

## Supporting South Africa's Vaccine Production Hub

Report on kENUP Foundation Mission  
to the Republic of South Africa  
held between August 11 and 14, 2021

*South Africa is setting up a global manufacturing hub for contemporary vaccines and other biologicals, starting with COVID-19 vaccines.*

### Preamble

The COVID-19 pandemic made visible the dependency of many countries, especially in the Global South, on a small number of vaccine producing countries:

- Globally, only a few countries are responsible for the bulk of COVID-19 vaccine exports. Meanwhile, it is widely recognized that vaccines are distributed unevenly.
- High income countries have multiple times the number of vaccines doses per inhabitant available to them compared to low- and middle-income countries (LMICs). Only 1.6 percent of people in low income countries have received at least one dose of COVID-19 vaccine.
- In the international community, the realization is growing that decentralized production is vital. Dr Tedros Adhanom Ghebreyesus, Director-General of WHO stated that “vaccine equity is the challenge of our time, and we are failing”.

In May 2021, WHO recognized the importance of producing locally by adopting the resolution ‘Strengthening local production of medicines and other health technologies to improve access’ calling for local manufacturing of vaccines. In parallel, WHO is initiating several Tech Transfer Hubs on the African continent.

Following the summit on vaccine manufacturing organized by the AU, the Africa CDC has launched the Partnerships for African Vaccine Manufacturing (PAVM) Task Force with a

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clear mandate, operating model, and governance structure to enable sustainable African vaccine manufacturing.

kENUP supports companies and governments in this important effort.

## **Situation**

To address a critical unmet need, the Republic of South Africa is setting up a pan-African manufacturing hub for contemporary vaccines, starting with vaccines against COVID-19. The project is managed by the Presidency, and led by the Department of Science and Innovation, receiving notable support from the Ministry of Health and other competent public authorities as well as from corporations and academia.

Until about twenty years ago, South Africa has been a producer of vaccines through the State Vaccine Institute (among others, BCG, rabies, smallpox), SAIMR/SAVP (among others, polio, cholera, typhoid), and the National Institute for Virology (OPV, yellow fever). Vaccine production skills were lost as all operations ceased in 2001. Only South African Vaccine Producers (SAVP), a subsidiary of The National Health Laboratory Service, is still producing snake, spider, and scorpion antivenoms.

Today, there are four major domestic industry players active in South Africa as well as a notable initiative of the World Health Organization (WHO):

1. The Biologicals and Vaccines Institute of Southern Africa (Biovac) in Cape Town is currently doing fill & finish for Sanofi Pasteur of foreign-produced hexavalent pediatric vaccine. Fill & finish for BioNTech/Pfizer's imported Comirnaty bulk is in preparation in the same production suite, which is currently being extended for that purpose. In addition, a cooperation with Pfizer on the local formulation of Prevenar 13 is under way.
2. Aspen Pharmacare, headquartered in Durban is a global specialty and branded pharmaceutical company, holding market leading positions in anesthetics and thrombosis products. Being primarily a small-molecule and chemicals company, Aspen has some segment expertise in biologicals, especially in its subsidiaries in

Notre Dame de Bondeville, France, in Oss, the Netherlands, as well as in Sioux City, USA. Currently, Aspen is doing fill & finish of Johnson & Johnson's single dose COVID-19 vaccine in its primary manufacturing site in Gqeberha, formerly known as Port Elizabeth.

3. Afrigen Biologics and Vaccines Limited is a small, Cape Town based biotechnology company, driving vaccine product development and biologics manufacturing set-up through a consultancy model.
4. Cape Bio Pharms and its daughter company Cape Biologix Technologies in Cape Town are producing pharmaceutical proteins in plants. The facility currently provides research and development material to academia and industry globally and is currently preparing for high-yield production through their animal-free expression system.
5. With support from the World Health Organization (WHO) and in alignment with the Africa CDC, a consortium led by Afrigen Biologics and Vaccines and BioVac Institute have established a vaccine technology transfer hub in Cape Town.

## Strategy

Biovac is in the process of raising capital for new and larger facilities to obtain the capability for global scale production. The new manufacturing facilities will be developed at a new site, providing ample space for the eventual relocation of Biovac fill-finish manufacturing facilities from its current site as well as for the establishment of multiplatform drug substance facilities and capability.

