ECBS report to SAGE immunization

SAGE meeting, April 2018

Prof Klaus Cichutek,
ECBS Chair

Outline

Expert Committee on Biological Standardization (ECBS)

- WHO Expert Committees
- New written standards established in Oct 2017
- New measurement standards established in Oct 2017
- Update on strategic issues
- Next ECBS meeting: vaccine standards under development

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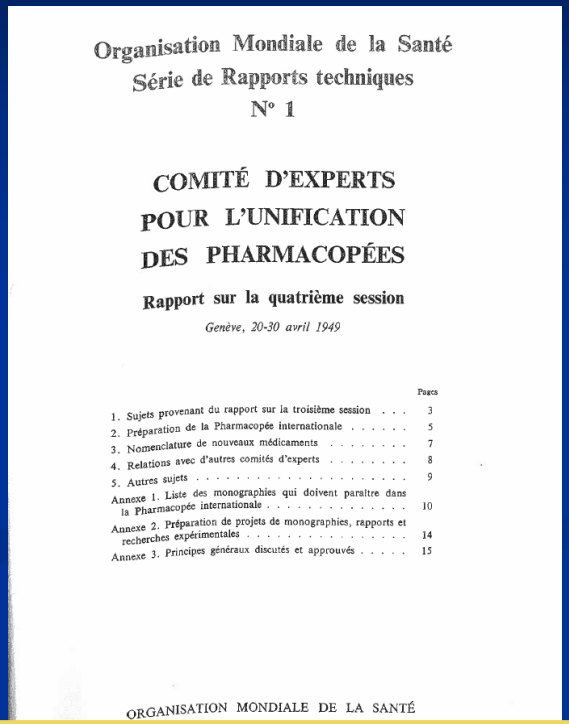
WHO'S CORE BUSINESS

The Constitution requires WHO…

"…to develop, establish and promote **international standards** with respect to biological and pharmaceutical products".

The norms and standards are established by Expert Committees



Organisation Mondiale de la Santé
Série de Rapports techniques
N° 1

COMITÉ D'EXPERTS
POUR L'UNIFICATION
DES PHARMACOPÉES

Rapport sur la quatrième session

Genève, 20-30 avril 1949

ORGANISATION MONDIALE DE LA SANTÉ

WHO's normative work on biologicals, diagnostics, medicines and vaccines has been part of our core business since the very start….

WHO Technical Report Series Number 1

WHAT IS A WHO EXPERT COMMITTEE?

- Official Advisory Body to Director-General of WHO
- Established by World Health Assembly or Executive Board

  - WHO Expert Committee on Specifications for Pharmaceutical Preparations, Secretary: Dr Sabine Kopp
  - WHO Expert Group on International Non-proprietary Names, Secretary: Dr Raffaella Balocco
  - WHO Expert Committee on Biological Standardization
    Secretary: Dr Ivana Knezevic

