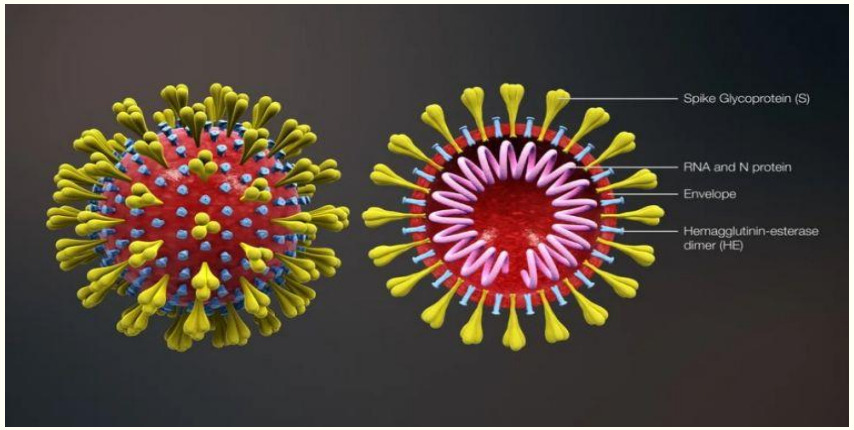
Regulatory Pathway for COVID-19 Vaccine



AIDCOC Webinar

30th Jan 2021

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Agenda

01 Introduction to COVID-19

02 Serum COVID-19 Candidate Vaccine Technology

03 Global Regulatory Pathway and Consideration

04 Country wise Registration Pathway

Vaccination

- Vaccination is most **effective public health intervention**
- A vaccine is a preparation intended to **produce immunity** to a disease by stimulating the **production of antibodies** to protect the person against subsequent infection or disease.

- **Value of Vaccination:**
  - Vaccination saves life
  - Vaccination saves money

Diseases and Vaccines

- Cholera
- Dengue
- Diphtheria
- Hepatitis
- *Haemophilus influenzae* type b (Hib)
- HIV/AIDS
- Human papilloma virus (HPV)
- Influenza
- Japanese encephalitis
- Malaria
- Measles
- Meningococcal meningitis
- Mumps
- Pertussis
- Pneumococcal disease
- Poliomyelitis
- Rabies
- Rotavirus
- Rubella
- Severe Acute Respiratory Syndrome (SARS)
- Tetanus
- Tick-borne encephalitis
- Tuberculosis
- Typhoid
- COVID-19

COVID-19 Disease

- Coronavirus disease (COVID-19) is an infectious disease caused by a novel coronavirus.

- A novel coronavirus (nCoV) is a new strain that has not been identified in humans previously. Once scientists determine exactly what coronavirus it is, they give it a name (as in the case of COVID-19, the virus causing it is SARS-CoV-2).

- The routes of transmission of COVID-19 remains unclear at present, but evidence from other coronaviruses and respiratory diseases indicates that the disease may spread through large respiratory droplets and direct or indirect contact with infected secretions. It has been found that it having high mortality and morbidity. The World Health Organization (WHO) declared spread of the novel coronavirus COVID-19 a pandemic.

- The most common symptoms of COVID-19 are fever, tiredness, and dry cough. Some patients may have aches and pains, nasal congestion, runny nose, sore throat or diarrhea. These symptoms are usually mild and begin gradually.

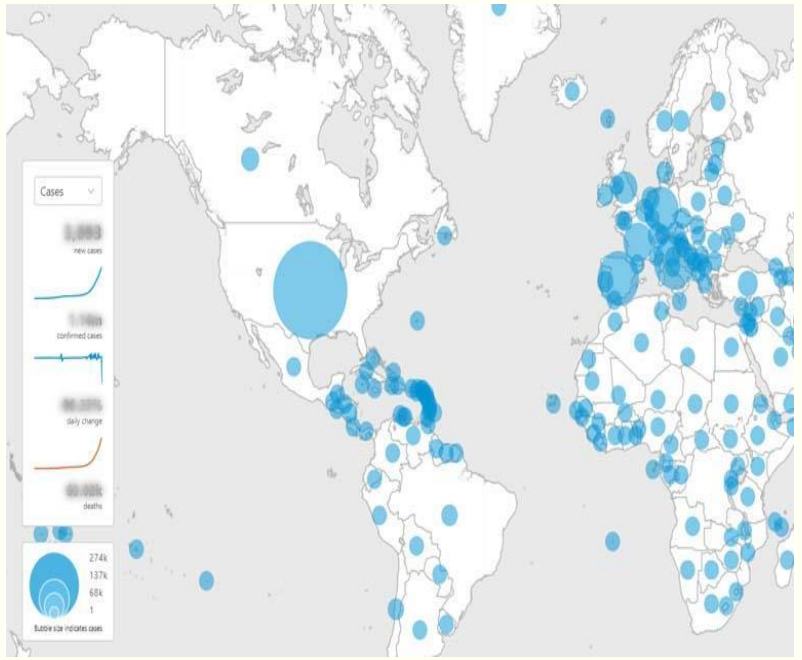
- Since early April 2020, COVID-19 disease has become the leading cause of death in the world outpacing cancer and cardiovascular disease in daily mortality.