Simultaneously, the vaccine technology transfer hub has been legally established on July 29, 2021. The Medicines Patent Pool (MPP) and the World Health Organization (WHO), Afrigen Biologics Limited, the Biologicals and Vaccines Institute of Southern Africa (Biovac), the South African Medical Research Council (SAMRC) and Africa Centres for Disease Control and Prevention (Africa CDC) have signed a letter of intent. The aim of the hub concept is to

boost Africa's manufacturing capacity, initially for COVID-19 vaccines and starting in South Africa, with more regional hubs across Africa to follow.

In coordination with the Republic of South Africa, the WHO Vaccine Technology Transfer Hub aims to copy the licensed COVID-19 vaccine of Moderna Inc. without acquiring licenses from the company. This is assumed to be possible as Moderna had announced in October 2020 it would not enforce patents related to its COVID-19 vaccine during the pandemic, raising hopes that other entities might be able to copy it without being prosecuted. It can be assumed that initial doses of the copied vaccine shall be produced by Afrigen, with scale manufacturing expected to occur at BioVac Institute later. In practice, though, it is close to impossible to replicate a vaccine manufacturing process without close cooperation with the inventor. The resulting product, even if successfully manufactured, would need to go through a full program of clinical trials. Afterwards, having completed these trials positively, the manufacturer must apply for a novel marketing authorization and WHO pre-qualification. Provided that the release from patent cover will be granted by Moderna only during the pandemic, the sustainability outlook for this project of the WHO Vaccine Technology Transfer Hub is not favorable.

On August 27, 2021, President Paul Kagame of Rwanda, President Macky Sall of Senegal, and President Ursula von der Leyen of the European Commission met Uğur Şahin, CEO and Co-Founder of BioNTech in Berlin at the Barenboim-Said-Akademie to discuss the development of sustainable vaccine production for Africa. On the fringes of this convention, following Africa CDC's request, in coordination with WHO and supported by the Mastercard Foundation, kENUP has started compiling a "White Book" on the regulation of the "transfer of mobile factories with embedded product-specific production processes and the associated regulatory approvals from the European Union to Africa". The upcoming document will compile commonly accepted practices, stipulations from relevant laws and regulations alongside explanatory texts to create maximum transparency and ease for those regional regulators, Government bodies and companies involved in the upcoming rapid set-up of vaccine manufacturing capacity in Africa. Following its initial completion, the White Book will be maintained by the African Medical Agency in formation.

## kENUP Findings

### A

kENUP recommends to both BioVac Institute and Company #1 (see Appendix) to partner on the manufacturing of mRNA Vaccines in South Africa. The following scheme could provide guidance to a swift and flawless process:

1. Company #1 intends to establish and operate vaccine manufacturing (drug substance & bulk drug product) in South Africa. To achieve this goal within 24 months, the company expects to import a “container factory” consisting of 12 large, pre-equipped, -configured and “-regulated” sea containers.
2. These containers will be placed in a suitable (empty) manufacturing hall. This facility needs to be built and managed by a third party to the Company’s specifications. The Company will sign a long-term lease for the facility and pay a local market rate rent for its use.
3. As announced by Pfizer and BioVac on June 30, 2021, a fill & finish facility is already being made available. With BioVac, it is planned and managed by an experienced fill & finish operator and is thus expected to comply with the Company’s requirements. The Company expects to conclude a commercial deal with BioVac for using these fill & finish services.
4. The Company expects to consider handing over ownership and operational responsibility of the "container factory" to BioVac Institute in due time, applying terms and conditions to be agreed upon.
5. All product manufactured under this scheme shall be dedicated to the African Union market.

The timing of this process will be dependent on the availability of the manufacturing hall described above under 2. This is a function of the initiation and subsequent progress of the real estate development for the novel manufacturing park in Cape Town, as BioVac’s current venue does not provide for the necessary extension space, at least not under sustainable operational conditions. Thus, kENUP expects the bulk vaccine manufacturing to start not before the end of 2022.

In general, the degree of the Republic of South Africa's endorsement and support of BioVac Institute in the pursual of such project is currently not clear to kENUP.

**B**

Further, kENUP recommends to Aspen Pharmacare and to Company #2 to partner on the set-up and operation of vaccine manufacturing on a recombinant nanoparticle vaccine platform.

For this cooperation, a different container manufacturing solution should be pursued. Due to the somewhat lower complexity, timelines could be quicker here, and there are further options for tech transfer with the aim of establishing a multiclient, manufacturer agnostic CDMO in South Africa.

**C**

Regarding Company #3, kENUP has initiated conversations with the Department of Science and Innovation and is currently awaiting feedback. kENUP has recommended to include a substantive African facility for the cost-efficient manufacturing of monoclonal antibodies as a second anchor into the upcoming biologicals manufacturing park in Cape Town.

