List of WHO guidance on COVID-19 vaccines

Contents

Target Product Profiles for COVID-19 vaccines (17 April 2020)

https://www.who.int/publications/m/item/who-working-group-target-product-profiles-for-covid-19-vaccines

Extract of the section on 'programmatic suitability' below:

'Considerations on Programmatic Suitability':

In addition to meeting quality, safety and efficacy requirements, it is also important that developers and manufacturers understand WHO's preferences for parameters that have a direct operational impact on immunization programs. Low programmatic suitability of new vaccines could result in delaying introduction in routine immunization programmes. for example, introduction of new vaccines that have higher packaging or presentation volumes, low formulation stability will highly impact on cold chain capacity or disposal demands therefore may have negative impact on existing operations of immunization programs. Therefore, early stage consideration of presentation and packaging parameters is encouraged.

EUL-related guidance

Emergency use listing procedure

(version 14 Dec 2020)

https://www.who.int/publications/m/item/emergency-use-listing-procedure

Emergency Use Listing (EUL) procedure to streamline the process by which new or unlicensed products can be used during public health emergencies. The EUL replaces the Emergency Use Assessment and Listing (EUAL) procedure, which was used during the West Africa Ebola outbreak of 2014-2016.

Considerations for the assessment of COVID-19 vaccines for listing by WHO

WHO Considerations for evaluation of COVID-19 vaccines: Points to consider for manufacturers of COVID-19 vaccines (version 25 Nov 2020)

https://extranet.who.int/pqweb/sites/default/files/documents/considerations-who-evaluation-of-covid-vaccine_v25_112020.pdf

The general principles described in the WHO Guidelines below apply to all Covid-19 vaccines and should be followed: (extracts of the pages 5 and 6)

The general principles described in the WHO Guidelines below apply to all Covid-19 vaccines and should be followed:

1. "Procedure for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies", WHO Technical Report Series 978, Annex 6, 2013 [1]
2. WHO EUL document [2]
3. "Guidelines on clinical evaluation of vaccines: regulatory expectations", WHO Technical Report Series 1004, Annex 9, 2017 [3]
4. COVAX SAGE Compendium of Covid-19 vaccine research questions [4]

[1] http://www.who.int/immunization_standards/vaccine_quality/TRS_978_61st_report_Annex_6_PQ_vaccine_procedure.pdf?ua=1
[2] https://www.who.int/medicines/publications/EULprocedure.pdf?ua=1
[3] http://www.who.int/biologicals/expert_committee/WHO_TRS_1004_web_Annex_9.pdf
[4] https://www.who.int/docs/default-source/immunization/sage/2020/october/sage-wg-critical-questions-

5. "Guidelines for assuring the quality, safety, and efficacy of plasmid DNA vaccines" adopted by the Seventy-first Meeting of the World Health Organization Expert Committee on Biological Standardization, 24–28August 2020.[5]
6. "Points to Consider for assuring the quality, safety and efficacy of RNA vaccines"[6] (currently under development)[7]
7. WHO guidelines on nonclinical evaluation of vaccines. TRS 927, Annex 1[8]
8. Guidelines on the nonclinical evaluation of vaccine adjuvants and adjuvanted vaccines. TRS 987, Annex 2 [9]
9. Recommendations for the Evaluation of Animal Cell Cultures as Substrates for the Manufacture of Biological Medicinal Products and for the Characterization of Cell banks. TRS 978, Annex 3[10]
10. WHO good manufacturing practices for biological products. TRS 999, Annex 2 [11]

Based on the current status of development of Covid-19 vaccines candidate, the extent of the available quality, safety and efficacy data and regulatory approvals by relevant NRAs, WHO shall follow either EUL process or Prequalification. Once a product has been listed under the EUL procedure, the development of the product must continue to completion for marketing authorization and be submitted to WHO for prequalification.

The decision for listing will be based on a risk-benefit assessment, of existing evidence of quality, safety and efficacy and will include a set of post-listing commitments.

