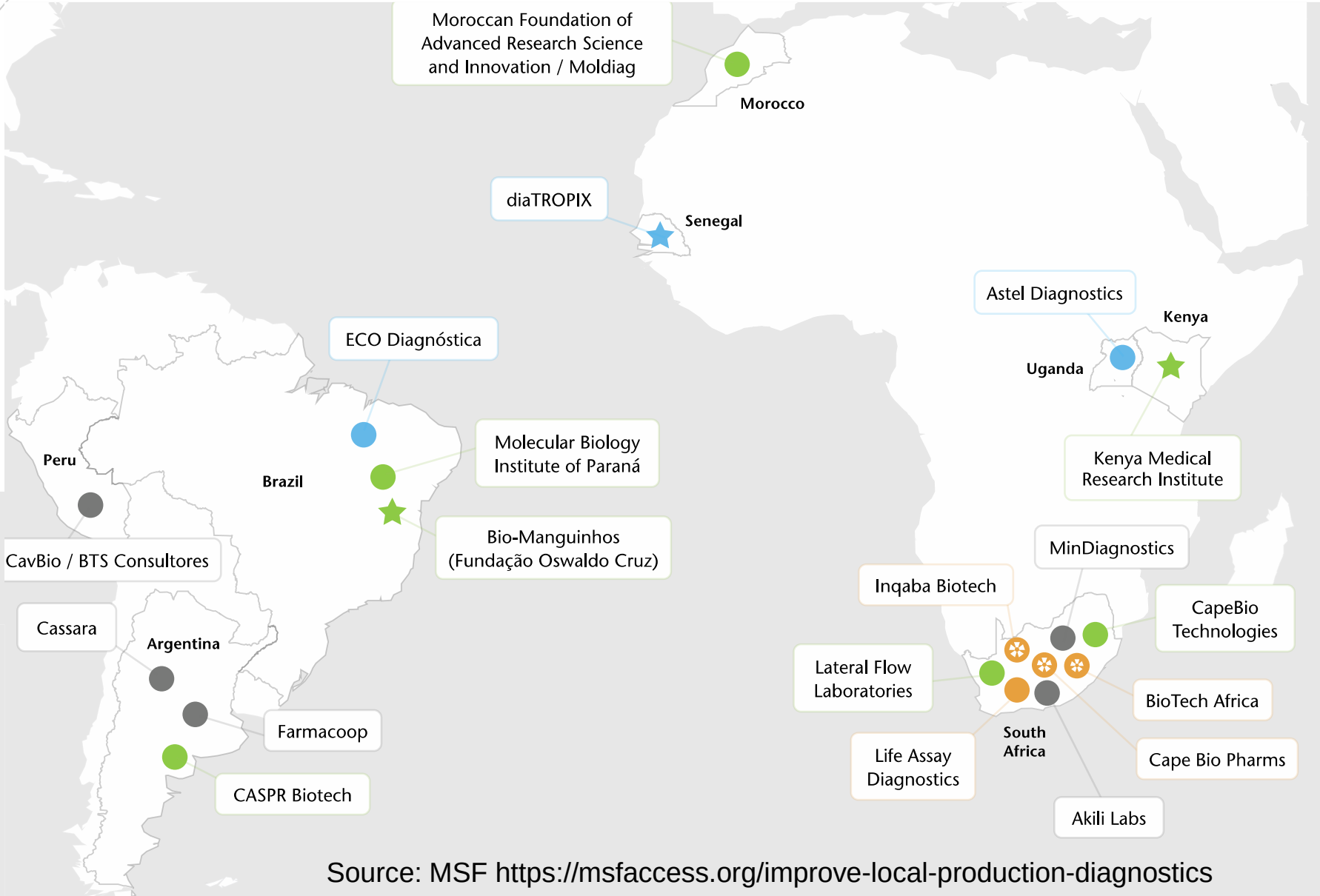
Figure 1 highlights examples of local manufacturers in Africa and South America, categorised by business model and level of local production, ranging from local assembly of imported semi-finished end products to full local production starting from raw materials, including local research and development (R&D). LMICs in any region may have limited diagnostic manufacturing capacity nationally; however, LMICs in Africa and South America were prioritised for this initial mapping given the limited local diagnostic production capacity region wide. An online supplement provides a more detailed, non-exhaustive list of manufacturers involved in technology transfer and local production of diagnostics in LMICs.[c] A second online supplement provides an analysis of global health organisations and initiatives to accelerate technology transfer and local production of COVID-19 diagnostics in LMICs.[d]

