BUILDING LOCAL CAPACITY FOR INTERNATIONAL VACCINE TRIALS IN NIGERIA

A Presentation at the 23rd National Conference & Annual General Meeting (AGM) of the Guild of Medical Laboratory Directors.

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BY

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Introductions

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Instructor: Dr. Ali Onoja

- Public Health Specialist, Vaccinologist and Knowledge Management Consultant
- Over 35 years working experience at the national and international arena in the area of Disease Control as well as research, project management, health promotion, epidemiology, and health systems strengthening.

Expertise:

- Vaccine Production
- Epidemiological Surveillance
- Laboratory and Extensive Field Experts
- Operational Methods in Biomedical Sciences
- Monitoring And Evaluation, Project Design and Implementation

Prior Vaccine Related Professional Experience:

- Federal Vaccine Production Laboratory Yaba Lagos
- National Programme on Immunization (NPI), Federal Ministry of Health, Abuja
- National Institute for Pharmaceutical Research and Development (NIPRD)
- Institute of Human Virology, Baltimore Maryland, USA.

Outline of Presentation

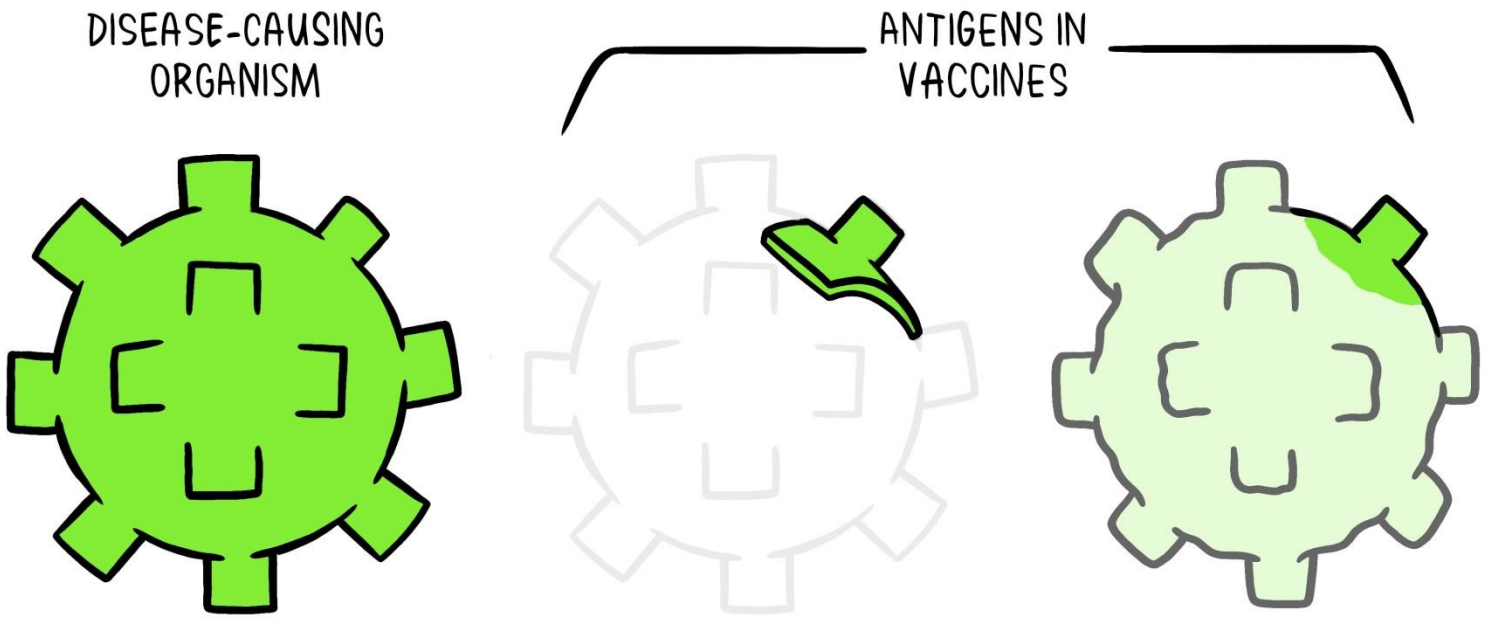
- What is in a vaccine?
- Vaccine Development Process
- Stages of Vaccine Trial
- Preparing Nigeria for International Vaccine Trial
- Site Development
- Population Activities
- Current Vaccine Trial Activities in Nigeria

What is in a vaccine?

