WHO Target Product Profiles for COVID-19 Vaccines

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Purpose of the document

Selected disease areas are identified as WHO priorities for research and product development. In the case of COVID-19, target product profile development followed the COVID-19 Global research and innovation forum: towards a research roadmap. The target audience includes vaccine scientists, product developers, manufacturers and funding agencies.

All the requirements contained in WHO guidelines for WHO policy recommendation and prequalification will also apply. The criteria below lay out some of the considerations that will be relevant in WHO's case-by-case assessments of COVID-19 vaccines in the future.

Therefore, should a vaccine's 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. Likewise, preferred characteristics should not be considered as the maximum desirable characteristics; vaccines that exceed these characteristics may find advantages in WHO's processes.

A generic description of WHO's Vaccine Emergency Use Listing (EUL) and Prequalification process can be found at the end of this document.

Modelling of the potential impact of COVID-19 vaccines with different efficacy profiles, administered using different immunization strategies, at different stages of the epidemic is a high priority to further refine desired characteristics. For certain vaccine characteristics, additional footnotes are provided on the rationale and assumptions made.

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I. Background

On 31 December 2019, WHO was informed of a cluster of cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province of China. The coronavirus disease (COVID-2019) was identified as the causative virus by Chinese authorities on 7 January. As of 10 April 2020, there have been over 1.6 million cases and almost 100,000 deaths world-wide.

Experts in relevant disciplines met at the World Health Organization's Geneva headquarters from 11 to 12 February 2020[1] to assess the current level of knowledge about the new virus, agree on critical research questions that need to be answered urgently and ways to work together to accelerate and fund priority research that can contribute to curtail this outbreak and prepare for future outbreaks.

This document describes the preferred and minimally acceptable profiles for human vaccines for long term protection of persons at high ongoing risk of COVID-19 such as healthcare workers and for reactive use in outbreak settings with rapid onset of immunity.

This Target Product Profile (TPP) was developed through a consultation process with key stakeholders in human and animal health, scientific, funding and manufacturing communities. It is intended that it will guide and prioritize the development of vaccines. As new scientific evidence is generated, this TPP may require further review and revision.

[1] https://www.who.int/blueprint/priority-diseases/key-action/Global_Research_Forum_FINAL_VERSION_for_web_14_feb_2020.pdf?ua=1

II. Target Product Profiles

Roadmap strategic goal: Develop and license vaccines **for use in outbreak settings (Outbreak) and/or** with **long-term protection for administration to those at high ongoing risk of COVID-19 (LT).**

Vaccine characteristic	**Preferred**	**Critical or Minimal**
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. 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 LT: For active immunization of at-risk persons to prevent COVID-19
Contraindication	None	Some contraindications (e.g., immunocompromised) may be acceptable
Target population	All ages[2]. Suitable for administration to pregnant and lactating women.	Adults, including elderly
Safety/Reactogenicity	Safety and reactogenicity sufficient to provide a highly favourable benefit/risk profile in the context of observed vaccine efficacy; with only mild, transient adverse events related to	Outbreak: Safety and reactogenicity whereby vaccine benefits outweigh safety risks[3]. LT: Safety and reactogenicity sufficient to provide a highly

[2] Recognize that herd immunity (and transmission blocking) will depend on broad immunization, likely including children.

[3] Benefit/risk may depend on age, other factors. Benefit/risk assessment should take potential for enhanced disease into account

Vaccine characteristic	Preferred	Critical or Minimal
	vaccination and no serious AEs.	favourable benefit/risk profile in the context of observed vaccine efficacy; with no severe adverse events related to vaccination.
Measures of Efficacy	At least 70% efficacy (on population basis, with consistent results in the elderly)[4]. Endpoint may be assessed vs. disease, severe disease, and/or shedding/transmission. Outbreak: Rapid onset of protection (less than 2 weeks). LT: rapid onset of protection is less important	Clear demonstration of efficacy (on population basis) ideally with ~50% point estimate[4]. Endpoint[5] may be assessed vs. disease, severe disease, and/or shedding/transmission[6].
Dose regimen	Outbreak: Single-dose primary series[7]. LT: Lower frequency (Yearly or less) of booster doses is preferred	Outbreak: No more than two dose regimen[8] LT: Booster doses[9] permitted

[4] The lower confidence limit of the efficacy estimate could be lower. These levels of efficacy are chosen based on their ability to confer important individual, public health, and indirect effects, recognizing that achievement of herd immunity might also require non-vaccine interventions. It should be understood that other factors held constant, higher levels of efficacy are more desirable than lower levels of efficacy.