Poor access to quality-assured diagnostics is a challenge in many LMICs, in part because of the limited number of local manufacturers, leaving these countries largely reliant on imported diagnostic tests from the US, Europe and Asia. These LMICs struggle to import the tests they need to detect diseases that primarily affect LMICs, especially when only low volumes of tests are needed, for example for neglected tropical diseases (NTDs). Manufacturers in HICs and high-volume manufacturers, primarily based in China, India and South Korea, have limited interest in developing these tests or may discontinue production because of the limited market.

LMICs also struggle to import the tests they need when they are in high demand globally, leaving LMICs competing for supply with HICs that can outbid them, such as for COVID-19 diagnostics.

Continued overleaf

Local manufacturers in Africa, South America



★ Non-profit or public manufacturer

✲ The finished product is a test component, not a complete diagnostic test

Level of local production

1. Local assembly of semi-finished products
2. Local production of finished products
3. Local production of finished products and some raw materials
4. Local production of finished products and some raw materials and/or local innovation

● Level of local production unknown

Source: MSF https://msfaccess.org/improve-local-production-diagnostics

Sunday Times
Times LIVE

SOUTH AFRICA

SA company gets the green light to manufacture Covid-19 rapid test kits

It is hoped the local manufacture of the kits will reduce the reliance on imports, with positive implications for access and pricing.

Belinda Pheto
Reporter

17 August 2021 - 06:00

The South African Minister of Science, Technology and Innovation, Dr Blade Nzimande, is pleased to announce that SAHPRA (South African Health Products Regulatory Authority) has authorised local biotechnology company CapeBio to manufacture rapid COVID19 polymerase chain reaction (PCR) test kits.

- Given Africa's dependence on imports, the government, through the Department of Science and Innovation (DSI), the South African Medical Research Council (SAMRC) and the Technology Innovation Agency (TIA), led an initiative to respond to the local and continental demand for testing by setting up a fund to develop diagnostic tools, among other resources
- The kits were co-developed by CapeBio and the Council for Scientific and Industrial Research (CSIR)
- In developing the test kits, the research team had access to the CSIR's existing know-how in areas such as enzyme biomanufacturing technologies. As a result, in under a year, the team was able to deliver a COVID-19 test kit that could pass CapeBio's internal tests and external evaluation by the National Health Laboratory Service. The end result is a 100% locally developed, soon to be manufactured PCR test kit, including reagents to test for COVID-19 – a first for South Africa
- They will help to reduce South Africa's reliance on imports, making it easier for the country and the rest of the continent to gain speedy access to test kits.
- CapeBio has commenced industrial-scale manufacturing of the test kits and the first batches will be available for local market uptake before the end of August 2021.
- At full operational capacity, the company will be able to produce up to 5 000 kits a day, with each kit providing for 1 000 tests

Intellectual property & knowledge

- Codify pro-access global health policies in national & GHA law, contracts
  - Conditions for publicly supported-R&D for affordability, access, transparency, collaboration, etc.
  - Pressure social-responsible IP and open licensing or non-exclusive licensing
- Licensing hub or expansion of the Medicines Patent Pool
  Tech transfer hub
- Protect the commons of genetic sequencing