All the ingredients of a vaccine play an important role in ensuring a vaccine is safe and effective. Some of these include:

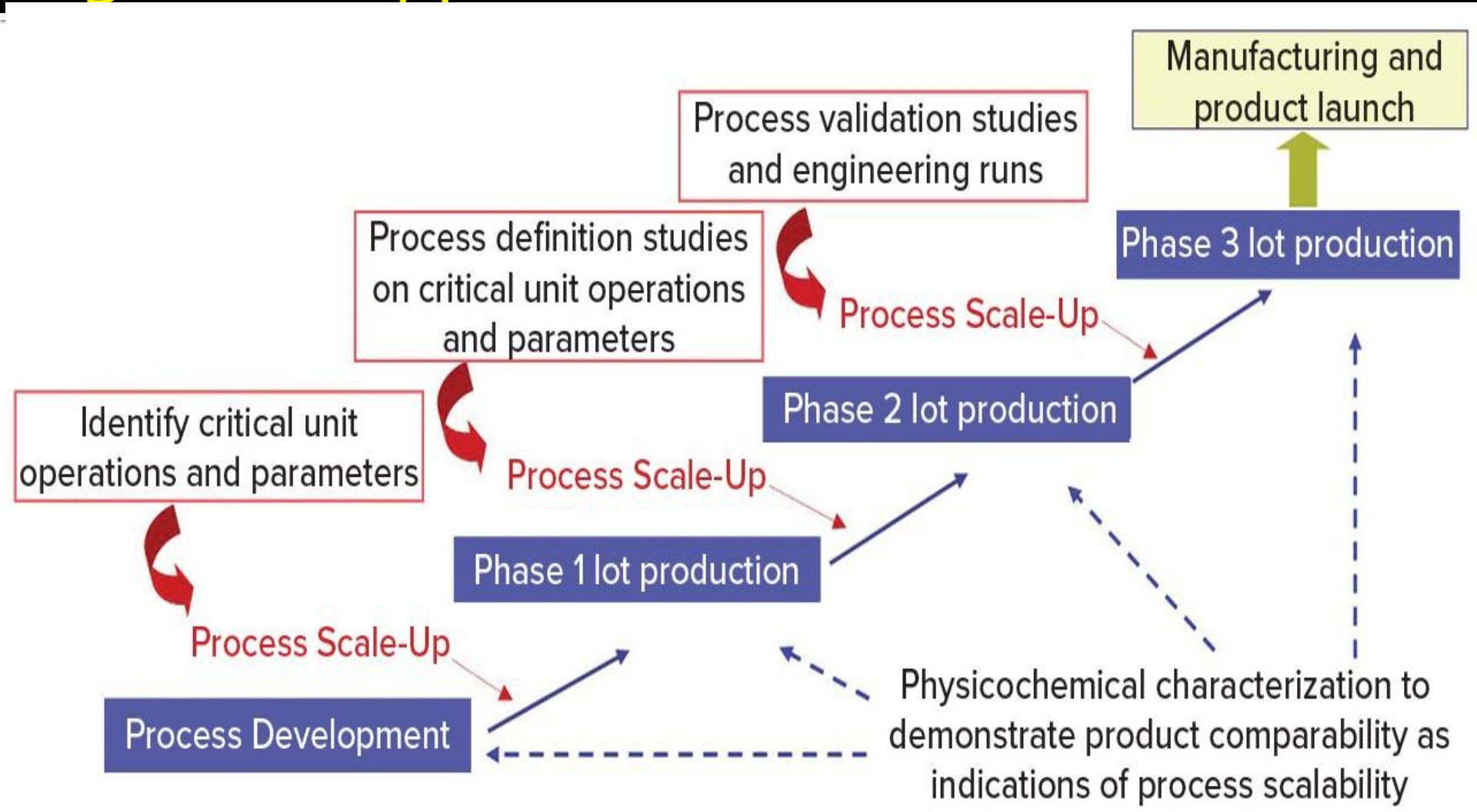
- The antigen.
  - This is a killed or weakened form of a virus or bacteria, which trains our bodies to recognize and fight the disease if we encounter it in the future.
- Adjuvants
  - help to boost our immune response. This means they help vaccines to work better.
- Preservatives
  - ensures a vaccine stays effective.
- Stabilisers
  - protect the vaccine during storage and transportation.

