

29 June 2023

Vaccine Manufacturing in PATH

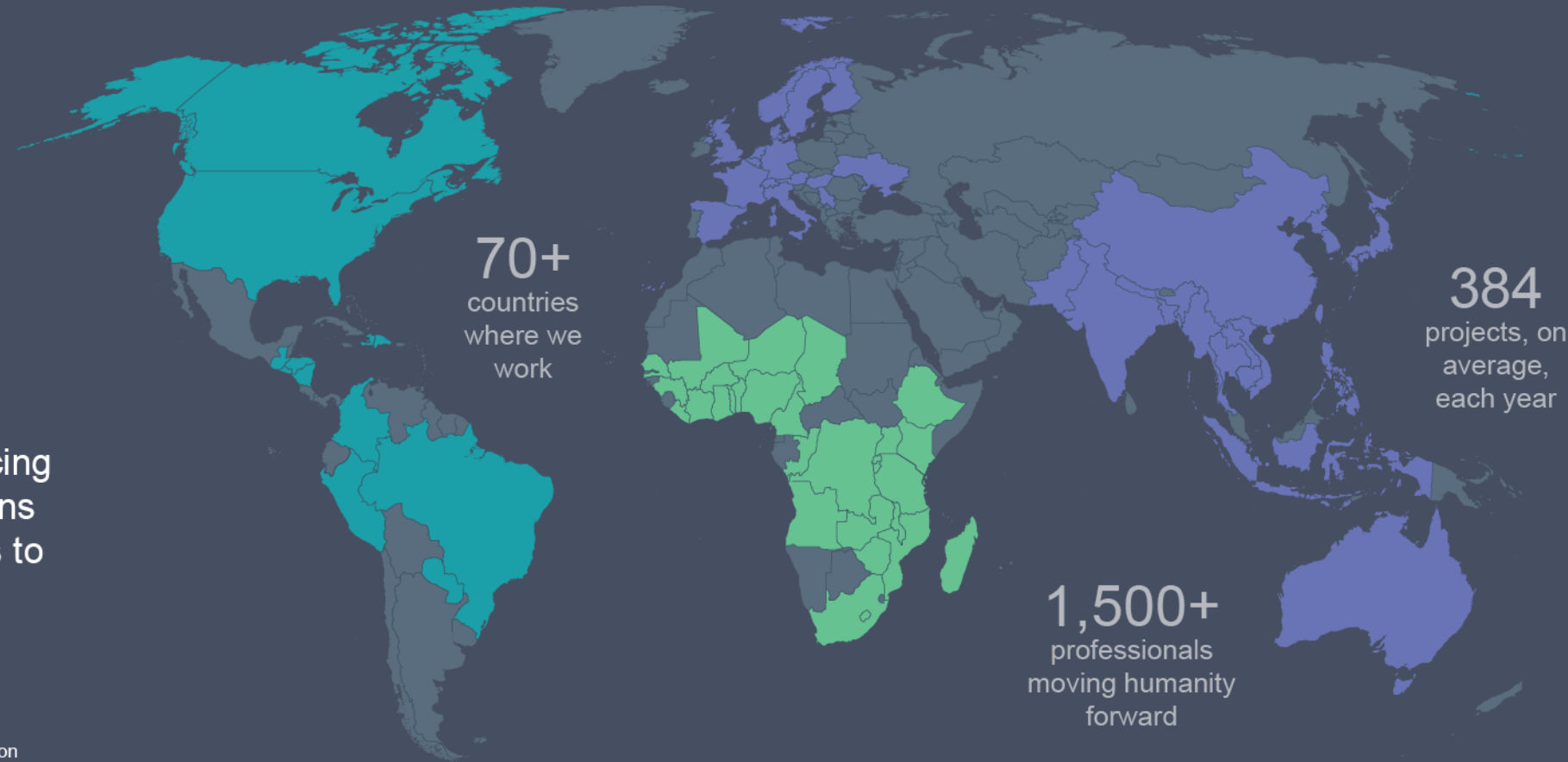
Simone Blayer, Global Head of CMC and Non Clinical
Toxicology

PATH
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PATH is a global organization working to advance health equity through innovation and partnerships.

With the help of local and global partners, PATH generates evidence, advances innovation, and strengthens local capacity to improve health in countries and communities experiencing disproportionate burdens of disease and barriers to well-being.