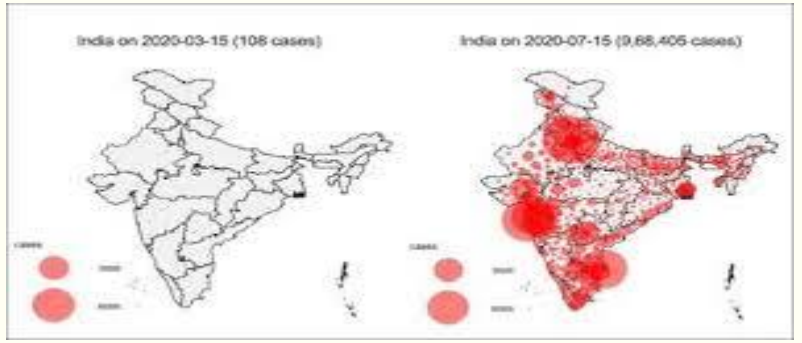
COVID-19 Disease

- As of January 28, 2021 WHO reported **100,455,529 confirm cases, 2,166,440 confirmed deaths** and these figures are continuously increasing day by day. Almost whole world, more than **216 countries** are currently suffering with COVID-19 pandemic situation.

- As of January 28, 2021 India reported total confirmed cases of more than **10.7 Million** as per data of Ministry of Health, Government of India.

- Organizations around the world are relentlessly pursuing to develop a vaccine to prevent COVID-19 and Indian organization is not an exception case, in order to overcome from COVID-19 pandemic situation and for well being and protection of mankind. We are working at unprecedented speed to support the broad, equitable and timely access of vaccine during the pandemic, should it prove effective and well-tolerated.