**D**

The Republic of South Africa should – represented by its relevant bodies and duly established regulators - participate in the White Book process described above.

**E**

The WHO Vaccine Technology Transfer Hub's project of copying the manufacturing process of Moderna's COVID-19 vaccine should be terminated immediately. This is to prevent damage to Afrigen, BioVac, and Moderna.

kENUP expects the WHO Vaccine Technology Transfer Hub, though, to play a crucial role in the continuous development of a skilled workforce, for South Africa and the entire Continent. As the first of its kind, the Cape Town Hub will also be involved in and shape the

necessary “reg & tech transfer” to the Continent. In addition, its convening and coordination function with industrial players globally is expected to contribute significantly.

## **Appendix A**

### **1. Company #1: European mRNA company**

Founded in 2008 to develop individualized immunotherapies for cancer and other diseases. Their mRNA-based vaccine product has been authorized or approved for emergency or temporary use or granted conditional marketing authorization in over 65 countries worldwide. The company is committed to invest the revenues they generate to accelerate the maturation of their oncology and infectious disease pipeline and the expansion into additional therapeutic areas, such as autoimmunity, allergy, regenerative medicine, and inflammatory diseases. Their immunotherapy product candidates span four distinct drug classes: mRNA therapeutics, cell therapies, antibodies, and small molecule immunomodulators.

They increased and will continue to increase their manufacturing capacity, including through their acquisition of a manufacturing site in Europe. Their latest site is one of the key factors in the expansion of their manufacturing network and will become one of the largest mRNA manufacturing sites in Europe with an annual production capacity of up to one billion doses once fully operational. The company's European manufacturing network has continually expanded from three partners in December 2020 to 13 sites as of March 2021 and is continuing to strengthen. The company currently investigates opportunities on the African continent.

### **2. Company #2: American-European nanoparticle and adjuvant company**

Headquartered in the US, the biotechnology company promotes improved health globally through the discovery, development, and commercialization of vaccines focusing on coronavirus, seasonal influenza, RSV, Ebola, MERS, SARS, and the combination of the aforementioned innovative applications to prevent serious infectious diseases. Established in 1987, the company has grown rapidly during the pandemic and now employs over 791 people with \$476 million in revenue. The company has attracted investments from national and international investors of more than \$2 billion to date and will establish a manufacturing capacity of 150 million doses by Q4 2021.



It uses a recombinant nanoparticle technology platform and a proprietary adjuvant in combination to create vaccines that address global public health threats. Its saponin-based adjuvant has demonstrated a potent and well-tolerated effect by stimulating the entry of antigen-presenting cells into the injection site and enhancing antigen presentation in local lymph nodes, boosting immune response. The company is seeking marketing authorization globally for the coronavirus vaccine after successful Phase 3 with efficacy of 96.4% against non-B.1.1.7 variants. Its seasonal influenza and RSV vaccines are in Phase 3, as well as the malaria (R21) development which is conducted by partners. Ebola proceedings are in Phase 1 clinical trials with MERS and SARS being preclinical to date.

The company is seeking opportunities to expand its manufacturing capabilities. With facilities in the US, Sweden and Czech Republic, antigen production across Europe and the US, and license and distribution agreements in India, South Korea, and Japan, as well as fill/finish capabilities in both in the US and Europe, the company has a global footprint.

*The company is considering partnering with a European manufacturing company:*

The group is offering manufacturing capacities to produce biologics to companies that are looking to expand or start their production. It increases access to biologics by offering a standardized sea-container-based manufacturing solution allowing production at substantially lower costs and at virtually any location. Headquartered in the EU, the organization consists of a group of companies that acts as a bioprocessing provider aiming to increase availability of biologics for all. The group offers manufacturing solutions to fill the supply gap in cell and gene therapies, vaccines and biotherapeutics. Established in 2013, the company has grown rapidly and now employs over 250 people. The companies have attracted investments from national and international investors. Multiple EIB loans have been received, as well as funds from the Bill & Melinda Gates Foundation and the Soros Economic Development Fund.

The group focusses on providing manufacturing solutions for cell and gene therapies, GMP clinical and commercial viral vector vaccines, biotherapeutics, and affordable pre-clinical platforms. The companies are in discussions with multiple parties to install the sea-container-based manufacturing units and are currently involved in 12 viral projects. Next to offering the sea-container-based manufacturing solution, the organization wants to co-develop a pipeline of COVID-19 vaccines.