Vaccine Development Process



The key ingredient in a vaccine is the antigen. It's either a tiny part of the disease-causing organism, or a weakened, non-dangerous version, so your body can learn the specific way to fight it without getting sick.

Vaccine process development – general approach

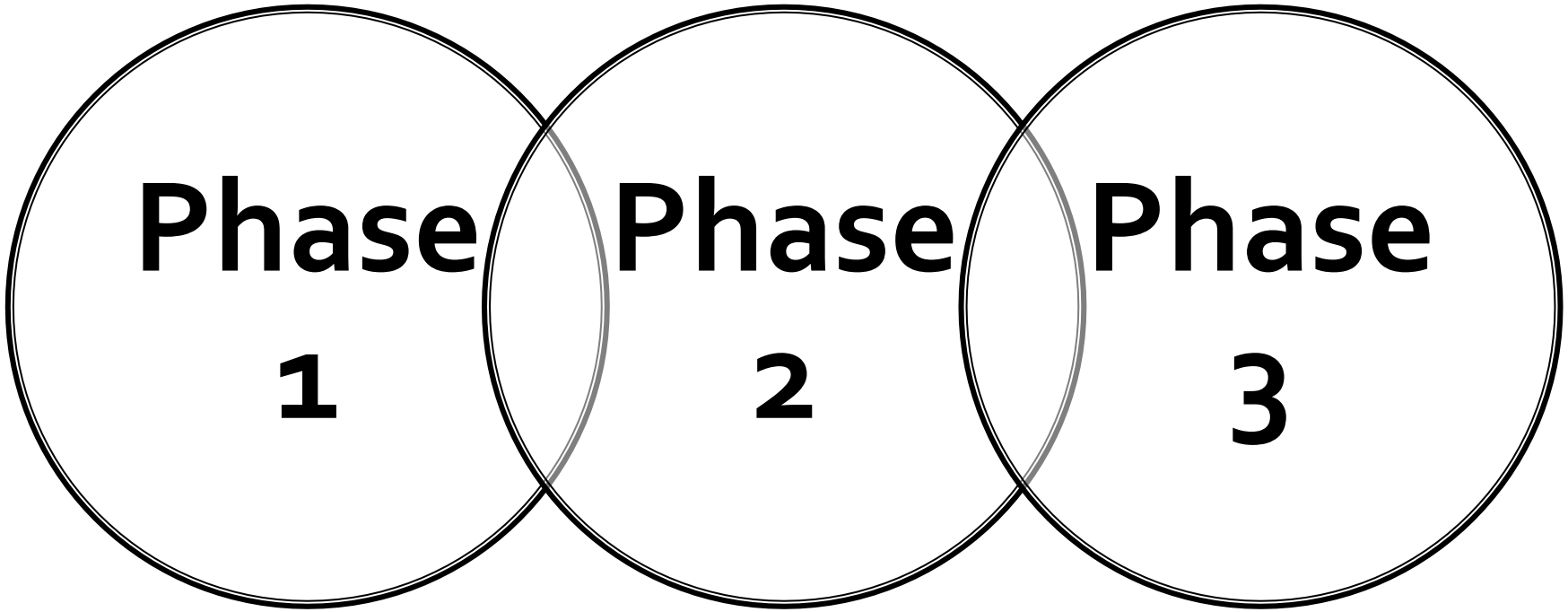


Typical Timelines for Vaccine Development (LCM = lifecycle management)

How are vaccines developed

- Most vaccines have been in use for decades, with millions of people receiving them safely every year. As with all medicines, every vaccine must go through extensive and rigorous testing to ensure it is safe before it can be introduced in a country's vaccine programme.
- Each vaccine under development must first undergo screenings and evaluations to determine which antigen should be used to invoke an immune response. This preclinical phase is done without testing on humans. An experimental vaccine is first tested in animals to evaluate its safety and potential to prevent disease.
- If the vaccine triggers an immune response, it is then tested in human clinical trials in three phases.