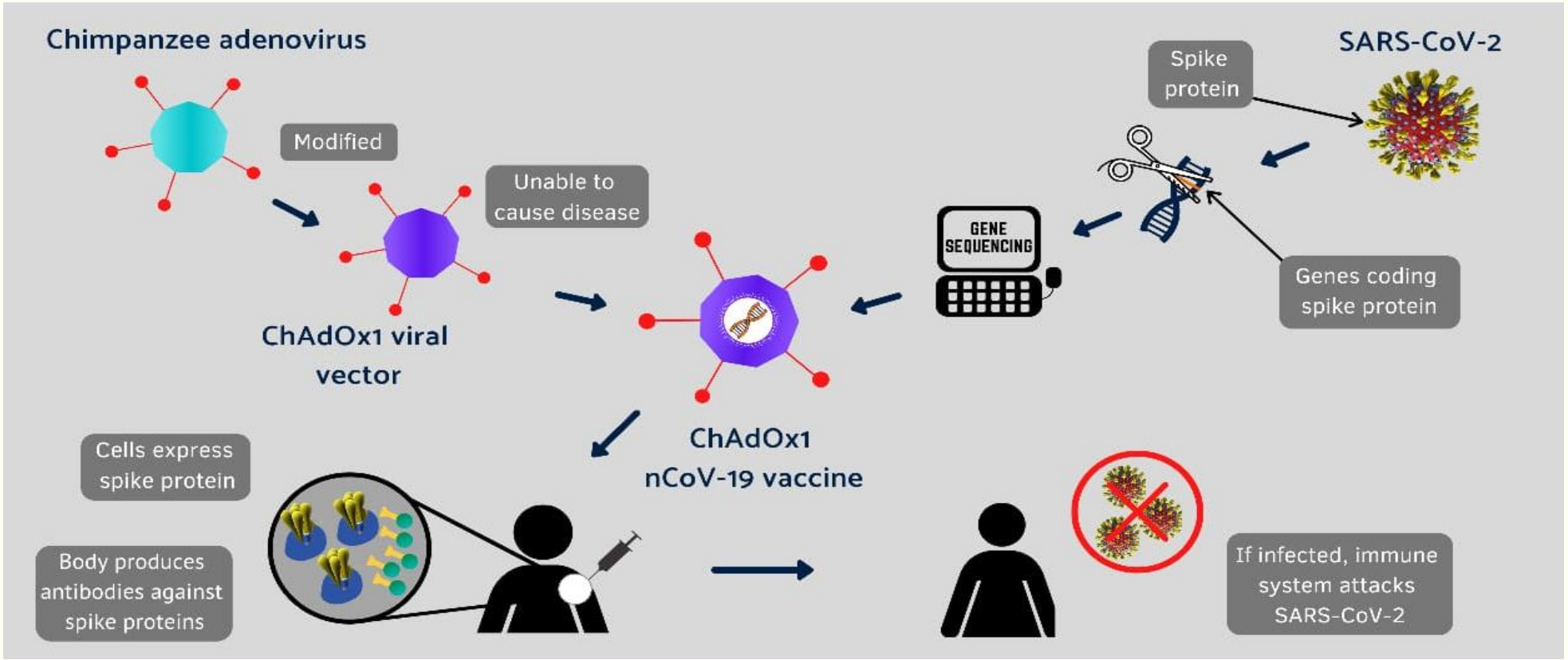
COVID-19 Candidates

SIIPL is developing following product candidates for addressing COVID-19

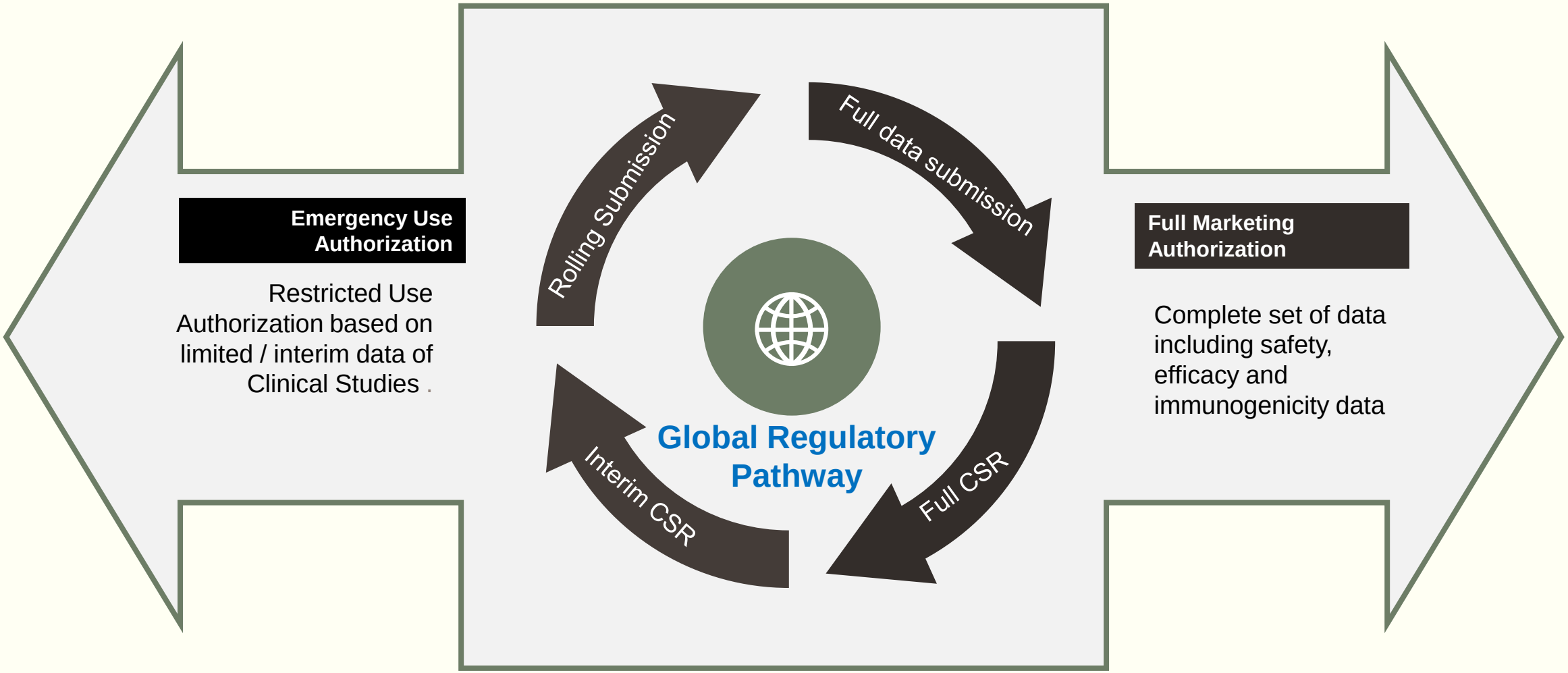
- COVISHIELD: Non-Replicating Viral Vector vaccine in collaboration with OU/AZ
- COVOVAX: Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M in collaboration with Novavax Inc
- COVIVAXX: RBD VLP display vaccine (Indigenous product)
- COVIVAC: De-optimised attenuated vaccine in collaboration with Codagenix - Intranasal
- rBCG (VPM1002) Immune boost

COVISHIELD™ (ChAdOx1 nCoV-19) Vaccine Technology

Replication-deficient simian adenoviral vectored vaccine expressing nCoV-19 Spike



Global Regulatory Pathway



Regulatory Pathways for Different Markets

Emergency Use Authorization (EUA)

To ensure that a widely deployed COVID-19 vaccine is effective, the primary efficacy endpoint point estimate for a placebo-controlled efficacy trial should be at least 50%, and the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate is >30%.