COUNTRIES WHERE PATH WORKS

- Africa Region
- Asia, Middle East, Europe (AMEE) Region
- Americas Region

How we improve public health

At PATH, we are constantly evolving to better meet the needs of the people and communities we serve. Over our 40+ year history, our expertise has grown broad, deep, and contextualized through local partnership and collaboration.

Capacities

- Advocacy and public policy
- Diagnostics
- Digital health and data systems
- Epidemic and pandemic preparedness and response
- Health system strengthening
- Infection prevention and control
- Market development
- Medical devices and health technologies
- Modeling and analytics
- Monitoring and evaluation
- Primary health care
- Public health and science communications
- Vaccines

Health Areas

Infectious Disease

- Antimicrobial resistance
- COVID-19
- Diarrheal disease
- Ebola
- HIV/AIDS
- Human papillomavirus
- Influenza
- Japanese encephalitis
- Malaria
- Measles
- Meningitis
- Neglected tropical diseases
- Pertussis
- Pneumonia
- Polio
- Respiratory syncytial virus
- Tuberculosis
- Yellow fever

Noncommunicable Disease

- Cancer
- Diabetes
- Heart disease
- Hypertension

Prevention and Promotion

- Early childhood development
- Maternal and newborn care
- Nutrition
- Public health and science communications
- Sexual and reproductive health

PATH's Center for Vaccine Innovation and Access (CVIA)

CVIA accelerates the development and delivery of lifesaving vaccines for the most vulnerable children and communities around the world. We focus on deadly and disabling diseases that pose the greatest threats to long-term health and development.

Our functional capabilities include:

- Clinical
- Regulatory
- Manufacturing and supply
- Quality assurance/quality control
- Pharmaceutical and vaccine technology
- Integrated portfolio and financial management
- Policy, access, and introduction
- Preclinical and nonclinical R&D
- Alliance management

DISEASE AREAS

Enteric and Diarrheal Diseases

rotavirus • enterotoxigenic *Escherichia coli* •
Shigella • typhoid

Malaria

Plasmodium falciparum • *Plasmodium vivax*

Polio

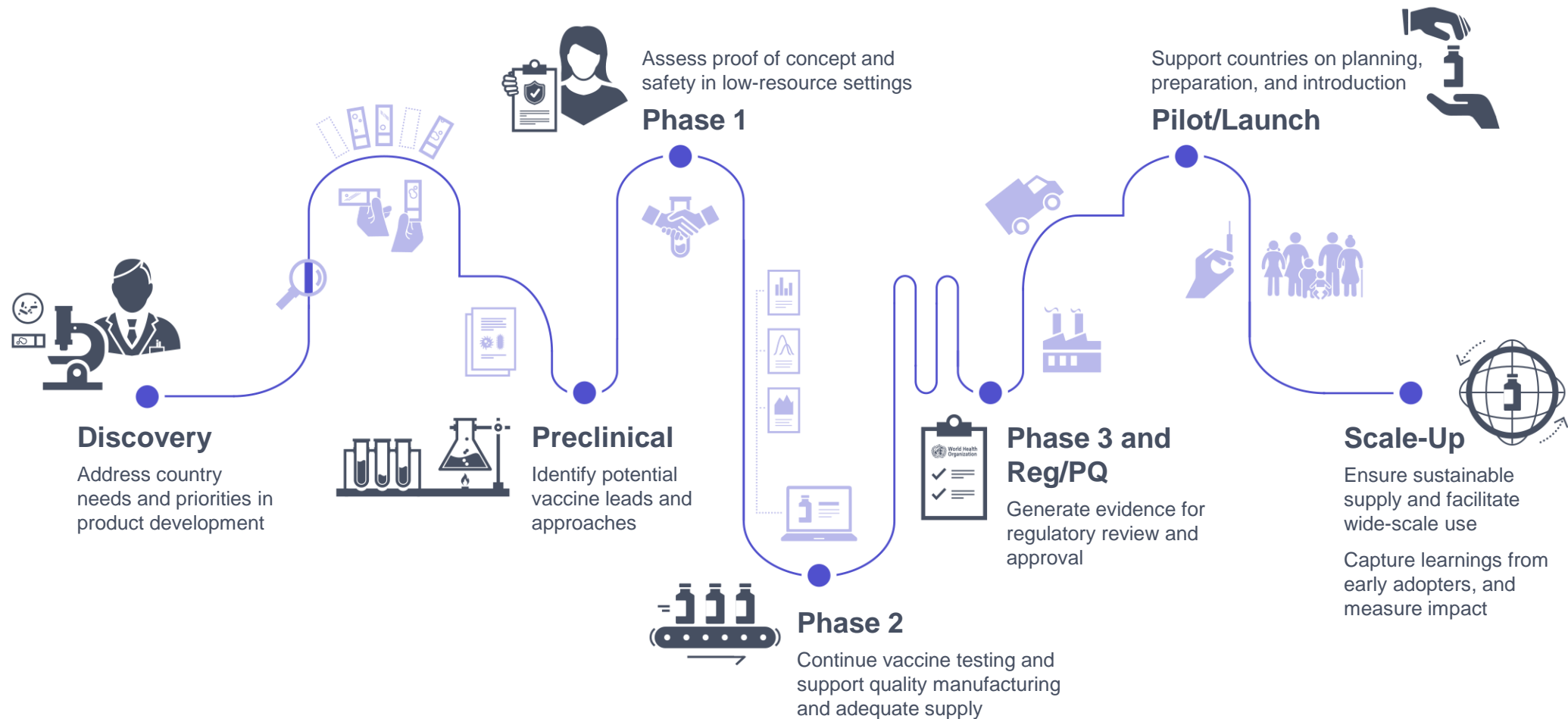
Respiratory Infections and Maternal Immunization