Stages of Vaccine Trials



Phase 1

The vaccine is given to a small number of volunteers to assess its safety, confirm it generates an immune response, and determine the right dosage.

Generally in this phase vaccines are tested in young, healthy adult volunteers (about 20 to 80).

Phase 2

The vaccine is then given to several hundred volunteers (about 100 to 300) to further assess its safety and ability to generate an immune response.

Participants in this phase have the same characteristics (such as age, sex) as the people for whom the vaccine is intended. There are usually multiple trials in this phase to evaluate various age groups and different formulations of the vaccine. A group that did not get the vaccine is usually included in phase as a comparator group to determine whether the changes in the vaccinated group are attributed to the vaccine, or have happened by chance.

Phase 3

The vaccine is next given to thousands of volunteers (from 1,000 to 3,000)– and compared to a similar group of people who didn't get the vaccine, but received a comparator product – to determine if the vaccine is effective against the disease it is designed to protect against and to study its safety in a much larger group of people.

Most of the time phase three trials are conducted across multiple countries and multiple sites within a country to assure the findings of the vaccine performance apply to many different populations.

Stages of Vaccine Trial (2)

- During phase two and phase three trials, the volunteers and the scientists conducting the study are shielded from knowing which volunteers had received the vaccine being tested or the comparator product. This is called "**blinding**" and is necessary to assure that neither the volunteers nor the scientists are influenced in their assessment of safety or effectiveness by knowing who got which product.
- After the trial is over and all the results are finalized, the volunteers and the trial scientists are informed who received the vaccine and who received the comparator.

Stages of Vaccine Trial (3)

- When the results of all these clinical trials are available, a series of steps is required, including reviews of efficacy and safety for regulatory and public health policy approvals. Officials in each country closely review the study data and decide whether to authorize the vaccine for use. A vaccine must be proven to be safe and effective across a broad population before it will be approved and introduced into a national immunization programme. The bar for vaccine safety and efficacy is extremely high, recognizing that vaccines are given to people who are otherwise healthy and specifically free from the illness.
- Further monitoring takes place in an ongoing way after the vaccine is introduced. There are systems to monitor the safety and effectiveness of all vaccines. This enables scientists to keep track of vaccine impact and safety even as they are used in a large number of people, over a long time frame. These data are used to adjust the policies for vaccine use to optimize their impact, and they also allow the vaccine to be safely tracked throughout its use.
- *Once a vaccine is in use, it must be continuously monitored to make sure it continues to be safe in*

Stages of Vaccine Trial (4)

- Phase IV clinical trials are done after the vaccine has been approved by the NAFDAC and marketed for public use.
- These studies continue testing the vaccine to collect information about its effect in various populations and gather data on any side effects associated with long-term use.

Preparing Nigeria for International Vaccine Trials

Regulatory Processes

- NAFDAC
- NHREC

Site development

- NIPRD
- NIMR
- NVRI
- International Organizations
- Universities and other institutions with Lab infrastructure
- Private Labs

Population Activities

- CAB
- Education
- Willingness to Participate

Clinical Trial Regulatory Authorities in Nigeria

National Agency for Food and Drug Administration and Control (NAFDAC):

The Agency is responsible for protocol review and authorization of clinical trial before it is conducted in Nigeria. It is also responsible for carrying out inspection of trial sites to monitor the conduct of authorized studies to ensure that well-being and safety of the participants is protected and credible data is obtained from the study.

National Health Research Ethics Committee (NHREC):

The Committee is responsible for accreditation of Independent Ethics Committee (IEC) and or Institutional Review Board (IRB) that give ethical opinion on study protocols depending on the number of trial sites involved.

In order to reduce processing timeline for Clinical Trial applications, the study protocol can be submitted simultaneously to NAFDAC and Ethics Committee. However, ethical opinion must be obtained before NAFDAC issues final authorization for the conduct of the trial subject to satisfactory review.

Site Development for Participation in Vaccine Trials

- Buy in by the Institutional management
- Study team (Clinicians, Laboratory Scientists, Pharmacists, Nurses, Social Health Workers)
- Study PI and Study Coordinators
- Payment of stipends and renumeration
- Ethical Consideration
- SOP
- GLP
- GCP
- Good and Standard Infrastructure
- Power
- Storage Facilities (+4 up to) - 80^{o}C
- Adequate Water Supply

Population Activities

- Study population and study communities
- Disease incidence
- Sensitization
- Community Advisory Boards (CABs)
- Willingness to Participate
- Informed Consent processes and procedures

Example of a Vaccine Trial Site in Nigeria- CLINICAL RESEARCH CENTER (CRC), Abuja.