Conditional marketing authorization by rolling reviews

To facilitate COVID-19 candidate vaccines attaining emergency use designation, the European Medicines Agency has started rolling reviews of leading candidate vaccines, which enable European regulators to quickly analyze results as they become available, rather than wait for a full application. Efficacy should be 50%

Interim Order (IO) pathway

This interim order facilitates timely access for Canadians to drugs and vaccines that have demonstrated the ability to diagnose, prevent, treat or cure COVID-19. The interim order introduces temporary regulations to expedite the authorization for importing, selling and advertising COVID-19-related drugs without compromising patient safety.

Emergency Use Listing (EUL)

WHO's evaluation will determine "whether, in light of available WHO/international standards, the submitted data demonstrate a reasonable likelihood that the vaccine quality, safety and efficacy are acceptable and that the benefits outweigh the foreseeable risks and uncertainties"

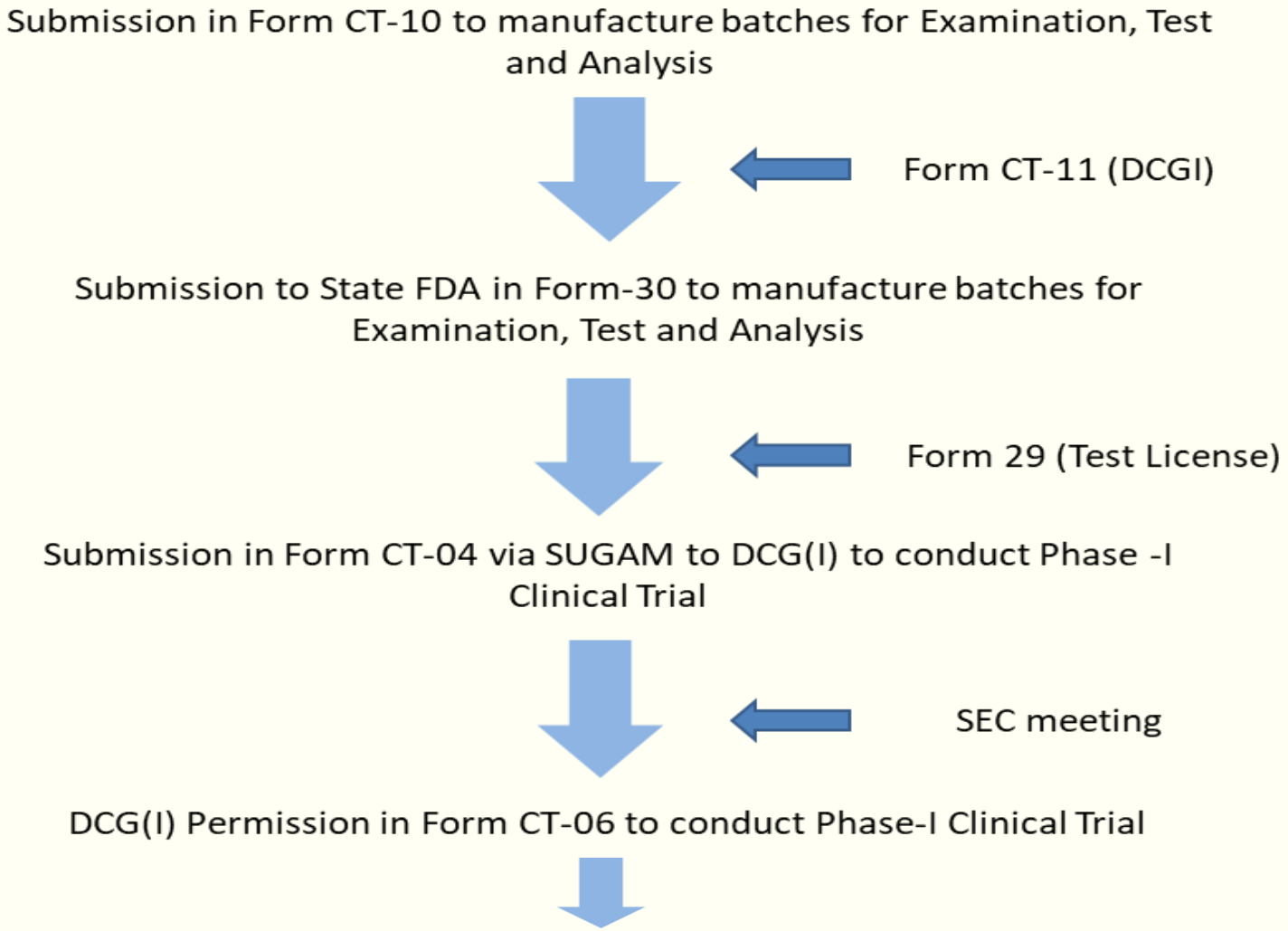
Regulatory Pathway for India

- DCGI has published DRAFT REGULATORY GUIDELINES FOR DEVELOPMENT OF VACCINES WITH SPECIAL CONSIDERATION FOR COVID-19 VACCINE.