ADDENDUM: Considerations for evaluation of modified COVID-19 vaccines:

Points to consider for manufacturers of COVID-19 vaccines (version 12 March 2021)

https://extranet.who.int/pqweb/sites/default/files/documents/Addendum_Evaluation_Modified_Covid-19%20Vaccine.pdf

Q&A: Use of EUL procedure for vaccines against COVID-19

30 September 2020 | Q&A

this Q&A should be read as a supplement to the general Q&A document for the EUL

https://www.who.int/news-room/q-a-detail/coronavirus-disease-use-of-emergency-use-listing-procedure-forvaccines-against-covid-19

Product eligibility under the COVAX Facility

https://extranet.who.int/pqweb/sites/default/files/documents/Product-Eligibility_COVAX-Facility_Dec2020_0.pdf

Extract of the first paragraph below:

Products procured and/or supplied under the COVAX Facility must be quality assured to

covid19-vaccine.pdf?Status=Temp&sfvrsn=6a98fce2_6&ua=1

[5] https://www.who.int/publications/m/item/DNA-post-ECBS-1-sept-2020

[6] Currently under development and to be published at https://www.who.int/biologicals

[7] https://www.who.int/publications/m/item/WHO-ECBS-aug-2020-executive_summary

[8] https://www.who.int/biologicals/publications/trs/areas/vaccines/nonclinical_evaluation/ANNEX%201Nonclinical.P31-63.pdf?ua=1

[9] https://www.who.int/biologicals/areas/vaccines/TRS_987_Annex2.pdf?ua=1

[10] https://www.who.int/biologicals/vaccines/TRS_978_Annex_3.pdf

[11] https://www.who.int/biologicals/expert_committee/WHO_TRS_999_FINAL.pdf?ua=1

ensure positive impact on the population that receive them and to preserve the trust that that has been placed in the Facility. Information about these products should be available to member states to enable them to make quick decisions on their importation and/or use and facilitate their continuous monitoring and oversite.

To achieve this, the COVAX Facility should only consider:

1. products listed by WHO Emergence Use Listing (EUL) or Prequalification (PQ) or,

2. under exceptional circumstances, products approved by a Stringent Regulatory Authority (SRA), hereunder to include Australia-TGA; EU-EMA; Canada-Health Canada; Switzerland Swissmedic; UK-MHRA and USA-FDA.

Please also see the Background information provided on the following topics:

a) Countries for reliance and streamlining assessment (abridged assessment)

b) Functional NRAs

First invitation to manufacturers of vaccines against COVID-19

https://extranet.who.int/pqweb/sites/default/files/documents/1_EOI-Covid-19_Vaccines.pdf

Rolling review of COVID-19 vaccines

https://extranet.who.int/pqweb/sites/default/files/documents/Note_Rolling_Review_May2021.pdf

Technical Advisory Group for Emergency Use Listing

(established December 2020)

The Technical Advisory Group for Emergency Use Listing (TAG-EUL) is an independent advisory group that will provide a recommendation to WHO whether an unlicensed vaccine can be recommended for emergency use under the EUL procedure, and if so, under what conditions.

https://extranet.who.int/pqweb/vaccines/TAG-EUL

TAG ToR

https://extranet.who.int/pqweb/sites/default/files/documents/TOR_TAG-EUL_DEC2020.pdf

WHO operational tool for efficient and effective lot release of SARS-CoV-2 vaccines

https://extranet.who.int/pqweb/sites/default/files/documents/WHO_OperationalTool_EfficientLotRelease_v20Jan2021.pdf

Scope of the tool

This operational tool was developed to assist national regulatory authorities in all countries to apply principles described in WHO Technical Guidelines to implement efficient and effective lot release of COVID-19 vaccines, including those granted WHO Prequalification or Emergency Use Listing, to mitigate potential bottlenecks and unnecessary wastage of these urgently needed products under the public health emergency of international concern.