Financial support

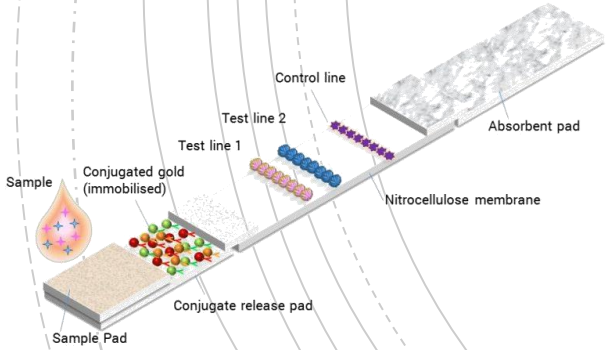
- WHO efforts should be supported
  - WHO Local Production & Assistance Unit (LPA)
    - A lack of funding for diagnostics since 2015 once funding from the Italian government ran out. So while LPA has developed a framework, it remains unpublished and has not been acted upon.
  - "WHO will need $69.54 million to implement the resolution from now to 2030. WHO already has a resource gap of $4.60 million to implement it for 2021." (Source: Devex)
- Government supported R&D and regional networks & initiatives
- Development banks: regional regulatory efforts, manufacturing hubs
- Access to Covid-19 Tools Accelerator (ACT-A)
- Unitaid
- New pandemic prevention, preparedness, & response funds & initiatives

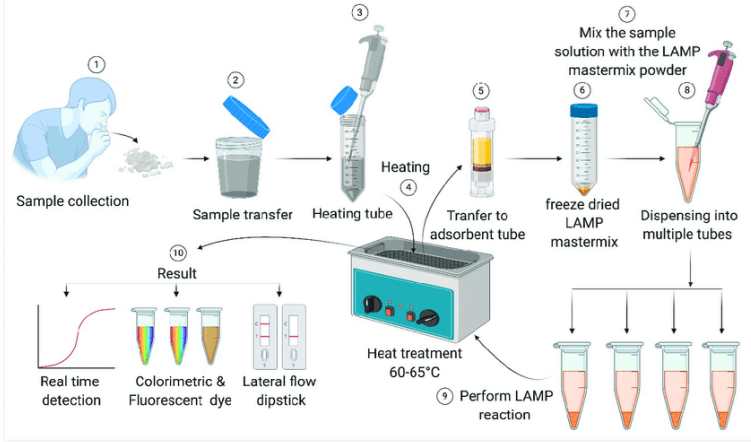
Regional coordination

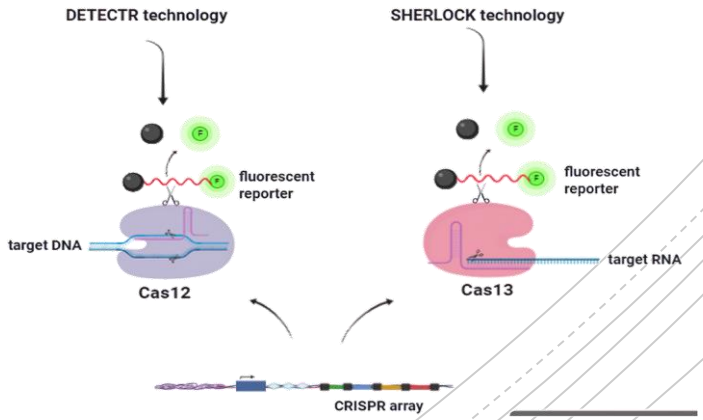
- African Medicines Agency (AMA)
  - Although the treaty to create the AMA was adopted in 2019, of 55 African countries, only 9 of the necessary 15 countries have ratified it as of June 2021, causing a delay in implementation.
  - Africa Medical Devices Forum (AMDF) already exists within the African Union, which aims to establish a harmonised framework for regulation of medical devices in Africa, including diagnostics, based on the WHO's Medical Devices Regulatory Framework Model. This sits within the African Medicines Regulatory Harmonisation (AMRH) initiative, which intends to serve as the foundation of the AMA.