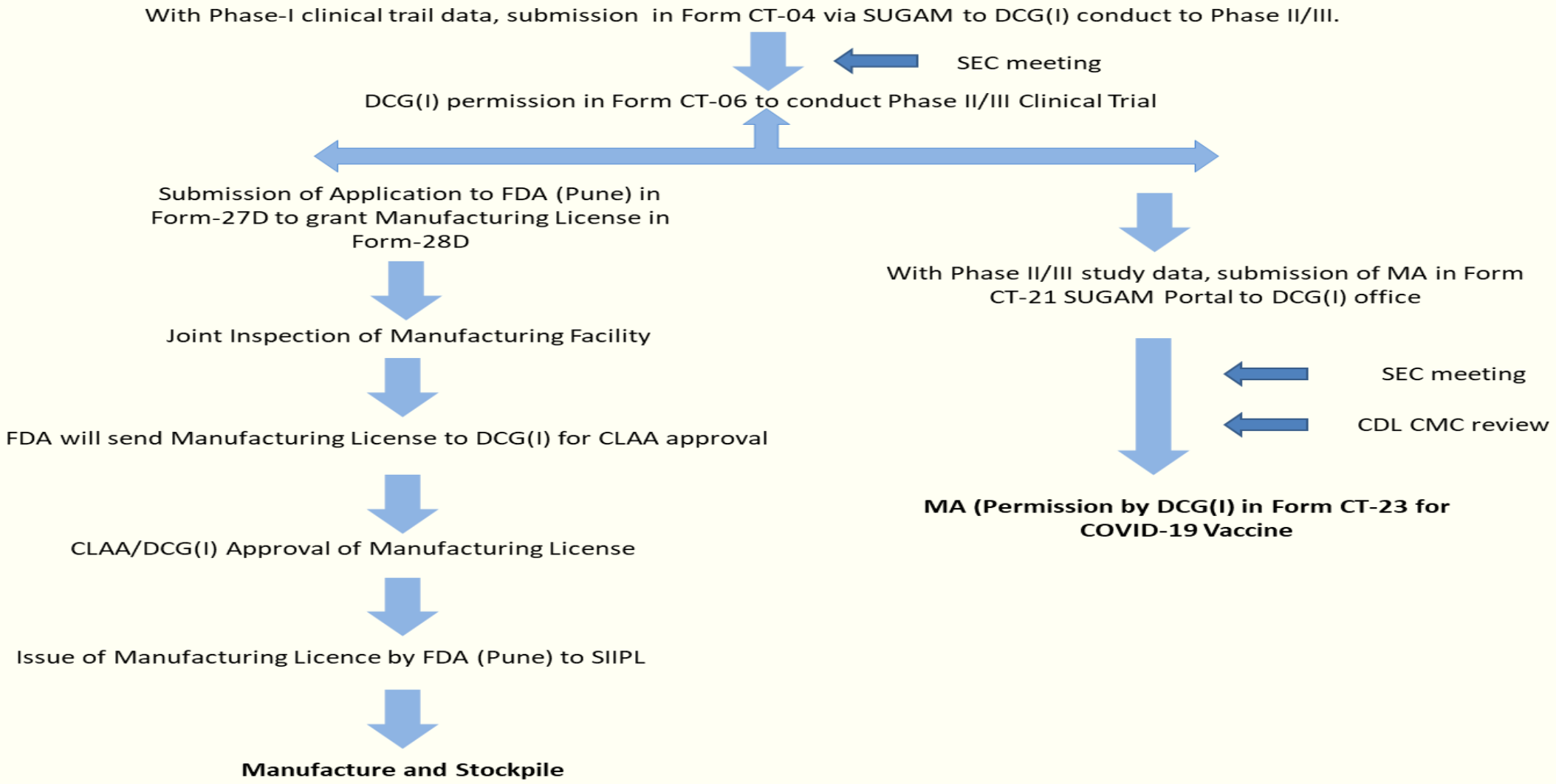
- Early in 2020, the DCGI office has offered several measures for speeding up the process, from giving fast-track approval for repurposed drug to waiving animal study and offering flexible pathways which earlier would have taken months. It said, that the COVID-19 related applications from companies will be given “high priority” and that it will assist the companies in speeding up their research. In parallel to the Clinical Trial in India, exceptional application and grant of license to manufacture and stockpile was introduced (Notification dated 18 May 2020)