[5] If regulatory authorization is provided with incomplete clinical efficacy data, effectiveness data are to be generated during use

[6] Efficacy in reducing the proportion of individuals who shed viruses may be an acceptable marker predicting efficacy against transmission

[7] Note strong preference for single-dose, but do not desire to discourage development of 2-dose vaccines if that is what is feasible

[8] note cholera is 2 dose, and many 2 dose vaccines confer partial protection after a single dose. For two-dose vaccines, protection after single dose should be assessed

[9] Booster doses are defined in the context of protection from the primary regimen

Vaccine characteristic	**Preferred**	**Critical or Minimal**
Durability of protection	Confers protection for at least 1 year.	Confers protection for at least 6 months[10].
Route of Administration	Outbreak: Non-parenteral (syringe/needle or other adjunct equipment-avoiding) is preferred for ease of rapid administration and other logistical issues. LT: any route of administration is acceptable	Any route of administration is acceptable, if vaccine is safe and effective.
Product Stability and Storage	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.	Outbreak: Shelf life of at least 6-12 months as low as -60—70°C[11], and demonstration of at least 2-week stability at 2-8°C. LT: Storage at -20°C or higher;
Co-administration with other vaccines	Outbreak: stand-alone product LT: potential for coadministration[12] with other vaccines that are typically administered in campaigns preferred	Stand-alone product

[10] This might not be demonstrated in initial clinical studies, but could be supported by follow-on studies, animal data, etc.

[11] For drug product, storage at temperatures below -20C would require additional infrastructure and may impede distribution of vaccine, and would thus need to be addressed. This concern may be overcome by providing data supporting some storage at -20 and higher degrees.

[12] Defined as separate administration but on the same day

Vaccine characteristic	Preferred	Critical or Minimal
Presentation	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[13].	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.
EUA/WHO EUL Registration and Prequalification	Outbreak: WHO pre-qualified and/or made available under EUA/WHO EUL 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

[13] If feasible, vaccines consistent with an "open vial" policy may have additional advantages

III. Considerations on Programmatic suitability

Vaccine for human use

WHO Prequalification
Except in cases of Emergency Use Listing (https://www.who.int/who-documents-detail/emergency-use-listing-procedure), vaccines that are procured by United Nations agencies and for financing by other agencies, including Gavi, the vaccine alliance, require WHO Prequalification. The WHO prequalification (PQ) process acts as an international assurance of quality, safety, efficacy and suitability for low and middle-income country immunization programs. WHO encourages vaccine developers and manufacturers to be aware of the WHO prequalification process, even at the early stages of development and to discuss the product and the regulatory requirements with the WHO prequalification staff early in the process. Licensure by a national regulatory authority (NRA), or European Medicines Agency in the case of the centralized procedure for marketing authorization in Europe, will be required prior to any consideration of prequalification. Furthermore, the prequalification process requires regulatory oversight by the NRA of Record, which is usually the NRA of the country where the vaccine is manufactured or the NRA of the country of finishing and distribution, and such an NRA should have been assessed as functional by WHO. Vaccine developers should check that the planned NRA of Record for the prequalification procedure is considered functional by WHO.

The prequalification procedure is described in detail in the document Procedures for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies (WHO TRS 978) available here: http://apps.who.int/medicinedocs/documents/s21095en/s21095en.pdf. The WHO PQ process which assesses vaccine quality, safety, efficacy and suitability for use in low and middle-income countries has developed criteria called Programmatic Suitability for Prequalification (PSPQ) criteria to review vaccines submitted for prequalification. (http://apps.who.int/iris/bitstream/10665/76537/1/WHO_IVB_12.10_eng.pdf).

Considerations of Programmatic Suitability for Prequalification
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.