COVID-19 Research and Development in Uganda: What were the setbacks?

Overview

The advent of the Coronavirus Disease (COVID-19) in Uganda resulted in institution of several measures to curb its spread. Some of these included: suspension of public gatherings, closure of education institutions, and a national curfew. The Presidential Scientific Initiative on Epidemics (PRESIDE) was created as a mechanism to fast-track Research and Development (R&D) for local generation of essential and emergency response tools for the disease and similar epidemics. The response tools included but were not limited to vaccines, diagnostics, and therapeutics.

Since its inception in 2020, the PRESIDE has funded 29 projects in the last three financial years aimed at developing COVID-19 vaccines, diagnostics, therapeutics and establishment of central research facilities. However, by 31st October 2022, none of the funded projects had commercialized their outputs and the country still relies on imported vaccines and diagnostics.

This policy brief discusses the progress made and setbacks towards the development of vaccines, therapeutics and diagnostics.

Key Issues

1. Delayed delivery of equipment due to COVID-19 restrictions and the global disruptions in supply chains and logistics.
2. The PRESIDE was too ambitious and embarked on several projects simultaneously thus scattering the meagre resources to different institutions.
3. Stalling of projects due to technical impracticability and withdrawal of collaborators.
4. Delayed budgetary releases during the first half of FY2021/22.
5. Inadequate monitoring and reporting system at the PRESIDE secretariat to ensure that project deliverables are attained in time.

Introduction

The COVID-19 emerged as a global public health threat towards the end of 2019 and was declared a global pandemic on 11th March 2020. Globally, over 633,263,617 positive cases and 6,594,491 deaths had been confirmed by 17th November 2022.

The total number of confirmed cases and deaths in Uganda stood at 169,568 and 3,630 respectively over the same period. The number of new COVID-19 cases dropped to less than 100, and no death was registered in October 2022.

Some of the measures instituted by different countries to prevent and treat COVID-19 included: national lockdowns, suspension of public gatherings, and border closures except for the movement of essential commodities and health supplies. Other strategies included funding research and development of vaccines, therapeutics and diagnostics for CoV-2. By 12th January 2022, nine[1] vaccines had been issued emergency use licenses by the World Health Organization. Globally 12,885,748,541 COVID-19 vaccine doses had been administered, of which

[1] Pfizer, AstraZeneca, Johnson and Johnson, Moderna, Sinopharm, Sinovac, Covaxin, Covovax and Nuvaxovid.

25,783,131 vaccines were administered to Ugandans by 8th October 2022.

The Government of Uganda funded COVID-19 research and development through two fronts: the Presidential Scientific Initiative on Epidemics (PRESIDE), and the National Research Innovation Programme (NRIP). Funding under NRIP was a one-off during FY2020/21, whereas PRESIDE has received funding for the last three years: FY2019/20 to FY2021/22.

Performance

Financial Performance

The three-year budget for PRESIDE Research and Development was Ug shs 142.07bn, of which Ug shs 139.1bn (97.9%) was released to the project implementers and the defunct Ministry of Science, Technology and Innovations (MoSTI) for the purchase of R&D equipment. During the FY2019/20 and FY2020/21 Ug shs 5.23bn and Ug shs 15.787bn respectively was released to MoSTI for procurement of equipment. Ug shs 64.337bn was disbursed to the various project implementers during FY2020/221 and FY2021/22 to cater for project operational costs. Financing for FY2021/22 was through two Votes: Ug shs 52bn through the Office of the President (OP) and Ug shs 50.4bn through the State House.

Physical Performance

As of 30th June 2022, a total of 27 projects had received funding from PRESIDE, of which three (03) were for the development of vaccines, twelve (12) for therapeutics, eight (08) for diagnostics, and four (04) for infrastructure development. Seven[2] out of the 23 funded projects in FY20/21 had a prototype in place by 30th June 2022, and three projects for the establishment of central facilities were substantially complete. Ten projects registered slow progress, whereas three[3] were dropped. All projects relating to vaccine development were still at the exploration stage with candidate vaccines ready for pre-clinical trials.

Vaccine Research and Development

Four research projects were funded for the research and development of vaccines. These included: the COVID-19 sub-unit vaccine, inactivated COVID-19 vaccine, novel adenovector COVID-19 vaccine and; self-amplifying mRNA. The key implementing agencies were the Makerere University College of Veterinary Medicine and Biosecurity (COVAB), and the Uganda Virus Research Institute (UVRI). The development of the sub-unit vaccine was ongoing but at a rather slow speed. Isolation and coding of the spike protein was done and the protein was expressed and amplified in E.coli. The extracted protein was to be administered to humanized mice which were delivered in June 2022 and are currently being multiplied at COVAB. The project experienced procurement delays both for equipment and humanized mice from which preclinical trials of the vaccine were to be carried out.

Development of the adenovector COVID-19 vaccine was ongoing with adenovector backbone and vaccine candidates generated (E1 deleted adenovectors). The vaccine candidates were being validated in human sera. The project also experienced procurement delays and no funding during the first half of FY2021/22. The development of self-amplifying mRNA (messenger ribonucleic acid) was dropped due to

[2] PCR based diagnostic assays; PCR and anti-body diagnostic kits, COVID-19 sub-unit vaccine; Novel adenovector COVID-19 vaccine; Matooke starch as a pharmaceutical excipient in selected medical formulations for use in the treatment of COVID-1; Nano-adjuvant therapeutics, vaccine adjuvant and materials testing; and Production and clinical trial of therapeutic herbal drugs against COVID-19 (UBV-01N).