- At the time of submission of Emergency Use Authorization application by Pfizer, Serum and Bharat Biotech it was not decided by Indian agency that what should be the terminology used and at last they finalized the name as **“Restricted Use in Emergency Situation”**

Regulatory Pathway for India



Regulatory Pathway for India

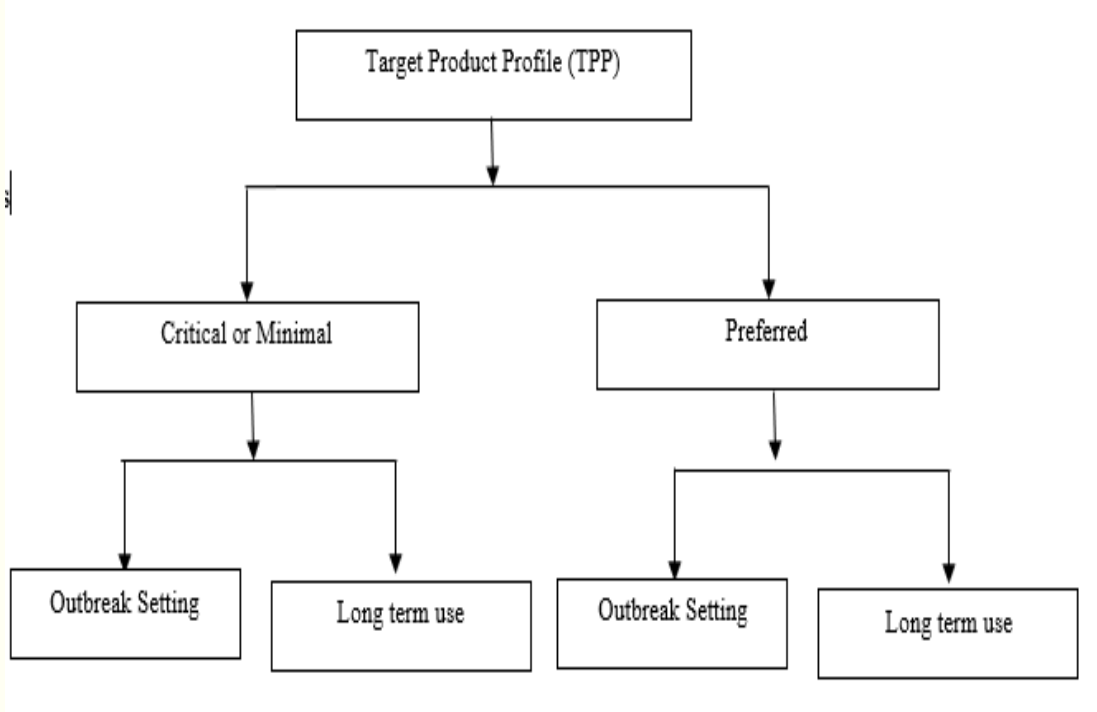


WHO Regulations for COVID-19 Vaccine

- WHO has published a separate guideline as “WHO Target Product Profiles (TPP) for COVID-19 Vaccine, Version 3.0, dated 29th April 2020. https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines

- WHO’s expectation is that the vaccine profile be sufficiently superior to the critical characteristics under one or more categories, this may outweigh failure to meet another specific critical characteristic. Vaccines which fail to meet multiple critical characteristics are unlikely to achieve favourable outcomes from WHO’s processes

- Preferred characteristics should not be considered as the maximum desirable characteristics; vaccines that exceed these characteristics may find advantages in WHO’s processes.



WHO Eligibility Criteria for EUL

- In order to qualify for assessment under EUL procedure, four criteria listed by WHO have to be been fulfilled

The disease for which the product is intended is serious or immediately life threatening, has the potential of causing an outbreak, epidemic or pandemic and it is reasonable to consider the product for an EUL assessment, e.g. there are no licensed products for the indication or for a critical subpopulation (e.g. children)
Existing products have not been successful in eradicating the disease or preventing outbreaks (in the case of vaccines and medicines)
The product is manufactured in compliance with current GMP in the case of medicines and vaccines and under a QMS in the case of IVDs
The applicant undertakes to complete the development of the product (validation and verification of the product in the case of IVDs) and apply for WHO prequalification once the product is licensed. For that purpose, the remaining clinical trials and other testing needed to complete the development of the product must already be underway at the time of the application for an EUL

