

How a global forum of scientists working on immune assays supported the development of SARS-CoV-2 medical countermeasures

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R&D Blueprint

Powering research
to prevent epidemics

To develop and standardize **assays** to support vaccine development

349 experts from **26** countries and **>100** entities were convened since Jan 2020

Live deliberations on **assay design and performance**

Researchers collaborating on **protocols** and access to reagents and proteins

Researchers collaborating on developing international and secondary **serology standards**



Improved **interpretability** of immune responses and harmonization of results

Enhanced **access** to assays, proteins and reagents



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Communicating information to research community

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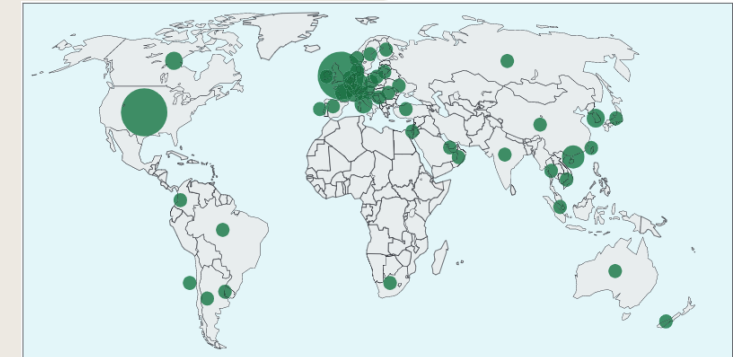
- Meeting reports posted on WHO R&D Blueprint website
- Special meetings of the expert group held with Vaccine Developers
- Reports from the group made at WHO R&D forums and public consultations
- Training sessions held for use of the WHO International Standard

- Viruses and other key reagents available
- Optimal conditions for culturing SARS-COV-2
- Binding assays – multiple antigens and formats (e.g. ELISA and multiplex)
- Neutralization assays – wtVNA, psVNA, sVNA
- Neutralization assays for Variants of Concern and Variants of interest
- Role of Fc-mediated effector functions
- Assessment of T cell responses
- Duration of immunity assessed
- Cross reactivity with other coronaviruses assessed
- 1st WHO International Standard established
- Secondary standards made available and new International Standard in development

Uptake of WHO IS for anti-SARS-CoV-2 immunoglobulin

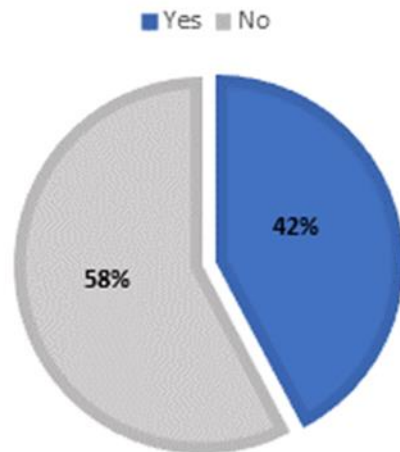
Over 2400 units 20/136 were shipped to 581 individual customers

Stocks of 20/136 depleted in August 2021



Knezevic et al. *Lancet Microbe* 2021

USE OF THE SARS-COV-2 IS
BY 26 VACCINE MANUFACTURERS



Kit manufacturers have adopted the WHO IS units (ELISA, sNeut)

