COVID-19 research: WHO International Units – a common language in evaluation of the immune response to vaccines for PHE

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External reference calibrants harmonise data

The WHO International Standard is the primary calibrant

- established by the WHO Expert Committee on Biological Standardization
- Defines the common language to express potency
- Reduces inter assay variation (harmonisation) allows dataset comparisons

So, what is the protective titre?

- 2450 unit/mL
- 330 ug/mL
- 1:50
Role of the WHO IS for anti-SARS-CoV-2 immunoglobulin

RAW data

Relative to candidate IS sample G

Reduction in interlab/assay variation
1st WHO IS for anti-SARS-CoV-2 immunoglobulin

- WHO IS established by WHO ECBS on 10th December 2020;
- Available in NIBSC catalogue on 18th December 2020;
- Production of reference materials is not a rapid process
  - identify infected and convalescent individuals
  - Characterise the antibody response
  - Filling and lyophilisation
  - Run a collaborative study to assess candidates
  - Report writing
  - Establishment by ECBS
Uptake of WHO IS for anti-SARS-CoV-2 immunoglobulin

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

Stocks of 20/136 depleted in August 2021

Ongoing analysis
Published studies only - many more vaccine manufacturers Published before IS available in December 2020?

Knezevic et al. Lancet Microbe 2021
Lessons learned

Rapid depletion of the WHO IS
Misuse of the standard: assumed to be a validation tool
Lack of secondary standards widely available

Barriers to the adoption of the International Standard
Users are unclear how to calibrate their assay
No internal standards/standards used in assays
Timelines for the production of the WHO IS – standards not available when assays are developed
Priorities to expand research capabilities so that we are better prepared for future pandemics.

Better understanding of purpose of International Standards

The IS should have a long duration of availability (5+ years) and are formulated as a lyophilised product for this purpose.

They are not a run control or a validation tool → need for secondary standards.

WHO manual for the establishment of national and other secondary standards for antibodies against infectious agents focusing on SARS-CoV2

https://www.who.int/health-topics/Biologicals#tab=tab_1
Priorities to expand research capabilities so that we are better prepared for future pandemics.

**Education on calibration of in house standards**

Understand of the need to report results as relative to an in house control instead of absolute value.

Protocols on how to perform the calibration: webinars, example provided in the manual.
Priorities to expand research capabilities so that we are better prepared for future pandemics.

Availability of research reagents while WHO IS is being prepared

20/130 example

Retrospectively calibrated
Priorities to expand research capabilities so that we are better prepared for future pandemics.

Provide a framework for source bulk materials collection

No coordinated framework for the sourcing of bulk materials with which to produce the International and secondary standards

WHO BioHub
Repositories

- Clinical laboratories/hospitals
- Blood collection services
- Public Health agencies
- Other agencies
Next steps

Support WHO Biohub and repositories initiatives

Work with funding organisations to provide a preparedness framework for known priority pathogens and for disease X

Develop a process to achieve 100 days to vaccine for PHE target

Improve methods to source materials for standards production

Provide education tools for calibration methods
Calibration methods

Commonly used example: parallel-line model, "parallel" sigmoid curves - used to determine relative potency

Calibration is the method to apply an International Unit to an internal standard
Performed on a regular basis (annually) or when a new internal standard is introduced
But...an internal standard is needed
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