mRNA TECHNOLOGY TRANSFER & TRAINING HUB

The African Growth and Opportunity Act (AGOA) CIVIL SOCIETY NETWORK

7th ANNUAL AGOA CSO NETWORK SPRING CONFERENCE

U.S. - Africa Trade and Investment: Current Threats, Challenges, and Opportunities
mRNA Hub design and objectives

Hub and Spoke model: a global network

The fast changing landscape of vaccine innovation in Africa

Success is not singular
Strengthening Africa’s vaccine manufacturing capacity through the South African mRNA technology transfer hub

A need for equity in access to COVID-19 vaccines
Similar to previous pandemics, COVID-19 has underscored (yet further) that gross inequity exists in relation to access to health products, especially vaccines. As of November 22nd, 2021, more than 7.71 billion vaccine doses have been administered globally, but about 74% have gone to high- or upper-middle income countries; while 7 in 10 people in North America have been vaccinated, only 1 in 10 people have been vaccinated in Africa.
OVERVIEW OF PROJECT STATUS AND SUMMARY OF COMMUNICATIONS TO DATE

2021

April 16th

WHO call for EOI to contribute by providing technology or hosting a hub, or One or more technology transfer hub(s) Will expand to other technologies in the future

June 21st

French President, SA president & WHO DG announcing establishment of SA mRNA hub

July 7th

Vaccine Manufacturing Working Group Proposed network could include additional hubs (3 to 6 in total), ensuring global coverage and training for spokes with different degrees of support

September 21st

WHO/PAHO announce selection of Argentina and Brazil as spokes in LatAm First hub is being set up in South Africa And this will start happening from the beginning of 2022

2022

November 10-11th

WHO call for EOI for additional spokes of SA mRNA and call for EOI to establish workforce training hub

February 18-25th

WHO announce selection of Egypt, Kenya, Nigeria, Senegal, South Africa and Tunisia and Bangladesh, Indonesia, Pakistan, Serbia and Vietnam as spokes

March 7-9th

Afrigen receives first spokes for training at lab-scale: Argentina & Brazil

Parallel initiative

BioNTech announced plan to develop capacity to produce mRNA Vx in Rwanda Senegal

Moderna announced ambition to build a mRNA facility in Africa

NantAfrica announced launch of prod. center in SA

Seeking interest from manufacturers elsewhere (i.e. low- or middle-income countries not in PAHO) Provide training on general biomanuf. processes in an industrial-type setting

WHO announce establishment of global biomanufacturing training hub in Republic of Korea

Global mRNA Technology Transfer and Training Hub
“The mRNA technology transfer programme is a global initiative to improve health and health security by establishing sustainable, locally owned mRNA manufacturing capabilities in and for low- and middle-income countries (LMICs). Its core concept is empowerment.

The hub at Afrigen, in South Africa, will transfer technology for COVID-19 vaccines and other mRNA products to 15-20 “spokes” in LMICs for commercial production creating a mega network of vaccine manufacturing capacity across LMICs. This programme will contribute to future pandemic preparedness in LMICs.”

In support of a sustainable initiative the WHO is further supporting the programme through a biomanufacturing workforce training hub, located in South Korea, and regulatory training and strengthening.
mRNA HUB NETWORK OF SPOKES (April 2022)
mRNA Vaccine Technology

### NON-LIVE
- No live pathogens
- Sequence specificity
- Flexible product design
- Well characterized

### SAFETY
- RNA does not integrate into the host genome and is degraded once the protein is made

### IMMUNOGENICITY
- Induces potent humoral and cell-mediated immune responses
- Self-adjuvanting

### MANUFACTURING
- *In vitro* transcription
- No cell culture
- Scalable to large capacity

---

SANOFI PASTEUR

*severe acute respiratory syndrome coronavirus 2, (SARS-CoV-2)*
mRNA Vaccine

**Components**
- mRNA (blueprint of protein)

**Production**
- Faster because mRNA molecules are easier to produce

**Process**
- Components are injected into the arm and serve as instructions for the body to make microbial protein

**R & D**
- Antigen determined for immune stimulation

**Result**
- Teaches the body to protect itself against a microbe

Traditional Vaccine

**Components**
- Microbial protein or inactive microbe

**Production**
- Slower and more difficult to produce the right type of protein

**Process**
- Components are made in a lab and injected into the arm to stimulate immune response

Vanderbilt Vaccine Research Program | Vanderbilt Institute for Infection, Immunology and Inflammation
Pfizer-BioNTech COVID-19 Vaccine
WHAT’S IN IT AND WHY?