[3] Stem cell research, therapeutic intervention for COVID-19 using antivirals, immune modulators and anti-platelet agents, and self-amplifying RNA.

the withdrawal of the United Kingdom project partner.

COVID-19 Diagnostics Research and Development

Some of the funded projects under diagnostics registered success at the level of a prototype. The Joint Clinical Research Centre (JCRC) developed and validated an ELISA assay test kit with the ability to test 48 samples in a single run. However, mass production of the kit was yet to begin, despite JCRC reporting the ability to produce 100 kits per day. The Makerere Biomedical Research Centre (MAK-BRC), developed a polymerase chain reaction (PCR) diagnostic kit for COVID-19 testing using nasopharyngeal samples and was under regulatory approvals before commercial production is initiated. Some of the production equipment was shipped into the country in FY2020/21. The project experienced delays in the effective acquisition of the five acres of land to establish a production facility in Busunju. A private partner, Ndiyo Biosciences was brought on board to construct the production facility, however, the guidelines and legalities of the partnership were yet to be developed.

The development of a Cov-2 biomarker rapid test strip by COVAB was ongoing and two biomarkers were identified from samples of Cov-2 patients. Development of a saliva diagnostic kit was ongoing but at a rather slow pace with isolation of nucleocapsid protein; cloning and expression in *E.coli* done. However, assembly and field evaluation of the kit were yet to be achieved. Even though the development of diagnostics made great strides and some of the prototypes acquired regulatory approvals, there were no guidelines on how the private can partner with the government for the commercialization of the developed prototypes.

COVID-19 Therapeutics Research and Development

The PRESIDE supported nine projects aimed at developing and evaluating therapeutics for COVID-19 treatment. One project developed a therapeutic from natural herbs (UBV-01N) and was launched to undergo clinical trials in January 2021 and end by 30th June 2021 before rolling it out to phase two of the trial with more participants. The trial experienced challenges of withdrawal of participants before the end of the study and to date, the therapeutic has not progressed to phase two.

Development of nano-adjuvants and materials testing for COVID-19 vaccines was ongoing and chitosan and lipid nano-delivery systems were formulated. The developed nano-delivery systems were undergoing immunogenicity and toxicity assessments. The project was however awaiting a vaccine from other projects for the adjuvant and other delivery materials to be evaluated effectively. The development of *matooke* starch as a pharmaceutical excipient had registered some progress with evaluated samples of starch available. The starch was primarily to be used as a carrier for COVID therapeutics. The development of immune therapy for COVID-19 using convalescent plasma had not produced a prototype yet due to the withdrawal of the key project partner. Other studies on the development of therapeutics funded by PRESIDE were ongoing but at a slow pace whereas one project (stem cell research) was dropped. The decrease in COVID-19-positive cases implied the inability to test the efficacy of the therapies.

COVID-19 Research and Development Infrastructure

The PRESIDE supported the renovation and equipping of two facilities at the COVAB. The biomarker research facility was renovated, equipped and upgraded to level 2 bio-security. The central laboratory animal research facility was also renovated and upgraded to level three bio-security status. The MAK-BRC acquired two ultra-low temperature freezers, 5 PCR units and two sequencers and established a biobank of well-annotated and characterized samples of COVID-

19-positive patients. The performance of infrastructure projects was good.

Some of the procured equipment at the MAK-BRC in Mulago

Conclusion

The projects received 97.9% of the approved budget, however, most of the studies experienced delays in the acquisition of critical equipment, and technical gaps thereby not delivering the anticipated emergency solutions to COVID-19. The infrastructure and capacity improvement projects however performed well. The so many preventative measures instituted by the government significantly helped in containing the virus and the number of new positive cases reduced to less than 100 a month. However, COVID-19 patients are a key requirement in the clinical evaluation of both vaccines and therapeutics as well as field evaluation of diagnostics. It is therefore imperative to review the intervention goal of PRESIDE from addressing the COVID-19 challenge to emergency preparedness for future epidemics through human resource capacity and sustaining the infrastructure developed.

Recommendations

- The Government should ensure sustained funding for research and innovation conducted by universities, and public research institutions to better leverage time in case of future epidemics.
- The Government should establish and sustain strategic collaborations with key research institutions and countries to enable sharing of knowledge and techniques amongst scientists.
- The PRESIDE Secretariat should review the vetting process for projects to ensure that only those that are feasible are funded. The vetting committee members should not be implementers of projects to avoid bias and lower incidents of one scientist implementing several projects. This will reduce the incidences of stalled projects due to technical impracticability.
- The PRESIDE should embrace the existing health research and development structures and ensure that central research facilities are well equipped and sustainably maintained other than scattering equipment to every project.
- The PRESIDE should strengthen the monitoring and reporting system to ensure the timely attainment of project deliverables and quick decision-making.

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PRESIDE Magazine, Volume 2, April 2021

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