Accompanying document:

WHO model NRA/NCL lot release certificate for SARS-CoV-2 vaccines

https://extranet.who.int/pqweb/key-resources/documents/annex-who-model-nrancl-lot-release-certificate-sars-cov-2-covid-19-vaccines

Status of COVID-19 vaccines within WHO EUL

https://extranet.who.int/pqweb/key-resources/documents/status-covid-19-vaccines-within-who-eulpq-evaluation-process

Consent of manufacturers

Consent of applicants/manufacturers of a vaccine or a pharmaceutical product, diagnostics and vaccines for WHO to share information with the national regulatory authority(ies) confidentially in emergency situations

https://extranet.who.int/pqweb/key-resources/documents/consent-applicantsmanufacturers-vaccine-or-pharmaceutical-product

Confidentiality agreements with national regulatory authorities

Confidentiality agreement template

English:
https://extranet.who.int/pqweb/sites/default/files/documents/CA_NRA_English_20210204.pdf

French: Engagement de Confidentialité des Autorités Nationales de Réglementation
https://extranet.who.int/pqweb/sites/default/files/documents/CA_NRA_French_20210204.pdf

Russian: СОГЛАШЕНИЕ О СОБЛЮДЕНИИ КОНФИДЕНЦИАЛЬНОСТИ ИНФОРМАЦИИ НАЦИОНАЛЬНЫМ ОРГАНОМ РЕГУЛИРОВАНИЯ
https://extranet.who.int/pqweb/sites/default/files/documents/CA_NRA_Russian_20210204.pdf

Arabic: تعهد بالتزام السرية من قِبل السلطات التنظيمية الوطنية
https://extranet.who.int/pqweb/sites/default/files/documents/CA_NRA_Arabic_20210204.pdf

Roadmaps

Evaluation of AstraZeneca ADZ122 vaccine against COVID-19

https://extranet.who.int/pqweb/sites/default/files/documents/Astra-Zeneca-covid19-roadmap-301020.pdf

Evaluation of Jansen Ad26.COV2-S (recombinant) vaccine against COVID-19

https://extranet.who.int/pqweb/sites/default/files/documents/Janssen-Covid19%20Roadmap_Final_Dec20.pdf

References for WHO Technical Report Series

Relevant to the critical observations of the inspection:

- WHO TRS 961, Annex 6: WHO good manufacturing practices for sterile pharmaceutical products,
https://www.who.int/medicines/areas/quality_safety/quality_assurance/GMPSterilePharmac

euticalProductsTRS961Annex6.pdf

- WHO TRS 986, Annex 2: WHO Good manufacturing practices, main principle, https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS986annex2.pdf
- WHO TRS 996, Annex 3: WHO good manufacturing practices for biological products, https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS986annex2.pdf
- WHO TRS 1033, Annex 4: WHO Guideline on data integrity, https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

Draft guidance and update on international reference materials / standards

- WHO draft guidance on Regulatory considerations in the evaluation of mRNA vaccines – status report in 72nd and 73rd report: WHO TRS N°1030: 2020 (pages 38-39) https://www.who.int/publications/i/item/9789240024373
- International reference materials – standards for use in public health emergencies (Chapter 9 and Annex 5 of the 72nd and 73rd report: WHO TRS N 1030: 2020

  https://www.who.int/publications/i/item/9789240024373
- More references will be sighted in the main reports for the other observations.

Other WHO guidance and meeting reports

COVID-19 vaccine tracker and landscape

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

Global Consultation on SARS-CoV-2 Variants of Concern and their Impact on Public Health Interventions

10 June 2021
Selected regulators shared their perspectives and underscored the importance of the regulatory community continue to work together collaboratively and whatever is used, a booster dose of prototype vaccines or a variant-specific vaccine, induces broad protection.

Watch the recording: passcode: m#t9b!Tl

WHO Meeting on correlates of protection: COVID-19 vaccines

26 May 2021

A deeper understanding of correlates of protection would greatly help new vaccine and modified vaccines development (and extension of existing vaccines to new populations).

Meeting objectives are as follows:

1. To outline the role of immunobridging in the evaluation of COVID-19 vaccines (current vaccines, modified vaccines, new vaccines)
2. To enumerate the data that would be required to inform decisions on immunobridging and correlates of protection.