CRC Facility Includes:

- Data management office
- 2100 m2 , detached 2-story, leased commercial duplex house, with the outbuilding designed and developed into a well-equipped clinical laboratory
- Stand-alone meeting/ orientation/training rooms are also located within the compound
- Reception room
- Five consulting office spaces
- Emergency unit
- Phlebotomy section
- Biosafety cabinets and ventilation hoods
- Pharmacy
- Regulatory office
- Storage capacity for fixed assets
- On-site lab with -80˚C cold sample repository
- Community engagement unit:
  - The Centre works in collaboration with a number of international collaborators including the Walter Reed Army Institute of Research and its Emerging Infectious Diseases Branch and U.S. Military HIV Research Program. The Centre is supported by HJFMRI and the Nigerian Ministry of Defence.

Vaccine Trial Activities in Nigeria (CRC) Abuja

CURRENT STUDIES	Ebola Vaccine (Ad26.ZEBOV/MVA-BN-Filo)	Enrolled 38 participants – 22 healthy and 16 HIV+ adults Retention rate of 89.5% at 12 months
	Study of Severe Infectious Disease in West Africa	Multi-site study designed for early identification and characterization of cases of suspected emerging infectious diseases in Nigeria, Liberia and Ghana.
	African HIV Cohort Study (AFRICOS)	Large, long-term cohort study at multiple African sites that evaluates HIV prevention and treatment services supported through local facilities, funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR)