- WHO Expert Committee reports are presented to the Executive Board

Technologies Norms and Standards

Expert Committees

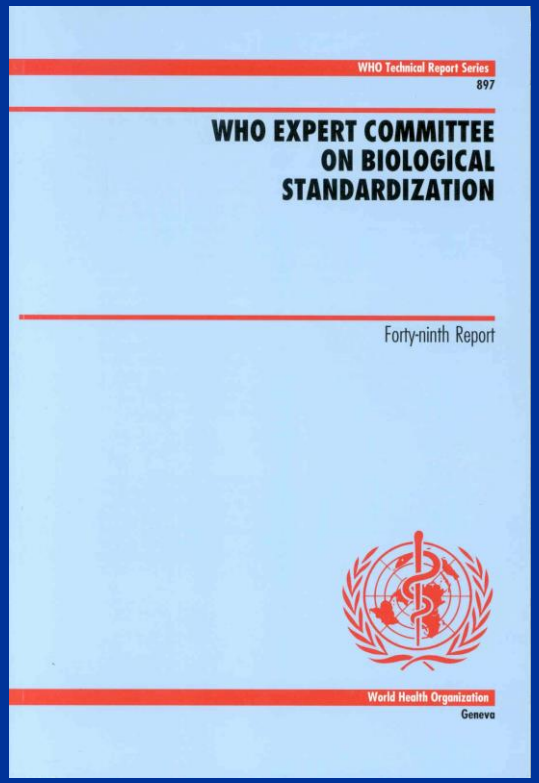
Expert Group

Long standing committees / group

periodic review of scope, priorities and ways of working

WHO GLOBAL STANDARDS AND NORMS

Global written standards
Tools for appropriate regulation of quality, safety and efficacy



Global measurement standards
Tools for product development, licensing and lot release

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New WHO written standards established by the ECBS in Oct 2017 (TRS 1011)

- ECBS 2017: establishment of written standards:
  - **Guidelines on the quality, safety and efficacy of Ebola vaccines**
  - **Procedures and data requirements for changes to approved biotherapeutic products**
  - **Rapid diagnostic tests for HIV infection for professional use and/or self-testing**
  - **Establishing stability of in vitro diagnostic medical devices.**
- ECBS 2017: report will be published in WHO TRS 1011, together with these standards

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Guidelines on the quality, safety and efficacy of Ebola vaccines (1)

History

- Need for guiding principles for vaccine evaluation (ECBS 2014)
- Drafted during the Ebola outbreak (2014-2016)
- Reviewed by ECBS 2016
  report to SAGE WG on Ebola vaccines
  input from SAGE on immunization
- Further revision made in 2017 addressed issues of multivalent Ebola vaccines and innovative clinical trial designs

Guidelines on the quality, safety and efficacy of Ebola vaccines (2)

Table 1. Description of candidate Ebola vaccines under clinical development

Candidate vaccine (manufacturer/developer)	Short description of vaccine	Clinical stages
Ad5-EBOV (monovalent) (CanSino Biologics & Beijing Institute of Biotechnology, China)	Non-replicative, recombinant human adenovirus serotype 5 expressing envelope GP of Zaire (Makona strain) Ebola virus species	1 & 2
Ad5 (bivalent) (National Institute of Allergy and Infectious Diseases, USA)	Non-replicative, recombinant human adenovirus serotype 5 expressing envelope GP of Zaire and Sudan Ebola virus species	1 (inactive)
Ad26.ZEBOV & MVA-BN-Filo (prime/boost, VAC52150) (Janssen Vaccines & Prevention B.V, The Netherlands)	Non-replicative, recombinant adenovirus serotype 26 expressing envelope GP of Zaire Ebola virus species and modified vaccinia Ankara expressing 4 filoviruses nucleoproteins (GP for Zaire Ebola [Mayinga strain], Sudan Ebola, and Marburg viruses and nucleoprotein of Taï Forest Ebola virus)	1; currently recruiting for phase 2/3 trials.
ChAd3-EBOZ (monovalent) (GlaxoSmithKline, Belgium)	Non-replicative, recombinant chimpanzee adenovirus serotype 3 expressing envelope GP of Zaire (Mayinga strain) Ebola virus species	1/2a
ChAd3-EBOZ & MVA-BN-Filo (prime/boost) (University of Oxford, UK and National Institute of Allergy and Infectious Diseases, USA)	See previous descriptions	1
ChAd3 (bivalent) (National Institute of Allergy and Infectious Diseases, USA)	Non-replicative, recombinant chimpanzee adenovirus serotype 3 expressing envelope GP of Sudan and Zaire (Mayinga strain) Ebola virus species	1
DNA plasmid vaccines (National Institute of Allergy and Infectious Diseases, USA)	Several candidate vaccines that either encoded both Zaire and Sudan Ebola virus species GP or Marburg virus. *Trials carried out in 2004–2010 and none is currently active under NIAID.*	1 (inactive)
GamEvac-Combi (rVSV & Ad5, prime/boost) (Gamaleya Research Institute for Epidemiology and Microbiology, Russia)	Replicative, recombinant vesicular stomatitis virus and human adenovirus serotype 5 expressing envelope GP of Zaire (Makona strain) Ebola virus (prime & heterologous boost). *MOH of Russian Federation registered vaccine on 28/12/2016 (no. LP-003390).*	1/2, 4
rVSVΔG-ZEBOV-GP (Merck, USA)	Replicative, recombinant vesicular stomatitis virus expressing envelope GP of Zaire (Mayinga strain) Ebola virus species with or without homologous boost	1–3
rVSV N4CT1 EBOVGP1 (Profectus BioSciences, USA)	Replicative, recombinant vesicular stomatitis virus expressing GP of Zaire (Mayinga strain) Ebola virus species. (Trivalent Ebola/Zaire, Ebola/Sudan and Marburg candidate vaccine is also been developed.)	1
Nanoparticle recombinant Ebola GP vaccine (Novavax, USA)	Nanoparticle recombinant vaccine with and without our Matrix-M adjuvant; Zaire (Makona strain) Ebola virus species	1
DNA vaccine (INO-4212) (Inovio Pharmaceuticals, USA)	INO-4212 (with 2 components INO-4201 [past Ebola Zaire virus outbreak strains] & INO-4202 [2014–2015 Ebola Zaire virus outbreak strains]), delivered with electroporation	1
HPIV3-EbovZ GP (National Institute of Allergy and Infectious Diseases, USA)	Live-attenuated human parainfluenza virus type 3 vectored expressing Zaire Ebola virus GP. *Trial is completed.*	1 (inactive)

