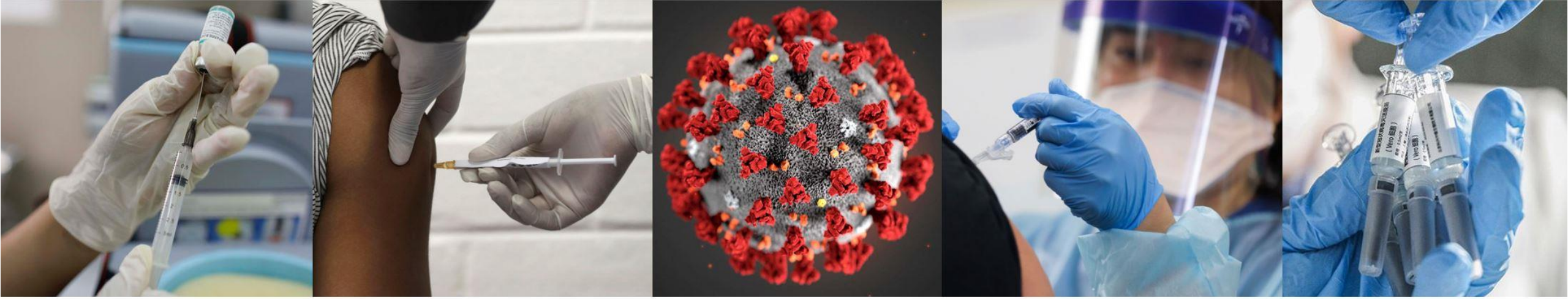


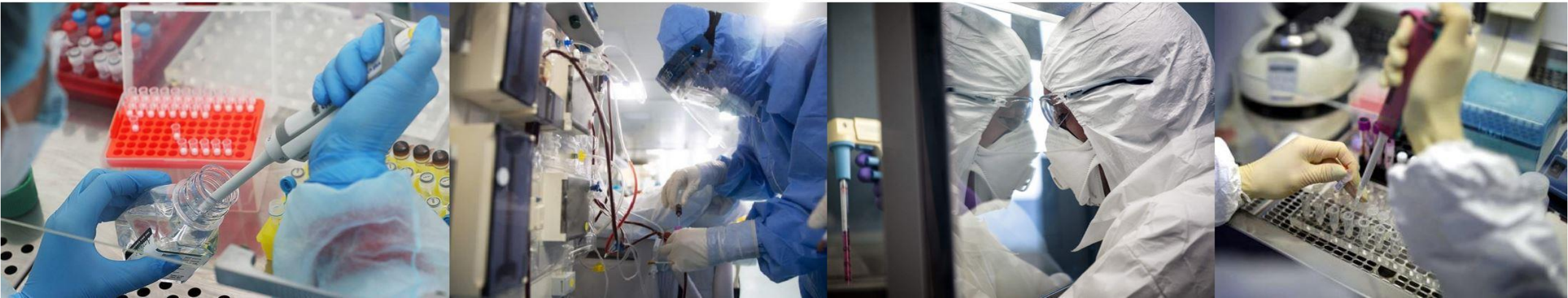
WHO updates/correlates of protection

World Health Organization

Rogerio Gaspar / David Wood
Regulation and Prequalification, WHO

24 June 2021

ICMRA COVID-19 Vaccine Development Workshop



Some current global priorities for regulators

Regulatory convergence:

- Evaluation of post-approval changes/modifications/extension of indications to approved vaccines with established efficacy
- Guidance on evaluation of second-generation vaccines that are still in development
- Responding to real-world scenarios e.g., pharmacovigilance if mix and match immunization schedules are used

Good Reliance Practices are the key enablers of convergence

WHO Technical Report Series 1033:
https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf

WHO publication announcement (29 April 2021)
https://www.who.int/news/item/29-04-2021-who-publishes-new-guidance-to-promote-strong-efficient-and-sustainable-regulatory-systems

29 June 13:00-15:00 CET
Launch webinar on WHO Good Regulatory Practices and Good Reliance Practices
Register: https://who.zoom.us/webinar/register/WN_1dkLBrc6Rw2pGWJZjC_naQ

Regulatory convergence: WHO support (1)

Prequalification and Emergency Use Listing (EUL) procedure

EUL Status of COVID-19 vaccines published on website (latest updated version)

- pre-submission meeting
- status of rolling submission
- EUL listing
- Additional DS/DP sites
- Post-approval changes