**Active Ingredient**

mRNA encoding the viral spike glycoprotein (S) of SARS-CoV-2

RNA is a template to produce a single specific protein.

In the vaccine, this is the message for our cells to produce the viral protein that will trigger the immune response to the virus.

**Lipids**

4 different fatty molecules (some with long names)

They form a protective capsule around the RNA.

This aids in delivery of the RNA, as well as protects the RNA from degradation (RNA is very unstable).

**Salts**

4 different salts

These buffer the vaccine to stabilize the pH, so that it matches the pH in our bodies.

**Sugar**

Sucrose

This is a cryoprotectant. It ensures the lipids don't get too sticky at the extremely cold storage temperatures.
GREENFIELDS: mRNA Hub forward innovation process of a mRNA vaccine

<table>
<thead>
<tr>
<th>PROCESS &amp; PRODUCT DEVELOPMENT</th>
<th>HUB MEMBERS</th>
<th>SCALE</th>
<th>PLASMID DESIGN &amp; CLONING</th>
<th>PLASMID PRODUCTION</th>
<th>mRNA SYNTHESIS</th>
<th>mRNA PURIFICATION</th>
<th>LNP FORMULATION</th>
<th>FILL &amp; FINISH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmid production</td>
<td>AFRIGEN AGTRU-WITS</td>
<td>µL – mL</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>mRNA synthesis via IVT &amp; capping</td>
<td>AFRIGEN CeBER-UCT</td>
<td>mL – 30-50 L</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Purification of mRNA</td>
<td>BIOVAC</td>
<td>≥50 L</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

- RNA structure improvement
- Cell-based: E.coli platform
- Cell-free (enzymatic) synthesis
- Encapsulation technology
- Liquid dosage form
- Novel lipids
- Reference product (mRNA-1273)
- Next-gen product

PRE-CLINICAL screening, safety & toxicity
CLINICAL TRIALS
Reference product
Next-gen product

<table>
<thead>
<tr>
<th>HUB MEMBERS</th>
<th>SCALE</th>
<th>PLASMID DESIGN &amp; CLONING</th>
<th>PLASMID PRODUCTION</th>
<th>mRNA SYNTHESIS</th>
<th>mRNA PURIFICATION</th>
<th>LNP FORMULATION</th>
<th>FILL &amp; FINISH</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFRIGEN AGTRU-WITS</td>
<td>µL – mL</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>AFRIGEN CeBER-UCT</td>
<td>mL – 30-50 L</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>BIOVAC</td>
<td>≥50 L</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

- TRAINING
- VIRTUAL
- HANDS-ON (small scale)
- HANDS-ON (Large scale)
Lots of players catching up with the leaders – some improved 2nd generation technologies

1. Best view from Adis as of 2021. Note: Overview of mRNA Vaccines by development stage; Imperial College taken out based on clinical results; Various indications in Phase I: Respiratory syncytial virus infections, Metapneumovirus infections, Cytomegalovirus infections, Rabies; Various indications in Preclinical: Influenza, Cancer, Multiple sclerosis, Epstein-Barr virus infections, HIV infections, Nipah virus infections, Lassa fever, Yellow fever. Source: ADIS
SUCCESS IS NOT SINGULAR
QUO VADIS AFRICA?
60 PERCENT OF VACCINE NEEDS PRODUCED LOCALLY BY 2040!!!

PAVM Framework for Action
Overall summary of the continental strategy

1. Potential disease prioritisation

Prioritized 22 diseases...