- **Candidate Ebola vaccines under clinical development**
- - refer to WHO SAGE meeting, April 2017: Update with the development of Ebola vaccines and implications to inform future policy recommendations. Background document prepared by the Ebola Working Group. http://www.who.int/immunization/sage/meetings/2017/april/1_Ebola_vaccine_background_document.pdf?ua=1

Guidelines on the quality, safety and efficacy of Ebola vaccines (3)

- Focus on
  - manufacture
  - development in clinical trials
  - evaluation for licensing
  - pharmacovigilance

- Evaluation of
  - quality
  - safety
  - efficacy

Guidelines on the quality, safety and efficacy of Ebola vaccines (4)

- ECBS 2017: adoption of the Guidelines
  - tool for regulatory preparedness in Member States for future public health emergencies
    - multivalent Ebola vaccines
    - innovative clinical trial designs
  - regulatory expectations for quality, safety and efficacy for full licensure
  - minimal data sets required during a public health emergency acceleration aspects

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WHO measurement standards established by ECBS in Oct 2017

- **1st IS for potency assays of Oral Polio Vaccines**
  - mOPV type 1, mOPV type 2, mOPV type 3, bOPV type 1+3
- **1st IS for anti-Typhoid capsular Vi polysaccharide IgG (human)**
- **1st IS for Vi polysaccharide**
- **3rd IS for Pertussis Toxin**
- **1st IS for Ebola virus antibodies**
- **1st IRP for Ebola virus antibodies**
- **1st IS for antiserum to Respiratory Syncytial Virus**

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ECBS – strategic issues under discussion

- Standards for priority pathogens in line with WHO Blueprint project (eg, Ebola, Lassa, Nipah, CCHF)
- Review of Terms of Reference
- Regular exchange with SAGE immunization and PDVAC
- Link with new expert group: SAGE IVD

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Next meeting of the ECBS: 29 Oct – 2 Nov 2018

- **New written standards** (consultations in 2017 and 2018) :
  - **Quality, safety and efficacy of Hepatitis E vaccines**
  - **Biosafety risk assessment and guidelines for the production and quality control of novel human influenza candidate vaccine viruses and pandemic vaccines**
  - **Safe production of polio vaccines**
- **Projects for ECBS 2019: Guidelines for RSV vaccines**
- **New project** "Nucleic acid based vaccines of importance for priority pathogens for PHE":
  - Revision of guidelines for DNA based vaccines
  - Points to consider on RNA based vaccines