pneumococcus • meningococcus • group B *Streptococcus* •
pertussis • influenza • respiratory syncytial virus

Zoonotic, Emerging, and Sexually Transmitted Infections

human papillomavirus • Japanese encephalitis • Nipah •
yellow fever • COVID-19 • outbreaks

CVIA's work spans the entire vaccine development and delivery lifecycle across five disease areas



Vaccine manufacturing at PATH: Chemistry, manufacturing, and controls (CMC)

CMC plays a pivotal role in the development, licensure, manufacturing, and ongoing monitoring of new and improved vaccines by ensuring product consistency and quality.

As part of CVIA, the CMC team provides capacity bridging support for vaccine manufacturers to ensure life-saving vaccines can be widely available to communities across the world.

Support for CMC partners

- For more than a decade, we've worked with vaccine manufacturers in low- and middle-income countries (LMICs) to address challenges in achieving their production objectives and milestones.
- We regularly works with manufacturing partners, funders, and other organizations to determine how we can best support their needs.

An experienced global team

- We are scientists, engineers, and quality, regulatory, and logistics specialists, with broad domain expertise across all platforms and aspects of vaccine manufacturing.
- We have a successful track record of productive and collaborative partnerships that have moved vaccines from early phase development to commercial licensure.

Project Management

PA

Analytical

Program
Lead, Fill
Finish

Finance

Conjugation

Missing:
Cindy (Finance)
Bia (Supply chain)
Guang (Quality)
Kutub (Virology)