<table>
<thead>
<tr>
<th>Legacy</th>
<th>Expanding</th>
<th>Outbreak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>HPV</td>
<td>Ebola</td>
</tr>
<tr>
<td>Whooping Cough</td>
<td>HIV</td>
<td>Chikungunya</td>
</tr>
<tr>
<td>Malaria</td>
<td>Cholera</td>
<td>Lassa fever</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Typhoid fever</td>
<td>Rift valley fever</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Pneumococcal</td>
<td>Influenza</td>
</tr>
<tr>
<td>Measles</td>
<td>COVID-19</td>
<td>Disease X</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>Rotavirus</td>
<td></td>
</tr>
</tbody>
</table>

... requiring a breadth of technology platforms...

2. Technology focus

- Traditional: Live attenuated, Inactivated virus, Subunit
- Innovative: Virus-like particle, Viral vector, RNA/DNA

3. Potential value chain focus

- Fill & Finish: Focus on highest volume vaccines (vaccine and modality agnostic) for economies of scale with potential for Africa to become cost-effective vis-à-vis other DCVM
- Drug Substance: Expand drug Substance mostly in established platforms where tech transfers are readily available; manufacturing will likely require developing a local raw materials industry
- R&D: Create regional R&D hubs to support more efficient manufacturing, improve vaccine characteristics and consider research centers to develop new vaccines for Africa
The ABCs of DIY vaccines: Why tech transfer is a big thing

By Adèle Sulcas and Linda Pretorius - November 18, 2021

A is for access
B is for building a vaccine
C is for capacity and continuity (REGULATORY KEY)
### COVID 19 TSUNAMI – TECHNOLOGY TRANSFER CHANGING LANDSCAPE

**Since 2020**

<table>
<thead>
<tr>
<th>COVID-19 vaccine</th>
<th>Africa partner</th>
<th>International partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria</td>
<td>GROUPE Saida</td>
<td>Sputnik V</td>
</tr>
<tr>
<td>Egypt</td>
<td>EVAPhoma</td>
<td>AstraZeneca</td>
</tr>
<tr>
<td>Morocco</td>
<td>PHARCO</td>
<td>sinovac</td>
</tr>
<tr>
<td>Senegal</td>
<td>Jothesma</td>
<td>Recipharm</td>
</tr>
<tr>
<td>South Africa</td>
<td>BIOVAC</td>
<td>UNIVERCELS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Johnson &amp; Johnson</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pfizer</td>
</tr>
</tbody>
</table>

**Before 2020**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>African partner</th>
<th>International partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV vaccine</td>
<td>South Africa</td>
<td>BIOVAC</td>
</tr>
<tr>
<td>Hexaxim vaccine</td>
<td>South Africa</td>
<td>BIOVAC</td>
</tr>
<tr>
<td>Pentavalent vaccine</td>
<td>Egypt</td>
<td>VACSEA</td>
</tr>
</tbody>
</table>

**mRNA Tech Transfer Hub**

South Africa

- AfriGen
- saMRC
- BioVac

- World Health Organization
- Medicines Patent Pool

---

Transfer included more upstream process steps (e.g. drug substance)
**Executive Summary (1/3)**

**Tech-transfers:** Viral Vector has been the most transferred vaccine platform for facilitating local vaccine production since the start of the pandemic.

- 113 Covid-19 vaccine technology transfers have been identified as of March 2022, including 19 transfers to Africa, 51 to Asia, 14 to Latin America, and 9 to the Middle East.

- The Gamaleya Research Institute’s Viral Vector and AstraZeneca’s Viral Vector have been the most outsourced Covid-19 platforms.

- For fill-finish production and end-to-end production, inactivated and mRNA platforms are also popular.

- African technology transfers have mainly been for fill-finish, Asia for end-to-end production, and the Middle East and Latin America for fill-finish/end-to-end production.