WHO Eligibility Criteria for EUL

- Tabulated below the list of **Target Products Profiles**

Vaccine Characteristics	Compliance Requirement as per the WHO guideline Critical or Minimal	Compliance Requirement as per the WHO guideline Preferred
Indication for Use	Outbreak: For active immunization of persons in the area of an on-going outbreak for the prevention of COVID-19; to be used in conjunction with other control measures to curtail or end an outbreak Long Term (LT): For active immunization of at-risk persons to prevent COVID-19	Outbreak: For active immunization of persons in the area of an on-going outbreak for the prevention of COVID-19; to be used in conjunction with other control measures to curtail or end an outbreak. Long Term (LT): For active immunization of at-risk persons to prevent COVID-19
Contraindication	Some contraindications (e.g., immunocompromised) may be acceptable	None
Target Population	Adults, including elderly	All ages Suitable for administration to pregnant and lactating women.
Safety/Reactogenicity	Outbreak: Safety and reactogenicity whereby vaccine benefits outweigh safety risks. Benefit/risk may depend on age, other factors. Benefit/risk assessment should take potential for enhanced disease into account . LT: Safety and reactogenicity sufficient to provide a highly favourable benefit/risk profile in the context of observed vaccine efficacy; with no severe adverse events related to vaccination.	Safety and reactogenicity sufficient to provide a highly favorable benefit/risk profile in the context of observed vaccine efficacy; with only mild, transient adverse events related to vaccination and no serious AEs.

