IABS conference on HCT

World Health Organization

WHO Guidelines

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Outline of presentation

- WHO standards for vaccines and other biologicals
- Concept of WHO Guidelines
- Guidelines on clinical evaluation of vaccines
- Scientific and regulatory considerations on HCT
- Implementation workshops

WHO standards and other services to facilitate regulatory oversight of vaccines in developing countries

- Facilitating registration (regulatory standards – Guidelines, Recommendations and measurement standards)
- Prequalification and emergency assessment procedures
- Collaborative procedures and joint assessments
- Vaccine safety initiatives

WHO norms and standards for biologicals

Global written standards

Total 91 docs (Recommendations/ Guidelines)
General docs that apply to both vaccines & BTP: 9
General documents that apply to all vaccines: 12
Vaccine specific: 62
BTP specific: 8

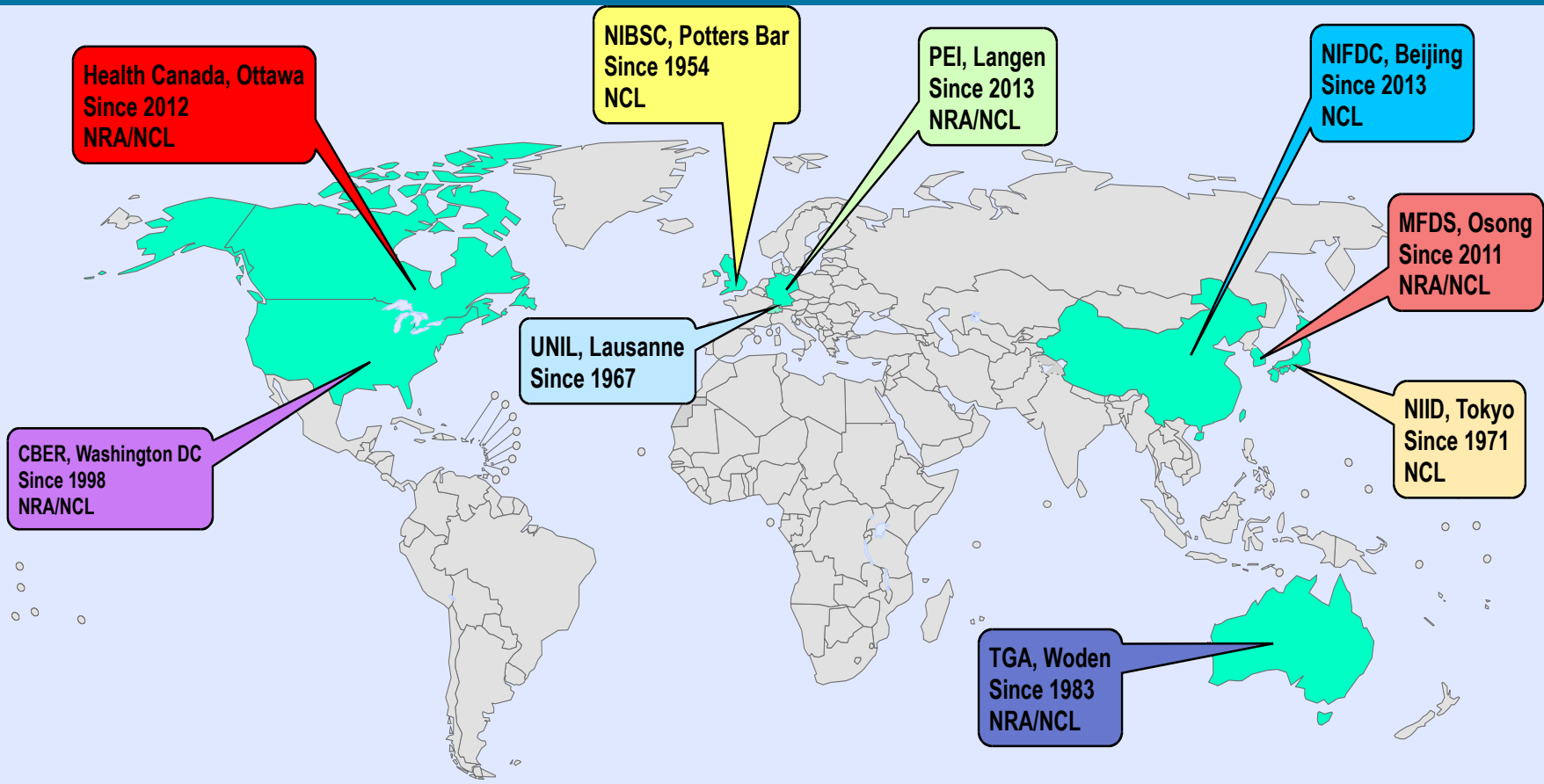
Scientific evidence

1) Standardization of assays
2) Further development and refinement of QC tests
3) Scientific basis for setting specifications

Measurement standards: essential elements for development, licensing and lot release