---

**Top 12 identified sources of TTs as at Mar 2022**

- **Protein Subunit**: CanSino
- **Conjugate**: ICGEB, SDN Bio
- **DNA**: Pfizer BioNTech, Bharat Biotech, Novavax, Sinovac
- **Protein subunit**: Sinopharm
- **Inactivated**: AstraZeneca
- **Viral vector**: Gamaleya

---

Source: Airfinity [Link]; Chart uses data from CHAI’s “LVM-Landscape-Baseline-March-01-2022” database of LVM commitments; CHAI staff calculations.
SUCCESSFUL VACCINE INNOVATION IN AFRICA WILL REQUIRE IP SYSTEMS REFORM
Increase in launched initiatives with varying tangibility

**Tunisia**
- Announced ambition to establish Vx production unit with Japanese partners
- Recipharm F&F capacity development incl. for mRNA Vx ($500M investment, 300M capacity, pledged start in 2023)
- Sothema & Sinopharm for Covid-19 F&F (60M capacity)
- RDIF* to fund Galenica for production options of Sputnik V

**Morocco**
- Advanced projects with COVAX partners
- Sothema & Sinopharm for Covid-19 F&F (60M capacity)
- RECIPHARM to develop capacity by end of 2022

**Senegal**
- IFC2, Universcells and Team Europe funding the building a COVID-19 Vx manufacturing facility, starting with packaging, with Institut Pasteur de Dakar (IPD) ($220M investment, 300M capacity by end of 2022)
- BMGF3 funding IPD to develop short-medium-long term strategy as well as set up Delivery Unit and build capacity to contribute to vaccine security on the continent ($5M investment)

**Nigeria**
- Plan to establish a Biovaccines F&F facility then move up the value chain ($30M investment, capacity to vaccinate 10M people)
- Afreximbank to fund the development of infrastructural facilities like hospitals, vaccine production with Gateway Pharmaceuticals ($200M investment in total)

**Ghana**
- Plan to establish a national vaccine institute to develop and manufacture Vx ($20M investment) and to source additional private capital for the project (incl. promoting a viable venture and reaching out to stakeholders like GAVI, CEPI, UNICEF and WHO, as well as Africa Union and European Union)
- Government to invest $900M to establish local Vx plants, incl. potentially partnerships with DEK Vaccines to use F&F capabilities or IDT Biologika for Covid-19 Vx, and in the longer term other Vx, incl. EPI-managed or Atlantic LifeSciences to install a F&F plant
- Early engagements in the Phyto-Riker-ASPEN pharmaceutical partnership (collaboration with J&J)

**Rwanda and Senegal**
- BioNTech announced plan to develop capacity to produce upcoming mRNA-based vaccines (50M, pledged start in 2022 for Covid-19, then moving to Tuberculosis and Malaria)

**South Africa**
- mRNA tech transfer hub
- Aspen & J&J for Covid-19 F&F ($710M investment, 300M capacity, started in 2021, plan to boost capacity by a further 200M doses)
- BioNTech & Biovac for mRNA Covid-19 F&F (100M capacity, start in 2022)
- Patrick Soon-Shiong launched a production center in SA of Covid-19 2nd generation mRNA Vx with his company NantAfrica and ImmunityBio, in collaboration with SA CSIR, CERI, SAMRC, and SA universities. Plan to expand in Botswana, Ghana, Kenya and Uganda and work on cancer, TB and HIV (first doses planned in 2022 for CTs)

**Algeria**
- Saidaal & Sinovac for Covid-19 F&F (200M capacity, started in 2021) then move up the value chain

**Egypt**
- Egy Vac (Vaccera) & Sinovac for Covid-19 F&F (200M capacity, started in 2021), plan to boost capacity with a new F&F facility (1B capacity, pledged start in November 2021)
- RDIF* to fund Minapharm for production of Sputnik V (400M doses capacity)
- Pharco announced partnerships to produce Sinovac Covid-19 Vx (20-60M pledged start in 2021), and Sputnik V funded by RDIF* (2SM pledged start in 2021)

**Kenya**
- Establishing a F&F facility for COVID-19 Vx then moving up the value chain to set up an end-end manufacturing plant (pledged start in 2022)

**Tanzania**
- Health Permanent Secretary announced plans to establish local manufacturing of Vx for Covid-19 and other diseases to reduce importation costs

CONTRIBUTION AND RECOGNITION

WHO
Medicines Patent Pool (MPP)
University of the Witwatersrand
SA Government DSI
AU and Africa CDC (PAVM)
SAMRC
Biovac
PATH
Independent specialists and advisors
Civil Society Groups
Funders: France, Belgium, Germany, Norway, Canada, South Africa, EC.

Afrigen Team and Shareholders