Vaccine prioritization for WHO Phase IIb/III clinical trial

Purpose of the document

The proposed attributes and criteria provide considerations for the evaluation and prioritization of COVID-19 candidate vaccines to be considered for further development by WHO. The target audience includes vaccine scientists, product developers, manufacturers, regulators and funding agencies.

The attribute and criteria below lay out some of the considerations that structure WHO's case-by-case assessments of COVID-19 vaccines in the future, with emphasis on prioritization for Phase IIb/III evaluation.

Criteria that are considered of major importance in ranking the vaccines are reported in bold in the table. WHO will also provide a scoring guide to promote consistency and predictability of evaluation.

ATTRIBUTE	MINIMALLY ACCEPTABLE PROFILE	COMPLIANT yes/no	CRITERIA	Candidate Vaccine #1 Score	COMMENT
Safety profile 25 points	Adverse event profile supports advancement to phase IIb/III Data from animal and human studies support no apparent risk of enhanced disease in vaccinees		**Lack of significant disease enhancement risk supported by clinical and/or preclinical data from relevant/suitable animal model(s), and of unexpected serious findings (e.g. unexpected AE) that could require more investigations**		
			Availability and rigor of safety follow-up , e.g. diary card etc		
			Safety database size adequate to support phase IIb/III [1]		
			Type of population included, e.g **Elderly**, pregnant women and subjects with chronic conditions		
			Developmental and reproductive studies		
Potential for efficacy 25 points	Evidence that the selected dose induces adequate immune responses in humans that might confer protection		**Magnitude of the immune response in humans (at selected dose) as compared with putative protective levels, supported by challenge studies showing vaccine protection from disease (e.g., pneumonitis) in characterized animal model or by other data (including any surrogate marker derived from clinical trial or natural history of disease data). Immune responses measured are ideally pertinent to the mechanism of protection of the candidate vaccine, e.g. titre of neutralizing antibodies and CMI responses for vaccines intended to induce one.**		
			Quality of immune response assays for key immunogenicity read-outs[2]		
			Quality of data supporting putative protective levels[3]		
			Sufficient evidence supporting dose selection including dosing/response in the elderly		
			Rapidity/level of immune response after the first vaccine dose		
			Durability of the immune response		

[1] Minimum # of subjects required for entry to phase IIb/III will be indicated in scoring guide

[2] E.g., for vaccines inducing humoral immunity (even if they also induce cellular immunity): Use of international standards in human studies where feasible, Neutralizing titers evaluate both IC50 and IC80, and Sensitivity of any pseudovirion neut assays is understood relative to WT virus; and for vaccines inducing cellular immunity: Sufficient assay qualification to interpret results.

[3] E.g., for animal models, rigor of experiments and degree to which the model used has been characterized, and for human data, degree of confidence in surrogate markers

Vaccine stability 10 points	Stability data are sufficient to assure delivery of dose to be tested		The vaccine has adequate stability[4] Quality of stability studies		
Vaccine implementation 15 points	Manageable regimen considering resource settings Any special requirements for immunization can be addressed Maximum parenteral dose volume: 1 mL		Regimen: Single dose preferred Acceptability of route of administration, Dose volume (0.5 ml is preferred for parenteral) Special requirements that might interfere with implementation is not preferred		Moved regimen here from under “efficacy”, because it is critical for implementation.
Vaccine availability 25 points	Demonstrated capability to rapidly scale-up production to allow inclusion in the trial and for broader use[5]		**number of regimens of adequate quality available for Phase IIb/III clinical trial**		
			Forecast of phased production capacity including buffer and delivery device capacity		
OVERALL SCORE					

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[4] E.g, Demonstration of at least 2-week stability at 2-8°C, stability profiles at different temperatures, e.g. -20°C and studies in place to support shelf life of at least 12 months as low as -60 - -70°C.

[5] Number of regimens required will be indicated in scoring guide