Assay Dev
Formulation

Polio, MAbs

Talent Dev

Washington DC, Summer 2022

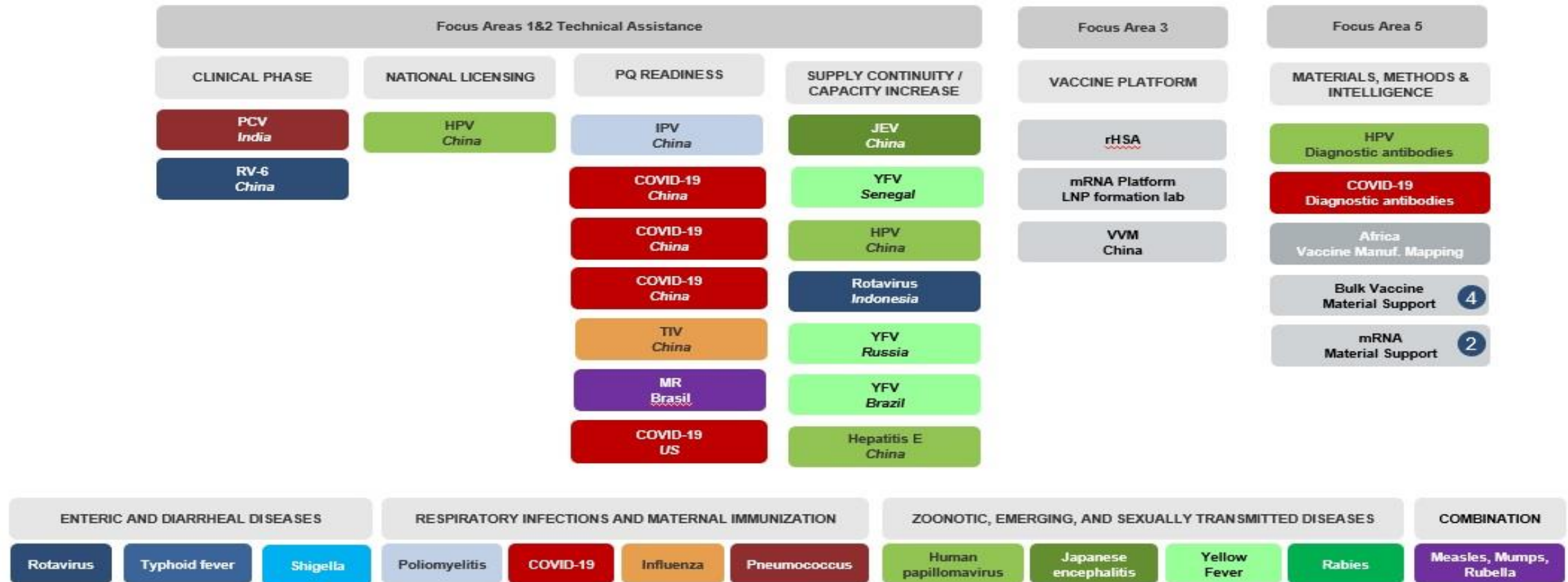


Geneva, Switzerland Feb 2023
The COVID Meeting

PATH CMC's vaccine domain experience

<p>Analytical</p> <p>Analytical methods development <i>In vitro</i> potency development and validation In-process assays Animal immunogenicity testing Reagent generation and screening Potency method transfer Extractables and leachable studies</p>	<p>Drug substance & drug product</p> <p>Process development Formulation development GMP manufacturing Upstream and downstream purification Scale up Yield improvement Cell banking Technology transfer Process validation Fill/finish Technology transfer Gap assessment Adjuvants</p>	<p>Logistics & supply chain</p> <p>Logistics advice Supplier research/identification Distribution planning and risk mitigation</p>
<p>CMC Regulatory</p> <p>Regulatory strategy (WHO, US FDA, China NMPA) WHO prequalification of viral vaccines Country registration</p>	<p>Facilities</p> <p>Facility design Equipment qualification Process validation</p>	<p>Management & strategy</p> <p>Global access strategy CMC project strategy Project management and leadership Partnership development Management of process and methods for technology transfer CMC landscaping assessments</p>
<p>Due diligence & audit</p> <p>GMP compliance Quality audit Quality by design Project risk assessments Root cause investigations</p>	<p>Nonclinical toxicology</p> <p>Preclinical and GLP toxicology study design IND-enabling toxicology studies in animals</p>	<p>Technology & platforms</p> <p>Recombinant protein cell culture Subunit Bacterial fermentation Cell culture Live and inactivated viral manufacturing mRNA vaccines Conjugate vaccines Egg-based vaccines Antibodies</p>

Sustaining Vaccine Manufacturers: A BMGF program to provide technical assistance to LMIC manufacturers of high-value, high-impact vaccines



*Portfolio snapshot current as of April 2020; does not include new/proposal development work on SARS-CoV-2

Case Study: Sustainable Vaccine Manufacturing in Africa: Estimating Capacity Needs



Partnerships for African Vaccine Manufacturing (PAVM) Framework for Action



2022 (Version 1)

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Propelling Africa toward manufacturing self-reliance

In 2021, the African Union and the Africa Centres for Disease Control and Prevention established the Partnerships for African Vaccine Manufacturing (PAVM) to “**ensure Africa has timely access to vaccines to protect public health security, by establishing a sustainable vaccine development and manufacturing ecosystem in Africa.**”

The [PAVM Framework for Action](#) (FFA), a blueprint for how to accelerate local manufacturing in a coordinated way, sets the goal of **manufacturing 60% of Africa’s immunization needs on the continent by 2040.**