Guidance for PQ/EUL assessments (see also Annex: WHO guidance documents)

https://extranet.who.int/pqweb/sites/default/files/documents/Addendum_Evaluation_Modified_Covid-19 Vaccine.pdf

Regulatory support to countries

Working with regional offices to support countries in issuing regulatory authorizations for vaccines supplied through the COVAX Facility

- with confidentiality agreement, access to product dossiers is granted to requested NRA
- 101 countries, out of 145 COVAX supported countries, issued import permit/regulatory authorizations for AZ SKBio/SII vaccines within 15 days

COVAX supported countries:
https://www.gavi.org/sites/default/files/covid/pr/COVAX_CA_COIP_List_COVAX_PR_12-05-21.pdf

Regulatory convergence: WHO support (2)

Global Standards

Multiple written standards are available, including

- Technical Report Series 1004, Annex 9, Clinical Evaluation of Vaccines
- TRS 1028, Annex 2, Guidelines on the quality, safety and efficacy of plasmid DNA vaccines
- TRS 1011, Annex 2, Guidelines on Ebola vaccines
- WHO guidance on mRNA vaccines for prevention of infectious diseases, *in development*

Reference preparations

- International Reference Panel and the first WHO International Antibody Standard for assay calibration

Naming of COVID-19 Vaccines

International non-proprietary names (INN) assigned to

- mRNA-based COVID-19 vaccines and
- plasmid-based DNA COVID-19 vaccine candidates

For variant vaccines

- Accelerated process and nomenclature scheme developed

  See INN Request form

Regulatory convergence:
Evaluation of Second-Generation Vaccines

World Health Organization

COVAX Regulatory Advisory Group (RAG)

Issues brought to the COVAX RAG:

- Data requirements to evaluate vaccines designed to address variants
- Immunobridging within same vaccine platform – endpoints and trial population
- Immunobridging across different vaccine platforms
- Evaluation of booster doses
- Evaluation of Immunobridging studies, in terms of choice of assays, choice of comparator, endpoints, margins and minimum threshold for acceptability for non-inferiority designs

The COVAX RAG is co-led by WHO and CEPI.
Its current members include Regulatory Agencies from Argentina, Australia, Brazil, Canada, Europe (EMA & EDQM), Ghana, India, Japan, Republic of Korea, Singapore, UK and USA

Outputs from meetings are published by WHO
https://www.who.int/publications/m/item/technical-brief-regulation-of-covid-19-vaccines

WHO Consultation on Correlates of Protection
R&D Blueprint, 26 March 2021

Assumptions:

- A deeper understanding of correlates of protection would greatly help new vaccine and modified vaccines development (and extension of existing vaccines to new populations)
- Definition of agreed correlates of protection will be a process
- An agreed research agenda will be an outcome from the meeting

  - To outline the role of immunobridging in the evaluation of COVID-19 vaccines (current vaccines, modified vaccines, new vaccines)
  - To enumerate the data that would be required to inform decisions on immunobridging and correlates of protection.
  - To discuss what is the role of the various assays and animal models and what are the current limitations with interpretation of results.
  - 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)
  - To review the current data and define a research agenda.

Watch the recording:
passcode: JBt*NW49

Current thinking expressed in CoP meeting

- Neutralizing and binding antibody show strong association with short-term vaccine efficacy
- An absolute threshold (i.e., a titer above which there is no risk of disease for an individual) may not exist, but a population-based correlate appears attainable
- Some regulators expressed comfort with immunobridging new products to authorized products, especially within the same platform and demonstrating superiority to comparator
- Standardization across labs/immunoassays, e.g. using the WHO International Standard, was emphasized

Issues raised by regulators* during CoP meeting

- Will CoP within a platform be the same as CoP across platforms?
- Will CoP differ according to the method of administration

  ex) i.m vs i.n?

- Is it necessary to have a complete understanding of all immunological parameters of the response to a vaccine before a CoP is usable by regulators?

*Regulators participating in the meeting:
Canada, China, EMA, Republic of Korea, UK, USA

Key messages on convergence

- A globally convergent regulatory response is essential to help address access and equity issues to COVID tools
  - ➢ *Requires exchange of information and clear dialogue for success*
- Implementation of reliance strategies is key to enhance regulatory convergence
  - ➢ *All regulators can benefit, through increased efficiency and collaboration*
- Further regulatory guidance is urgently needed for next generation COVID-19 vaccine candidates that are in earlier stages of development
- Urgent consideration is needed on pharmacovigilance preparedness for mix and match immunization scenarios
  - ➢ *Alignment on requests from NRAs to industry on PV studies and data collection*