### **3. Company #3: European mAbs manufacturing and research collaboration company**

Located in the EU, with established collaborations with numerous pharma companies through its unique business model enabling it to act as service provider for the life science industry while running its own discovery and development projects in co-owned (i.e., risk-reward sharing) models, both of which operate on the same scientific platforms and share a common workforce. The company focuses on various therapeutic areas: (i) anti-infectives, (ii) immunology and inflammation, (iii) metabolic diseases, (iv) neurosciences, (v) oncology, and (vi) respiratory.

The company has been active in R&D on small molecules with library of more than 1m compounds having delivered more than 50 pre-clinical and clinical candidates. It is a market leader in pre-clinical R&D and with a large pipeline portfolio operating in the EU and the US and has over 20 product opportunities in the clinical and pre-clinical pipeline, with another 20 in discovery.

Recently, the company has acquired a large-scale manufacturing system for humanized monoclonal antibodies (mAbs), and other complex biologicals. The capacity would be sufficient to serve the entire African continent with this novel class of powerful therapeutics that are currently, in most cases, not available to patients in Africa at all. Very similar to the operational model suggested for the mRNA manufacturer earlier in this document, the company could bring to Rwanda an exact clone of its existing facility in the United States, which it operates there for several pharmaceutical manufacturers and for the US Department of Defense. Timing for such a move appears to be favorable, as a Member State of the EU is currently procuring another clone to be located on its territory. The European Investment Bank (EIB) has expressed its interest to finance a potential factory in Africa.

## Appendix B

Visual documentation on kENUP Foundation's Mission to the Republic of South Africa from August 11 to 14, 2021

1. Policy Briefing on Vaccine Manufacturing in South Africa with the Acting Ambassador of the Federal Republic of Germany to South Africa

August 11, 2021 from 16:00h to 17:15h in Pretoria



*From right to left: Dr. Rüdiger Lotz, Chargé d'Affaires, Embassy of the Federal Republic of Germany o South Africa; Elke Wolf, Deputy Head of Cooperation, Embassy of the Federal Republic of Germany o South Africa; Dr. Susanne Kieffer, Head of Education and Science, Embassy of the Federal Republic of Germany o South Africa.*

2. Company Visit at aspen Pharmacare

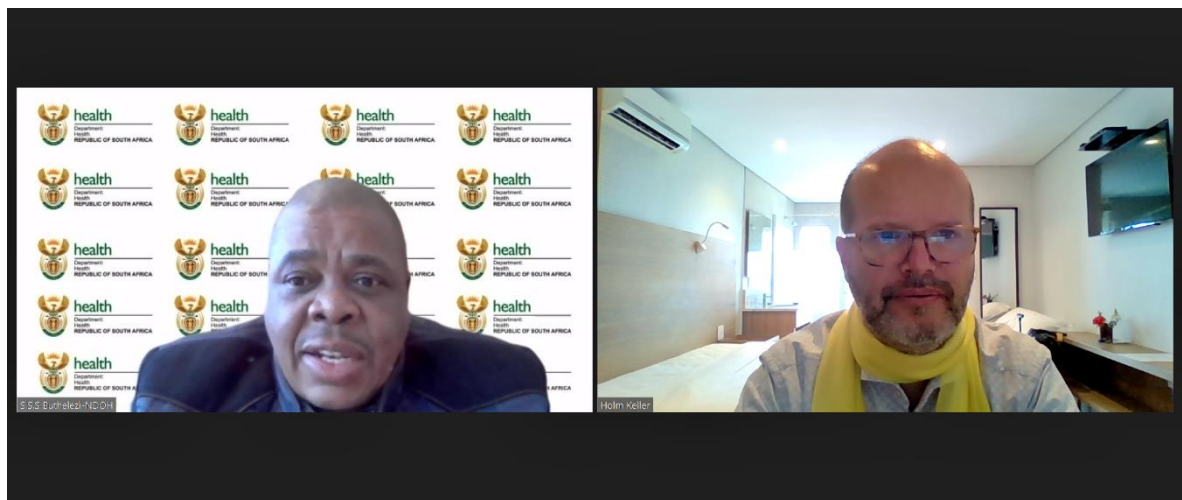
August 12, 2021 from 09:00h to 10:30h in Durban



*On the right: Stephen Saad, Founder and CEO of Aspen Pharmacare Holdings Limited.*

### 3. Policy Consideration with the Ministry of Health

August 12, 2021 from 11:30h to 12:30h, held by Zoom due to COVID-19 regulations



*On the left: Director-General Dr Sandile Buthelezi, National Department of Health, Republic of South Africa*