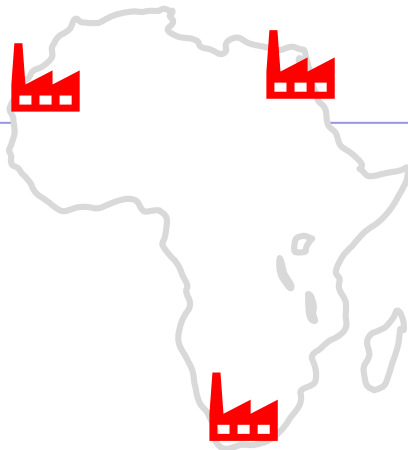
We’re working with Coalition for Epidemic Preparedness Innovations, KU Leuven, and PAVM to develop resources that identify existing and needed manufacturing capacity in Africa.

Funding support is provided by the UK Foreign, Commonwealth & Development Office and the Bill & Melinda Gates Foundation.

What resources do we need to advance sustainable manufacturing?

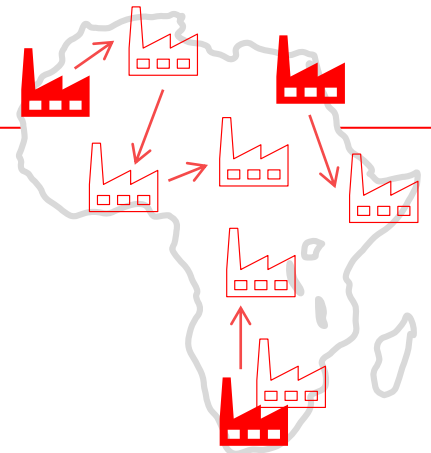
Current state map

Identifies the existing vaccine manufacturing capacity on the African continent.



Future state model

Identifies the capacity necessary to establish a sustainable vaccine development and manufacturing network in Africa.



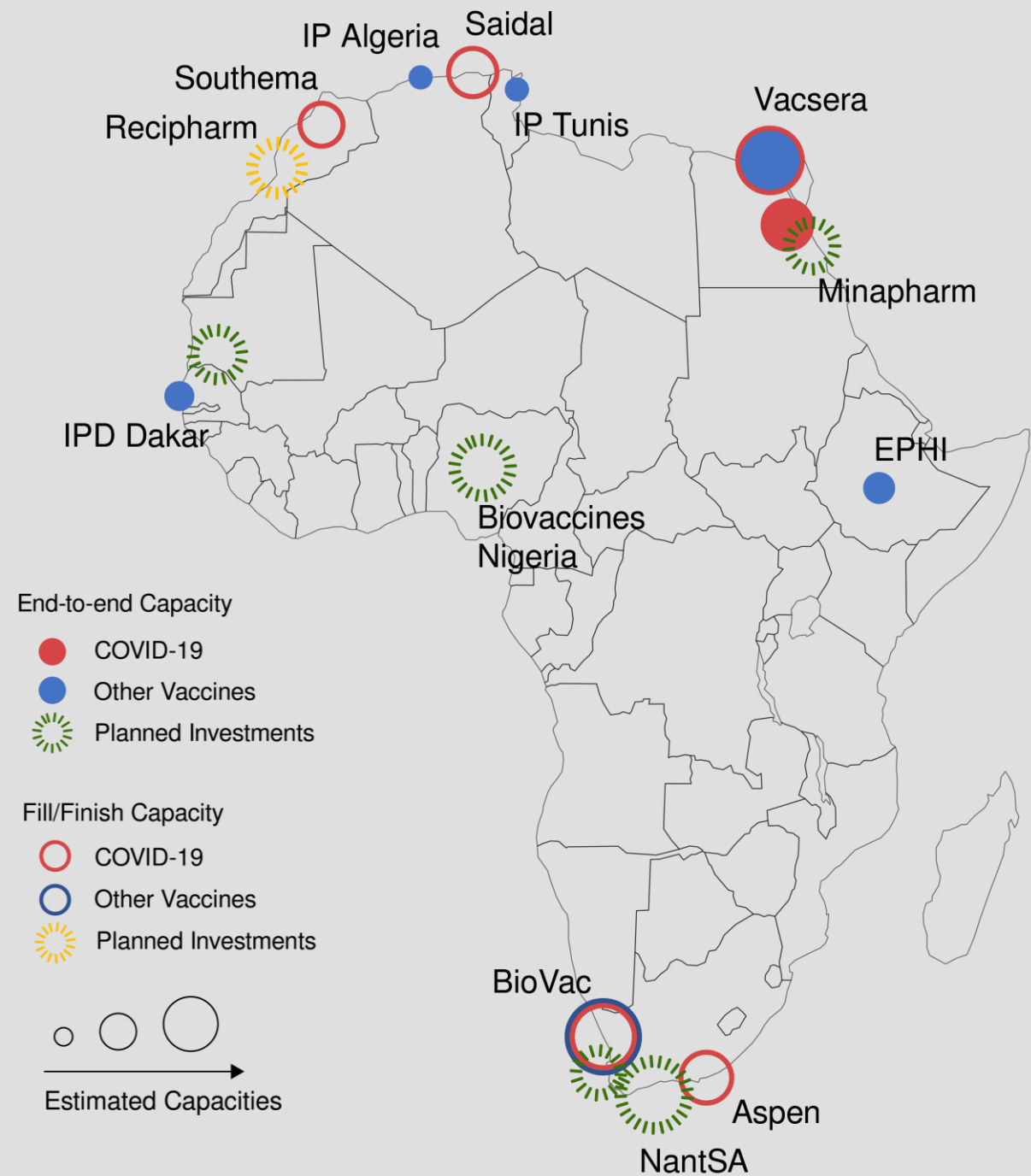
Current African vaccine manufacturing is limited by location, capability, and capacity

