World Health Organization

# COVID-19 vaccines
## WHO Meeting on correlates of protection

26 May 2021

**13:00 – 18:00 Central European Time CET**

## Agenda - outline

Version 2 – 18 May 2021



R&DBlueprint

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## BACKGROUND

The ability to assess the protective efficacy of a vaccine by measuring the proportion of vaccinees who generate a particular immune response, without having to measure clinical outcomes, has significant advantages. The availability and quality of such substitute endpoints are important for vaccine development, licensure and effectiveness monitoring. A better understanding of the interrelationships between vaccination, the immune response, protection, and clinical outcomes is thus of interest not only to regulatory authorities but also to microbiologists, immunologists, epidemiologists and statisticians. Different study designs, each with their strengths and weaknesses, have been used to evaluate immunological substitute endpoints of vaccine-induced protection. Various statistical tools have been developed to evaluate these endpoints, but few epidemiologists are familiar with the details of these methods. Immunological substitute endpoints can be relative or absolute quantities, and further information is needed on how they are affected by factors such as the challenge dose, the mechanism of action of the vaccine, the environment, or host characteristics. [1]

Regarding COVID-19 vaccines, while the data have been sufficient to warrant emergency use authorizations, many gaps in knowledge exist. Vaccines have not yet been tested in all population groups, their impact on subclinical disease and transmission remains to be determined, and the duration of protection and need for booster doses are not yet clear. Development of new products needs to continue, to provide a diversified portfolio of products and manufacturers, and to generate vaccines with more desirable properties, including single-dose use, no cold-chain requirements, and non-injectable delivery. More standardized preclinical models and assays would help to accelerate development and expedite regulatory review of second-generation products. Placebo-controlled trials remain the most powerful way to evaluate vaccines, but are becoming less appropriate as vaccine availability increases. Noninferiority active comparator studies are an appropriate alternative [2].

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

## OBJECTIVES OF THE MEETING

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.



[1] https://apps.who.int/iris/bitstream/handle/10665/84288/WHO_IVB_13.01_eng.pdf;sequence=1
[2] https://www.who.int/publications/m/item/covid-19-vaccines-knowledge-gaps-and-research-priorities---who-ad-hoc-consultation

**Chairperson: Stanley Plotkin**

| Time | Topic |
|---|---|
| 13:00 - 13:10 | **Welcome address**<br>Objectives of the meeting |
| 13:10 - 13:20 | **Why do we need correlates of protection**? |
| 13:10 – 13:20 | **What data would be required?**<br>(assays, animal models, trials, convalescent sera, mAbs) |
| 13:20 – 13:30 | **Assays to support development of immune correlates of protection** |
| 13:30 – 13:40 | **Development of next generation models to address correlates of protection** |
| 13:40 – 14:30 | **Analysis of available antibody data and plans to generate additional data.**<br>Vaccine developers |
| 14:30 – 15:10 | **T cells response** |
| 15:10 – 15:30 | Questions for clarification |
| 15:30 – 16:20 | **Statistical analysis**<br>o What end points?<br>o What is the comparator?<br>o Non-inferiority/superiority |
| 16:20 – 16:50 | Initiatives to analyse available data on correlates of protection |
| 16:50 – 17:10 | Questions for clarification |
| 17:10 - 17:30 | o **What is the role of immunobridging and correlates of protection in the regulatory evaluation of COVID-19 vaccines** (current vaccines, modified vaccines, new vaccines, *mix and match*)?<br>o **What data would be required to define correlates/surrogates of protection?**<br>o **What preliminary conclusions can be drawn-up from existing data?** |
| 17:30- 17:50 | **What is the research agenda moving forward?** |
| 17:50 – 18:00 | **Main conclusions and next steps** |
| 18:00 | **END OF MEETING** |