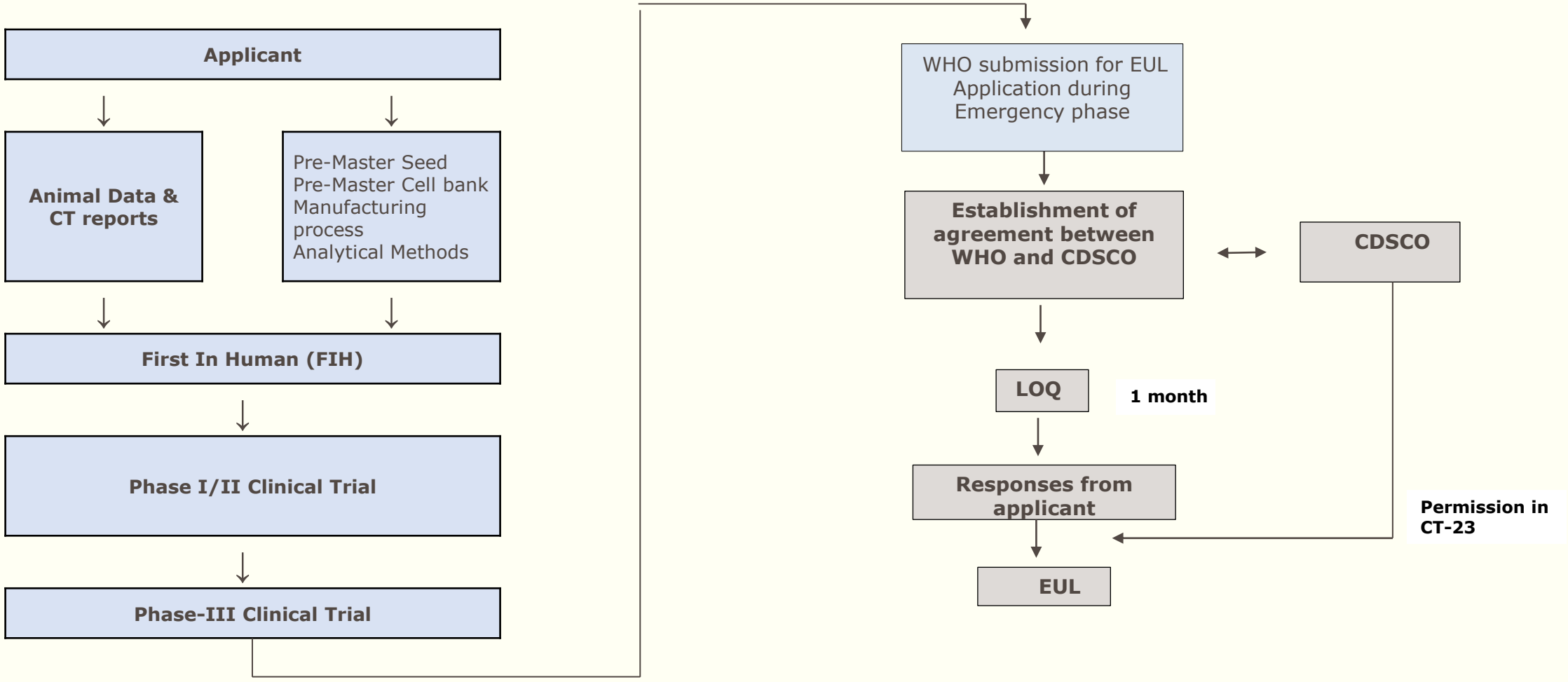
WHO Eligibility Criteria for EUL

Vaccine Characteristics	Compliance Requirement as per the WHO guideline Critical or Minimal	Compliance Requirement as per the WHO guideline Preferred
Measures of Efficacy	Clear demonstration of efficacy (on population basis) ideally with approx. 50% point estimate Endpoint may be assessed vs. disease, severe disease, and/or shedding/transmission	At least 70% efficacy (on population basis, with consistent results in the elderly) Outbreak: Rapid onset of protection (less than 2 weeks) LT: rapid onset of protection is less important
Dose Regimen	Outbreak: No more than two dose regimen LT: Booster doses permitted	Outbreak: Single-dose primary series LT: Lower frequency (Yearly or less) of booster doses is preferred
Durability of Protection	Confers protection for at least 6 months	Confers protection for at least 1 year.
Route of Administration	Any route of administration is acceptable, if vaccine is safe and effective	Outbreak: Non-parenteral is preferred for ease of rapid administration and other logistical issues. LT: any route of administration is acceptable
Product Stability and Storage	Outbreak: Shelf life of at least 6-12 months as low as -60 - 70˚C and demonstration of at least 2-week stability at 2-8˚C. LT: Storage at -20˚C or higher	Higher storage temperatures and higher thermostability will greatly enhance vaccine distribution and availability, and are thus strongly preferred. Vaccine vial monitor (VVM): Proof of feasibility and intent to apply a VVM to the primary container.

WHO Eligibility Criteria for EUL

Vaccine Characteristics	Compliance Requirement as per the WHO guideline Critical or Minimal	Compliance Requirement as per the WHO guideline Preferred
Co-administration with other vaccines	Stand-alone product	Outbreak: stand-alone product LT: potential for coadministration12 with other vaccines that are typically administered in campaigns preferred
Presentation	Multi- or mono- dose presentations are acceptable Maximum parenteral dose volume: 1 mL Multi-dose presentations should be formulated, managed and discarded in compliance with WHO's multi-dose vial policy.	Outbreak: Availability of multi-dose presentation is generally preferred for use in campaigns. LT: mono-dose or multi-dose presentations are acceptable Maximum parenteral dose volume: 0.5 mL Multi-dose presentations should be formulated, managed and discarded in compliance with WHO's multi-dose vial policy
EUA/WHO EUL Registration and Prequalification	Outbreak: Meets criteria for EUA/ WHO EUAL LT: WHO pre-qualified	Outbreak: Meets criteria for EUA/ WHO EUAL LT: WHO pre-qualified
Accessibility	Outbreak: Capability to rapidly scale-up production at cost/dose that allows broad use, including in LMIC. LT: Availability of sufficient doses at cost/dose that allows broad use, including in LMIC	Outbreak: Capability to rapidly scale-up production at cost/dose that allows broad use, including in LMIC. LT: Availability of sufficient doses at cost/dose that allows broad use, including in LMIC

WHO EUL Pathway



Regulatory Pathway for South Africa (SAHPRA)

Submission of **Section 21 authorization application** by local agent or directly to South African Health Product Regulatory Authority (SAHPRA).

Submission of Section 21 application along with information prescribed by **regulation 29 (2) of General Medicines Regulation** on online portal.

Evaluation and decision by SAHPRA within couple of weeks. Approval valid for **6 months.** Beyond this period extension may be requested

Conditional Approval for sale of unregistered medication granted.

Regulatory Pathway for Brazil (ANVISA)

Submission of an application for **authorization for Emergency use** directly or via local agent to Agência Nacional de Vigilância Sanitária (ANVISA) - Brazil National Health Surveillance Agency.

Submission of application for emergency use is done under the terms of Resolution RDC No. 444/2020 and Guide No. 42/2020

GGMED, GGFIS GGMON; These agencies along with ANVISA review the data of all phases conducted as well as the safety and efficacy data of the vaccine.

Grant of Emergency Use Authorization

Regulatory Pathway for UK

Evaluation of data as it is being generated (rolling review model) via Regulation 174

Review of pre-clinical studies, clinical trials, manufacturing and quality controls, product sampling and testing of vaccine as soon as data of each phase becomes available.

National Institute of Biological Standards and Control (NIBSC) conducts independent testing to confirm safety and quality of each batch.

Grant of EUA by MHRA based on recommendation by Commission on Human Medicines

QP Role is key in batch evaluation and release

Emergency Use Approval Pathway – United States of America

Upon total completion of phase 3 or upon generation of enough data to prove safety and efficacy of vaccine the data is assessed by data safety monitoring board (in accordance with FDA)

Emergency Use Authorization (EUA) data submission by applicant to FDA.

Evaluation of EUA by FDA personnel

Concurrent with FDA evaluation, conduction of public meeting of Vaccines and Related Biological Products Advisory Committee (VRBPAC)

Grant of EUA based on evaluation by FDA and input from VRBPAC.


thank you
gracias
danke
merci
obrigado
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