The current African vaccine manufacturing landscape is **mostly focused on fill/finish of COVID-19 vaccine.**

Per a 2021 CEPI survey and public data available, Africa is home to six vaccine manufacturers, mainly located in North Africa and South Africa. These manufacturers produce and distribute legacy vaccines.

Planned fill/finish capacity committed in 2022 exceeded 500 million doses per year and was **clustered in North and South Africa.**

- Manufacturers in South Africa, Morocco, and Egypt have already started, or will soon start, fill/finish activities.
- The capacity dedicated to vaccines could be increased by some manufacturers, should the opportunity arise; however, some facilities are not equipped to manufacture viral vaccines.
- Potentially, when the COVID-19 emergency ends, the fill/finish capacity could be transitioned to manufacture different vaccines.

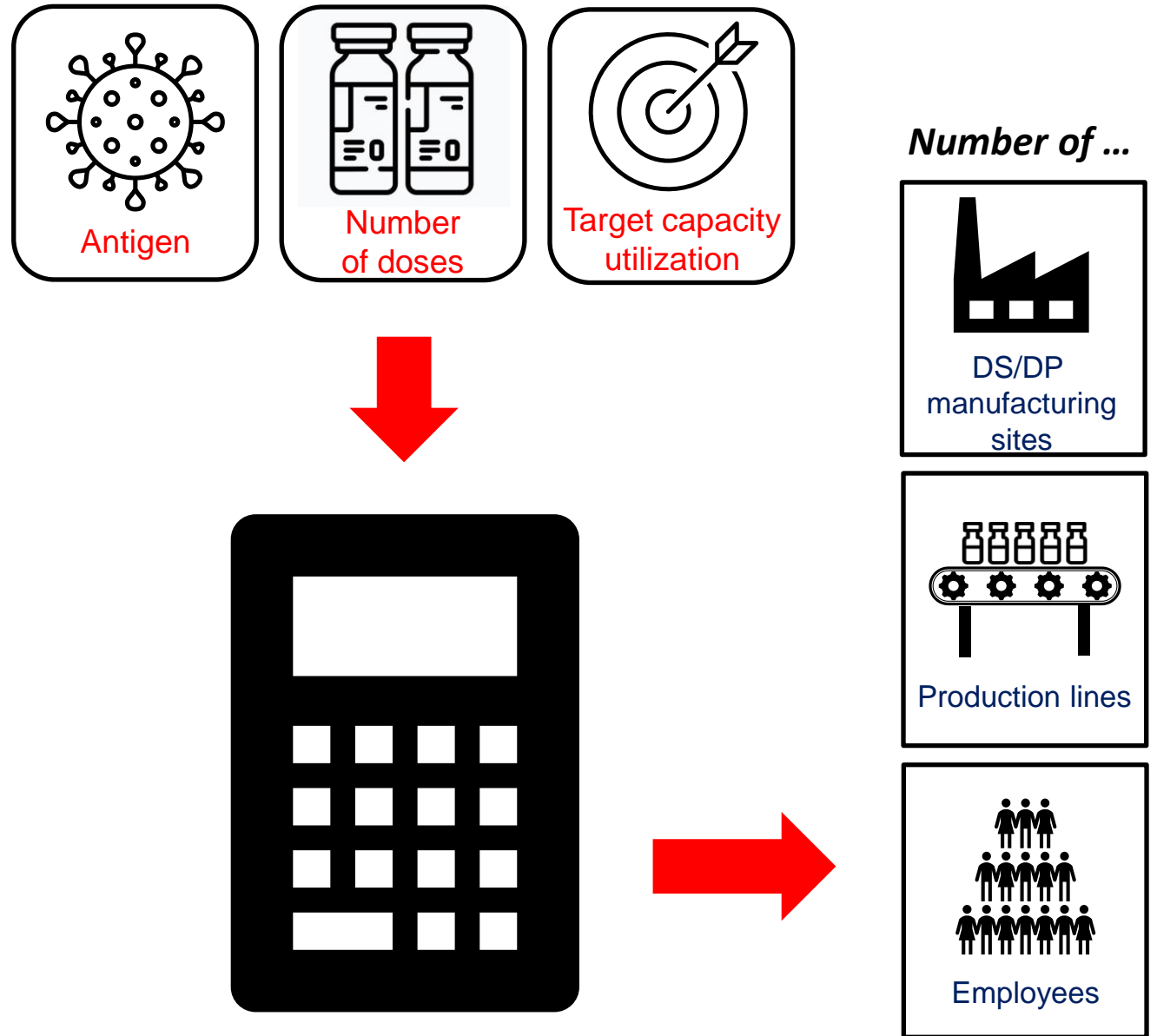


The future state model

The future state model estimates the manufacturing capacity and capabilities needed to produce enough doses of a given vaccine to meet the PAVM 2040 target demand.

For example: If African vaccine manufacturers are currently producing 5 million doses of pneumococcal vaccine annually but need to produce 140 million doses annually to meet the PAVM target, our model estimates the number of DS and DP production sites, production lines, and employees needed to meet that goal.

The model provides estimates for 15+ priority vaccines.



Determining how to combine facilities give us our first estimation of how many sites and employees are needed to fulfill the PAVM goal

Estimated number of sites	Vaccine(s) produced at site	Estimated total employees