Vaccine Trial Activities in Nigeria (CRC) Abuja

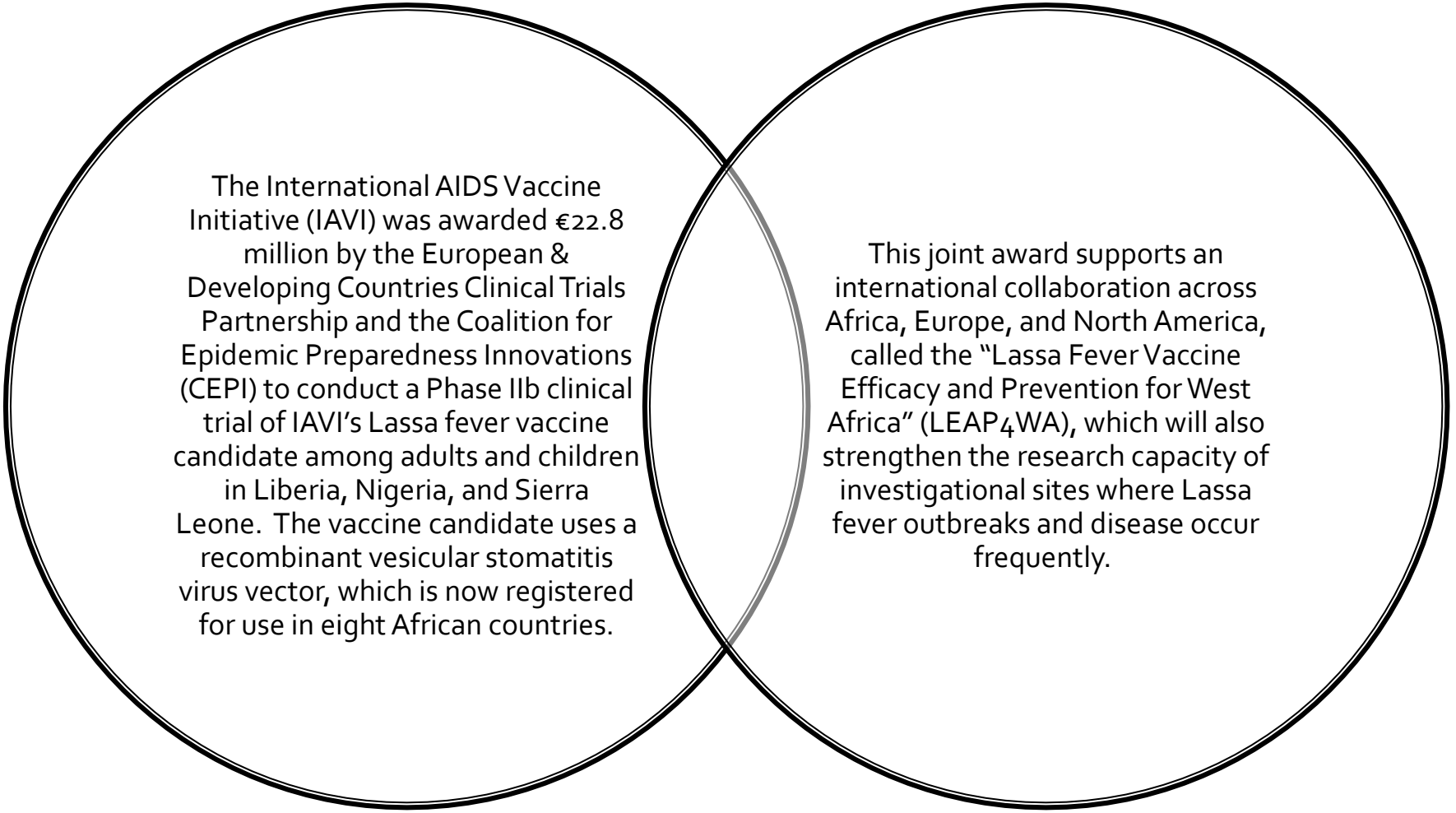
Completed Studies

- Ebola Vaccine (ChAd3-EBO-Z)
- The first Ebola vaccine trial in Nigeria, conducted between August 2015 and November 2016
- Enrolled 330 participants, exceeding the original sample size expectation for Nigeria by over 100%
- Retention rate of 99.4% at 12 months.

TRUST HIV Cohort Study

- Prospective cohort study characterizing HIV and STI prevalence, incidence and risk behaviors among men who have

New Lassa Vaccine Trial in Nigeria



New Lassa Vaccine Trial in Nigeria (2)

The LEAP4WA consortium consists of the following members:

- IAVI Inc., U.S.
- IAVI Stichting, Netherlands
- Tulane University School of Public Health and Tropical Medicine, U.S.
- Ministry of Health and Sanitation/Kenema Government Hospital in Sierra Leone
- Imperial College of Science Technology and Medicine, U.K.
- University of Liberia, Liberia
- Epicentre, France
- Henry M. Jackson Foundation Medical Research International Ltd/Gte (HJFMRI), Nigeria. In Nigeria, HJFMRI will conduct the study at its Clinical Research Center (CRC) supported by the Walter Reed Army Institute of Research.

New Lassa Vaccine Trial in Nigeria (3)

Other supported WRAIR Lassa projects being implemented at the CRC and other sites across Nigeria include

Lassa incidence study in collaboration with the African Center of Excellence for Genomics of Infectious Diseases (ACEGID),	Lassa seroprevalence study, and a potential opportunity for a CEPI-funded Phase IIa Lassa vaccine study through a WRAIR/IAVI collaboration.	Despite these outbreaks, there is yet no Lassa fever vaccine.

An estimated 300,000 to 500,000 Lassa fever cases are diagnosed annually, resulting in approximately 5,000 deaths. The World Health Organization has identified Lassa fever as one of the top emerging pathogens likely to cause severe outbreaks in the near future. In 2018, the Nigeria Centre for Disease Control (NCDC) reported the largest ever number of cases in Nigeria, with over 600 confirmed cases and over 170 deaths.

Conclusion

- Advances in vaccine R&D have not been paralleled by the regular introduction of new vaccines into the market.
- More vaccine trials need to happen in developing countries, where preventable infectious diseases still impose a major public health problem.
- Most of the new developments are being conceived to target the market of industrialized countries and it is foreseeable that their introduction in low-to-middle income countries will be difficult.
- Nigeria needs to strengthen her own capacities for R&D to ensure that new vaccines will become a sustainable reality.
- We need concerted efforts that draw together local capacities (industry and academy) with the experience of large global manufacturers.
- Nigeria can do it if only we decide to work together to break into this multi-million dollar enterprise through public private partnership.

International Collaboration for Vaccine Trials

Thank you and God Bless.