4. Understanding the state of Science in the Republic of South Africa

August 12, 2021 from 14:00h to 16:00h in Durban



*From right to left: Prof. Quarraisha Abdool Karim, Co-Founder of CAPRISA, UNAIDS Special Ambassador for Adolescents and HIV; Prof. Salim S. Abdool Karim, Director of Caprisa, Professor for Global Health at Columbia University, Adjunct Professor in Immunology and Infectious Diseases at Harvard University; Dr Sharana Mahomed, Research Clinicianat Caprisa.*

5. Policy Consideration with the Department of Science and Technology

August 13, 2021 from 09:30h to 10:30h in Cape Town



*On the right: Glaudina Loots, Director Health Innovation at the Department of Science and Innovation, Republic of South Africa*

6. Company Visit at The Biovac Institute

August 13, 2021 from 11:00h to 13:00h in Cape Town



*From right to left: Dr Patrick Tippoo, Head of Science and Innovation of The Biovac Institute, Executive Director of the African Vaccine Manufacturing Initiative (AVMI); Dr. Morena Makhoana, CEO of The Biovac Institute.*



7. Policy Consideration on the upcoming WHO mRNA Vaccine Hub

August 13, 2021 from 13:30h to 15:00h in Cape Town



*From left to right: Dr Caryn Fenner, Technical Director at Afrigen Biologics & Vaccines; Dr Petro Terblanche, Managing Director at Afrigen Biologics & Vaccines.*

8. Company Visit at Cape Bio Pharms and Cape Biologix Technologies

August 13, 2021 from 15:00h to 18:00h in Cape Town



*On the left: Belinda Shaw, CEO and Co-Founder of Cape Bio Pharms and of Cape Biologix Technologies.*

9. Discussing potential contributions of South Africa's Universities to human resources capacity building for vaccine manufacturing

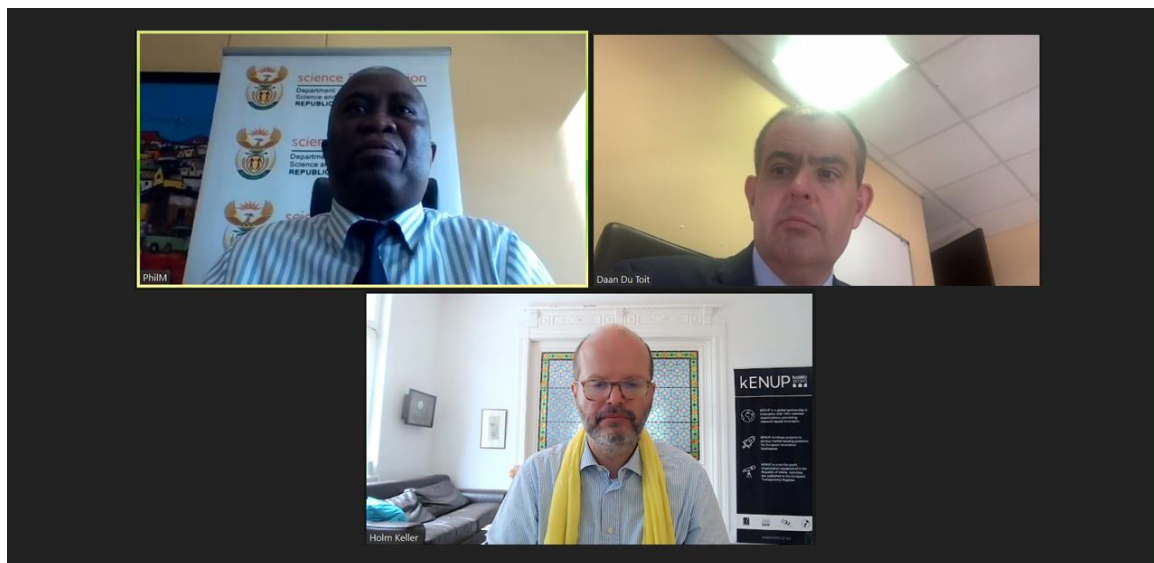
August 14, 2021 from 10:30h to 11:30h in Cape Town



*On the right: Prof. Mamokgethi Phakeng, Vice-Chancellor (=Rector) of the University of Cape Town.*

**10. Policy Consideration with the Department of Science and Innovation**

August 19, 2021 from 11:30h to 12:00h, held by Zoom due to COVID-19 regulations



*From left to right: Director-General Dr Phil Mjwara, Department of Science and Innovation; Daan du Toit, Deputy Director-General: International Cooperation and Resources, Department of Science and Innovation.*