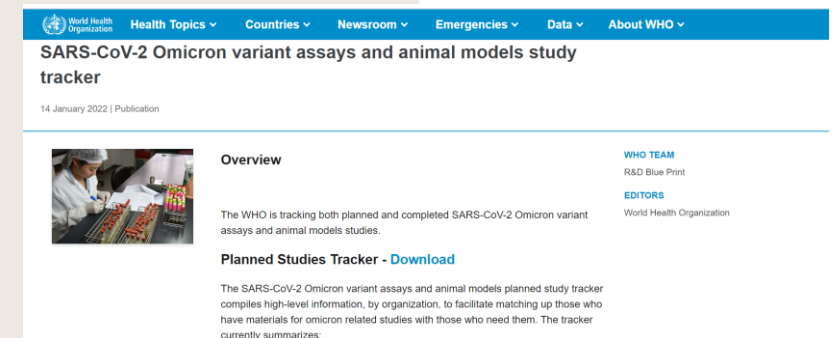
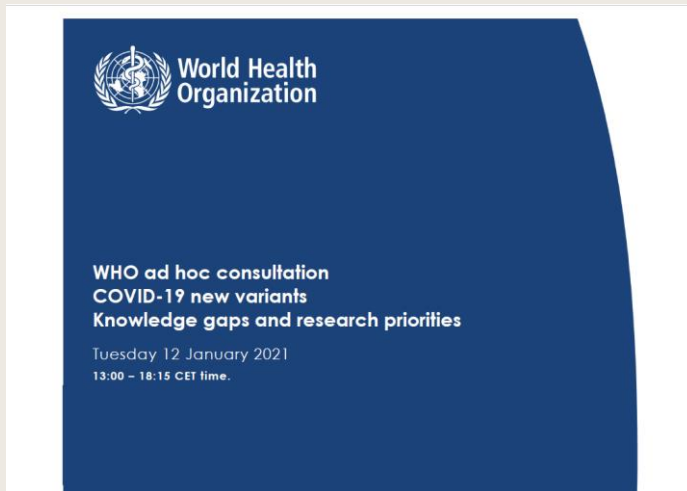
Secondary standards calibrated in IU:
NIBSC 21/234 and US Serology standard

- 2nd WHO International Standard candidates were evaluated and will be presented to the WHO ECBS
- Currently available working standard 21/338

Assessing effects of Variants of Concern

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- Rapid assessment and sharing of data on the effects of variants of concern (VOC) and variants of interest (VOI) on immunity
- Contribution to multiple consultations regarding variants
- Omicron – sharing of planned studies and publicly posted study tracker



Lessons learned

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- Rapid sharing of results to advance the field
- Reporting widely to research community and vaccine developers
- Challenges
 - Viruses and reagents
 - Distribution of viruses
 - Panels of sera
 - Proteins – Full Spike
 - Standards
 - Usage

International Standard

- International Standard - plasma with high titer anti-SARS-CoV-2 antibody collected early in the pandemic (prior to May 2020): pool from 11 donors
- Collaborative study to generate data - 50 laboratories from 14 countries with the standard and a common panel
- WHO IS established by WHO ECBS on 10th December 2020
- Available in NIBSC catalogue on 18th December 2020
- Assigned unitage – 1000 IU/mL



**WHO International Standard
First WHO International Standard for anti-SARS-CoV-2
immunoglobulin (human)
NIBSC code: 20/136
Instructions for use
(Version 2.0, Dated 17/12/2020)**

1. INTENDED USE

The First WHO International Standard for anti-SARS-CoV-2 immunoglobulin is the freeze-dried equivalent of 0.25 mL of pooled plasma obtained from eleven individuals recovered from SARS-CoV-2 infection. The preparation has been evaluated in a WHO International Collaborative study (1). The intended use of the International Standard is for the calibration and harmonisation of serological assays detecting anti-SARS-CoV-2 neutralising antibodies. The preparation can also be used as an internal reference reagent for the harmonisation of binding antibody assays. The preparation has been solvent-detergent treated to minimise the risk of the presence of enveloped viruses (2).

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The preparation contains material of human origin, and either the final product or the source materials, from which it is derived, have been tested and found negative for HBsAg, anti-HIV and HCV RNA. As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

3. UNITAGE

The assigned potency of the WHO International Standard for SARS-CoV-2 is 250 IU/ampoule for neutralising antibody activity. After reconstitution in 0.25 mL of distilled water, the final concentration of the preparation is 1000 IU/mL.

For binding antibody assays, an arbitrary unitage of 1000 binding antibody units (BAU)/mL can be used to assist the comparison of assays detecting the same class of immunoglobulins with the same specificity (e.g. anti-RBD IgG, anti-N IgM, etc.)