WHO Revised guidance on Emergency Use Listing

SAGE COVID-19 Vaccines Meeting

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CONSIDERATIONS FOR EVALUATION OF COVID-19 VACCINES
Points to consider for manufacturers of COVID-19 vaccines (25 Nov 2020)

World Health Organization

- Additional nonclinical info
  - **Novel adjuvants**
  - **Vaccine-enhanced disease**
- Clinical assessment
  - Placebo-controlled efficacy trial
    - primary efficacy endpoint of at least 50%
    - lower bound of the confidence interval >30%
  - **Non-inferiority to a COVID-19 vaccine already proven to be effective**
  - Endpoints of interest (infection, disease, severe disease, death)
  - Stratification (age, comorbidity)
  - Duration of protection / need for booster
  - Immunogenicity
    - correlations of protection
  - Safety
- Benefit-risk assessment report
- Risk management plan (RMP)
- Manufacturing and quality control

Addendum (12 March 2021)

- Purpose
  - **Variants of concerns (VOCs)**
  - **Possible need for monovalent modified vaccines**
- Additional non-clinical info
  - VOCs
- Clinical
  - **Non-inferiority study comparing the immune response induced by the modified COVID-19 vaccine to that by the prototype COVID-19 vaccine**
  - **Booster dose – same criteria**
- Risk management plan (RMP)
  - **Need for demonstration of effectiveness**

Revised guidance EUL document* (30 March 2022)

- **Discussed with regulators and the WHO R&D Blueprint Team**
- Published on 30 March 2022
- Revision
  - **Acknowledges applications for EUL based on immunobridging**
  - Indicates that careful **choice of comparators** is important
  - Indicates that **additional nonclinical and immunogenicity data** may be required
  - Indicates that **demonstration of efficacy will also be needed as a post-listing commitment**
    - **in-deployment clinical trials or**
    - of (more likely to happen in practice) **effectiveness by post-deployment observational studies**
  - Avoids being too prescriptive
  - Is **aligned with the**
    - **revised WHO Target Product Profiles (TPP) for COVID-19 vaccines**
    - **draft R&D Blueprint Team "Framework" document**

* Considerations for evaluation of COVID-19 vaccines: Points to consider for manufacturers of COVID-19 vaccines. Revised version, 30 March 2022
https://extranet.who.int/pqweb/sites/default/files/documents/Considerations_Assessment_Covid-19_Vaccines_v30March2022.pdf

WHO COVID-19 vaccines listed for emergency use and boosters (1)

For COVID-19 vaccines already listed aimed at homologous or heterologous boosting seeking approval based on immunobridging approach

- Non-inferiority to comparator (listed COVID-19 vaccine)
- Demonstration of immunobridging to the listed vaccine based on neutralizing antibodies; demonstration of cell mediated immunity and binding antibody response may confer supportive evidence of interest.
- These variations should be supported by reactogenicity and safety data; benefits should outweigh the risks.
- Individuals vaccinated with the candidate vaccine should be monitored over time for waning of protection and need for a booster dose

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WHO COVID-19 vaccines listed for emergency use and boosters (2)

For new COVID-19 vaccine candidates aimed at primary immunization or heterologous boosting seeking approval based on immunobridging approach

- Provide rationale for the selection of comparator(s)
- Whenever possible the comparator vaccine should be of the same vaccine platform.
  - If a comparator of the same platform is not available, there should be strong evidence that the new vaccine candidate is capable of inducing non-neutralizing protective (e.g., cell mediated and non-neutralizing humoral) immune responses comparable to that of the comparator
- Data on comparator effectiveness against severe disease caused by currently circulating VOCs (instead of the initial VE when it was first evaluated / recommended / approved)
- Non-inferiority (sometimes superiority) to comparator (EUL listed COVID-19 vaccine)
- In addition to demonstration of immunobridging to an appropriate vaccine comparator based on neutralizing antibodies, demonstration of cell mediated immune and binding antibody responses are required
- Post-EUL effectiveness studies also necessary

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WHO COVID-19 vaccines listed for emergency use and boosters (3)

For modified COVID-19 (monovalent, variant specific) vaccine candidates aimed at primary immunization or homologous boosting seeking approval based on immunobridging approach

- Non-inferiority to comparator (listed COVID-19 vaccine)
- In addition to demonstration of immunobridging to the already listed vaccine based on neutralizing antibodies, demonstration of cell immune immunity and binding antibody response may confer supportive evidence of interest
- Confirmatory vaccine effectiveness [estimated by observational sponsor-initiated or independent vaccine effectiveness study(ies)] will be requested as a post-EUL commitment for modified vaccines granted an EUL based on demonstration of immunobridging
- Individuals vaccinated with the candidate vaccine should be monitored over time for waning of protection and need for a booster dose

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Department of Regulation and Prequalification, WHO