1	Tetanus, Diphtheria, Pertussis, Hep B (DS only)	966
1	TT carrier, PRP (no conjugation) (DS only)	1183
1	IPV (DS only)	1436
1	PRP-T conjugation (DS), Hexa (DP)	1275
1	Measles-Rubella	1675
1	Rotavirus (DS & DP), Cholera (DP)	578
1	Pneumococcal (DS & DP), Meningococcal (DP), Typhoid (DP)	750
1	COVID-19 subunit protein, HPV	939
1	COVID-19 mRNA, HIV	670
1	COVID-19 viral vaccine	546
1	BCG	640
1	Malaria	1229
12 sites total		Approx. 12,000 total employees

Important: Site sizing is based on baseline capacity estimations, not model-adjusted capacities

Notes:
 1. Pandemic flu, Ebola, Chikungunya, Rift Valley, and Lassa Fever vaccines will be merged with an existing facility with similar technology
 2. Yellow Fever was excluded from the modelling as scale up of Yellow Fever production is already ongoing (IPD Senegal)



Where do we go from here?

The current state map and the future state model are huge steps forward, but the work doesn't end here. Both must be maintained and refined to ensure their use over time.

Current state map next steps:

- Together with CHAI, conduct visits to African manufacturers to **assess current and future vaccine capacity**, as well as identify commercial challenges to manufacturers' operations.

Future state model next steps:

- Perform new simulations with refined data to **update network estimations**.
- **Make model data available** to PAVM workstreams, local African vaccine manufacturers, and other stakeholders.

Our work on this project is planned to be complete in **September 2023 at the DCVMN Meeting in Cape Town.**



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