Which test - Comparison of Top PoC Tests

Lateral Flow	Reverse transcription loop-mediated isothermal amplification (**RT-LAMP**)	**CRISPR – CAS**
PROS: - **Cheap to manufacture** - Easy to reverse engineer - Thermostable - Easy to use/At home application	PROS: - **Cheap to manufacture** - **Easy to reverse engineer** - Thermostable - Easy to use/At home application	PROS: - Highly sensitive and specific - **Cheap to manufacture** - **Easily customizable** - **Lab protocols published** - Thermostable - Easy to use/At home application - **Sampling flexibility**
CONS: - **Poor sensitivity and specificity** - **Not easily customizable (1 bug, 1 test)** - Sampling bias - **Sample restriction**	CONS: - **Prone to contamination/Type 2 error** - **Potential for mishandling/Lab based** - **Not easily customizable** - Sampling bias - **Sample restriction**	CONS: - Patent uncertainty







Courtesy Angelique Corthals

Sustaining local production

What commercial manufacturers need

- Access to capital
- Diagnostic tools that are affordable to make and change (including production lines)
- Access to affordable raw materials
- Access to innovation through licensing
- Access to knowledge via tech transfer hubs
- Regulatory approval
  - National or regional regulatory drug regulatory authorities
  - ISO (International Organization for Standardization) certification
  - WHO Pre-Qualification (fee structure) or Stringent Drug Regulatory Authority (SDRA)
- Access to domestic markets - 'buy local' preference in national tenders allowed markups
- Access to external markets - smart market shaping and global actors
- Commercially sustainable margins over the cost of manufacture

Sustaining local production: tech transfer hub/diagnostics facility

Developers

- Clearing house for clinical trial information
- Tech transfer hub for know-how to regional hubs
- Clearing house for open platforms (& a market for use of such platforms)
- Seeks licensing for MPP for early promising tech

Producers

- Assistance with applications for NDRA, ISO, WHO PQ
- Access to external markets (sustainable prices + incentive for WHO PQ)
- Projections of future needs and volumes
- Diversity and stability in the raw materials market
- Technical hub for sequencing data and software downloads
- Tax to pay for IEC/WHO PQ

Buyers

- Stability of supply through attracting suppliers
- Pooled volumes and negotiations across pathologies (not happening now)
- Transparent reference prices to assist with national tendering processes
- Ability to buy on credit
- Assistance with national forecasting

Sustaining local production: regulatory reform

Set Standards

-Maintain priority in vitro diagnostics lists

-Set timelines from submission to approval

-Expedite pathways for priority or emerging needs

-National Essential Diagnostics Lists (EDLs)

Harmonize & Streamline

-Regional regulatory harmonization (e.g. AMA) and SRA harmonization

-Increase use of PQ collaborative procedures and investigate novel SRA collaborative procedures

-Identify least burdensome information requirements

Strengthen & Clarify

-Clarify and disseminate national and regional regulatory requirements

-Strengthen NRA procedures, including collaborative pathways and post-market surveillance

-Support SMEs to strengthen ability to navigate regulatory requirements

-Regulatory information should be publicly available on websites

National procurement

- Quality:
  - Don’t require clinical trials in country
  - Require WHO Pre-Qualification
- Registration
  - Enrol in the WHO Collaborative Registration Procedure (CRP)
- Price
  - Waiver from national tendering processes in order to tap global markets/pools
  - Regional pooling of demand or procurement
  - Open & transparent tenders/bids
  - VAT tax waiver
- Sustainability
  - Preference for national and regional suppliers

Re-thinking diagnostics

- **Technology**: REASSURED, **open-system**, and **flexible** to respond to pathogen and disease changes.
- **Access** provisions are tied to funding and international procurement, and clear expectations are set for time to patients. Enclosure of the commons is avoided through the diagnostic facility to remove IP barriers and ensure more open R&D and access to key tools, including big data.
- **Markets:** Organized via transparency, market intelligence, and the **diagnostic facility** to improve quality, prices, and reliable supply. Local/regional manufacturers supported for sustainability.
- **Regulatory:** Clarified, **harmonized, and streamlined**, with standards to judge efficiency

What we want

- **The platforms**: Open-source (rather than closed systems), multiplex, rapid, affordable to produce & procure, adaptable, and more effective at detecting bugs, viruses, evolving strains
- **The ecosystem**: public sector (de-risking) innovation, streamlined and collaborative regulatory policies, LMICs manufacturing, non-voluntary licensing, global pooled procurement, etc.

Thank you

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