WHO R&D Blueprint

WHO Working Groups on COVID-19 Assays & Animal Models

Outline of research priorities related to the Omicron variant

WHO reference number

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29 November 2021
Geneva, Switzerland
Background
The WHO R&D Blueprint Working Groups on COVID-19 Assays and Animal Models are two expert groups consisting of more than 600 global scientists with expertise in assays and animal models of viral diseases. Since February 2020 the groups have met weekly to discuss advances, to foster collaborations and to share, resources, reagents and research outcomes to avoid duplication of effort.

These working groups met on 29 November 2021 to discuss action plans and current knowledge about the emerging SARS-CoV-2 Omicron variant of concern first identified in the South Africa Gauteng province.

Due to the presence of multiple mutations in the SARS-CoV-2 spike protein, there is an urgent need to evaluate the cross reactivity, transmissibility, and pathogenicity of the omicron VOC. The WHO working groups met with the following specific objectives:

1- Identify the knowledge gaps and key research priorities
2- Identify any participating experts with access to omicron isolates and/or sequences. Establish mechanisms for rapid sharing of viruses and reagents.
3- Discuss any existing data or plans to test omicron variant antibody neutralization
4- Discuss and setup transmissibility experiments
5- Discuss any data or plans to test omicron variant interferon antagonism
6- Discuss plans to test infectivity and pathogenesis in animal models

More than 450 scientists participated in the meeting of Monday 29 November, 2021 to discuss the Omicron variant.

Key Research Priorities
The experts agreed that at the moment there are three main gaps of knowledge:

1- Ability of post-vaccination and convalescent sera to neutralize omicron.
2- Ability of current vaccines to prevent mild and/or severe disease
3- Ability of current therapeutic approaches, including monoclonal antibody therapy, protease inhibitors and nucleoside analogs to retain efficacy against the omicron VOC.

In order to address these gaps, the following research priorities were established

1a. Virus neutralization: Identify the neutralization titers against live omicron VOC in convalescent individuals, vaccinated and boosted individuals. Collection of sera needs to be considered a public health priority, not research.

Anticipated challenges: The major bottleneck is availability of virus, which is limited by the time to propagate sufficient quantities of virus, generate full genome sequences, obtain export/import permits and transport internationally in the context of flight bans being imposed by multiple countries.

Alex Sigal (AHRI) is growing the virus and willing to share. Other labs are growing independent isolates (UK-HSA and KU-Leuven). All groups can share viruses using the WHO-Biohub as a
facilitator (WHO BioHub) or other biorepositories (BEI, EVA, NIBSC). Category 3 laboratories are needed for virus propagation and storage.

1b. Pseudovirus neutralization: Identify the neutralization titres against recombinant pseudovirus in convalescent individuals, vaccinated and boosted individuals using international unitage.

**Anticipated challenges:** Reduced due to lower containment level required. Studies may be delayed by restrictions in shipping of sera, ethical approvals and access to recombinant virus. Sharing can be facilitated by WHO-Biohub ([https://www.who.int/initiatives/who-biohub](https://www.who.int/initiatives/who-biohub)) and other biorepositories (BEI, EVA, NIBSC).

2- T cell assays (ELISPOT): Are needed as cross-reactive T cells are likely essential to prevent severe disease.

**Anticipated challenges:** T cell assays are not easy to standardize. However, previous comparative data on variants exist.

3- Studies in animal models, primarily in hamsters and potentially non-human primates should be done to understand:

3.1. Pathogenesis: In comparison with other VOCs
3.2. Cross protection: Via passive transfer studies vaccination+challenge studies and/or rechallenge studies
3.3. Transmission: Competition transmission studies have been conducted for previous VOCs in hamsters, ferrets and cats. This same strategy can be used to address omicron transmissibility.
3.4. Drug resistance studies: Against mAb therapy, protease inhibitors and nucleoside analogs.
3.5. If reformulated vaccines are needed. Vaccination plus challenge studies are recommended to assess vaccine immunogenicity and protection in hamsters and NHP. Other models such as hACE2 mice can be used to accelerate the process (e. g. immunogenicity)

**Anticipated challenges:** Access to viral stocks, omicron convalescent sera, vaccines, and therapeutics.