Global measurement standards

WHO COLLABORATING CENTERS IN THE AREA OF VACCINE RESEARCH AND STANDARDIZATION



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Data Source: World Health Organization

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Development of measurement standards for Vaccines and Biologicals, 2013 – 2017: examples

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1) Trivalent inactivated polio vaccine (TIPV) for D antigen assay (3rd IS)

1) Tetanus toxoid for flocculation assay (3rd IS)
2) Anti-Toxoplasma Serum, Human (2nd IS)

1) Human serum anti-malaria Plasmodium falciparum (1st RR)
2) Haemophilus influenzae b polyribosylribitol phosphate polysaccharide (2nd IS)
3) Human anti-Vi polysaccharide IgG (1st IS)

1) Antibodies, human, to enterovirus type 71 (1st IS)
2) Meningococcal serogroup A polysaccharide (1st IS)
3) Meningococcal serogroup X polysaccharide (1st IS)
4) Diphtheria toxoid (3rd IS)

1) Antiserum to RSV (1st IS)
2) Anti-Vi IgG serum, human (1st IS)
3) Typhoid Vi Polysaccharide (1st IS)
4) Antibodies to Ebola virus (1st IS and 1st IR Panel)
5) Anti-CMV IgG (1st IS)

Subject of ECBS review in Oct 2017

WHO written standards: ECBS 2016 - 2018

Written standards (eg, Guidelines, Recommendations) - Vaccines

- **Influenza vaccines for non-producing countries – new (ECBS 2016)**
- **Maternal immunization – labelling of flu vaccines – new (ECBS 2016)**
- **Ebola vaccines – new (ECBS 2016)**
- **Clinical evaluation of vaccines – revision (ECBS 2016)**
- **Human Challenge Trials – new (ECBS 2016)**
- **Safe production of IPV – revision of TRS 926 (ECBS 2018)**
- **Biosafety of flu vaccines – revision (ECBS 2018)**
- **RSV vaccines –new guidelines (ECBS 2019)**

Written standards – Biotherapeutic products (BTP) /Similar biotherapeutic products (SBP)

- **Guidelines on Mabs developed as biosimilars - (ECBS 2016)**
- **BTP post-approval changes - new (ECBS 2017)**

Concept of WHO Guidelines

1) Provide key principles for evaluation of biologicals as a basis for setting national requirements;

2) Leave space to NRAs to formulate additional/ more specific requirements;

3) Living documents that will be developed further in line with the progress in scientific knowledge and experience

4) Assist with the implementation of the guidelines into regulatory and manufacturers practices through:

- **Global, regional and national workshops involving regulators, manufacturers and other relevant experts**
- **Trainings, advisory groups**

5) Consider guidance issued by other bodies – intention to complement them, not to create a conflict.

Revised Guidelines on clinical evaluation of vaccines (TRS 1004, annex 9)

- Introduction
- Scope
- Glossary
- Vaccine Clinical Development Programs
- Immunogenicity
- Efficacy and effectiveness
- Safety
- Authors and Acknowledgements
- References

Scientific and regulatory considerations for HCT, TRS 1004, annex 10 (1)

- Not all diseases are suitable for "challenge-protection studies"
- Regulatory framework
- Quality and safety of pathogenic challenge strain
- GCP
- Various purposes for HCT in vaccine development:
  - Often a type of efficacy indicating study
  - Better understanding of pathogenesis of , and immunity to, the organism to guide decisions on immune responses that a vaccine might need to elicit in order to protect against disease

Scientific and regulatory considerations for HCT, TRS 1004, annex 10 (2)

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Various purposes for HCT in vaccine development (cont.):

- Proof of concept
- to identify potential ICP and other elements which will be then validated in an efficacy study
- Down or up selection of vaccine candidates
- Provision of a basis for licensure (rare case)
- Post-licensure studies to explore waning immunity, need for booster or duration of protection
- other

Scientific and regulatory considerations for HCT, TRS 1004, annex 10 (3)

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Study design of human challenge trials:

- the purpose of the study is influencing study design
- Different models according to the purposes and study design
- Challenge organism
- Usefulness for positive or negative prediction

Operational aspects

- Relevant committees
- Qualified investigators
- Protocol
- Special facilities to prevent spread of challenge organism
- High level of control

Scientific and regulatory considerations for HCT, TRS 1004, annex 10 (4)

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- **Some key ethical considerations:**
  - Minimize risk to subjects and maximize benefits
  - Review by an independent ethics committee
  - Informed consent
  - Other issues and references to more detailed sources of information

Way forward

- Report to the ECBS in Oct 2017
- Discussion with regulators, vaccine developers, manufacturers, HCT specialists, ethical and other relevant experts to identify need for standards and other support
- Implementation workshops:
  - at the global and regional level are very much needed
  - Case studies and review of examples

Other ideas?

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3. Participants of WHO consultation held in July 2014: meeting report published in Vaccine 2015; 33 (17):1999-2003

Thank you

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