3. To discuss what is the role of the various assays and animal models and what are the current limitations with interpretation of results.
4. To debate on the design and analysis of clinical studies to define correlates of protection (non-inferiority vs superiority, selection of comparator and end points)
5. To review the current data and define a research agenda.

Watch the recording: passcode: JBt*NW49

COVID-19 Global Research & Innovation Forum

13 &14 May 2021

WHO research and scientific achievements in the fight against COVID-19 have just been released as a background piece to the 13-14 May Global Research & Innovation Forum. This report presents WHO led research and innovation achievements against the goals and knowledge gaps articulated in the Coordinated Global Research and Innovation Roadmap for COVID-19 released in March 2020. This research roadmap was the product of a two-day meeting convened by WHO with 350 of the top scientists worldwide on 11-12 February 2020 – just weeks after the pandemic was announced.

Using the R&D Blueprint framework, the roadmap aims to coordinate and accelerate global research, accelerate the development of diagnostics, medicines and vaccines, and ensure coordination of global research efforts towards the goals of the Roadmap.

https://www.who.int/teams/blueprint/covid-19/covid-19-global-research-innovation-forum

Overall achievements report

Recordings (available in 6 languages)

Detailed achievements report (by thematic area)

Animal-Human interface

Virology and diagnostics

Epidemiological studies

Clinical characterization and management

Infection, prevention and control

Therapeutics R&D

Vaccine R&D

Social sciences

Ethics

Infodemiology Research

Methodological approaches to assess variants effect on vaccine efficacy, effectiveness and impact

11 February 2021

The ad-hoc consultation was held with the following objectives:

- To outline current WHO efforts to set up a mechanism to provide guidance to developers/manufacturers and countries, and to coordinate changes that may be

needed for vaccines.

- To discuss the most robust methodological approaches to assess – during vaccine roll-out- if a circulating new COVID variant – considered of public health relevance- has an impact on vaccine effect.
- To deliberate on the research approaches that could be considered when assessing vaccines that have been adjusted to address vaccine efficacy issues with new variants.

https://cdn.who.int/media/docs/default-source/documents/r-d-blueprint-meetings/blueprint-covid-vaccines-and-variants-research-methods.pdf?sfvrsn=27feead4_1&download=true

Knowledge gaps and research priorities WHO ad hoc consultation

15 January 2021

The meeting concluded that, although the COVAX facility was making an important contributing to widening vaccine availability, there was still a need to ensure wider global access to COVID-19 vaccines. It was emphasized that all countries should have the potential to contribute to SARS-CoV-2 surveillance and vaccine research, and to gain access to the data generated by that research, as well as to the products that are developed on the back of such data.

As well as global equity arguments, global contributions to surveillance, research and vaccine access are also fundamental to global health security, as no country can be safe from COVID-19 until all are.

https://cdn.who.int/media/docs/default-source/blue-print/covid-vaccines-report-15-january.pdf?sfvrsn=ebf42ebd_3&download=true

COVID-19 new variants: Knowledge gaps and research

12 January 2021

In light of the potential risk posed by SARS-CoV-2 variants, in January 2021 WHO organized an ad hoc consultation to discuss the development of an R&D agenda in response to existing and emerging SARS-CoV-2 variants.

The key objectives were to identify the critical research questions related to variants and agree on a research approach to address them.

Six breakout groups covered a range of specific issues related to COVID-19 variants: Epidemiology and mathematical modelling; evolutionary biology; animal models; assays and diagnostics; clinical management and therapeutics; and vaccines.

This report is a summary of presentations and panel discussions.

https://cdn.who.int/media/docs/default-source/blue-print/covid-19-new-variants-meeting-report_20.03.2012.pdf?sfvrsn=5ac5785_3&download=true

Report of the WHO AG on human challenge studies

07 December 2020

WHO R&D Blueprint novel Coronavirus WHO Advisory Group Tasked to Consider the Feasibility, Potential Value and Limitations of Establishing a Closely Monitored Challenge Model of Experimental COVID-19 in Healthy Young Adult Volunteers

https://www.who.int/publications/m/item/report-of-the-who-ag-on-human-challenge-studies