Developments in traceability requirements around the globe

Activities in WHO

C. Micha Nübling
Blood Products and related Biologicals (BLD)
Technologies, Standards and Norms (TSN)

World Health Organization

WHO's Normative Work

WHO mandated by Member States to set global standards

- **Written standards**
  - International Pharmacopeia
  - INN
  - GMP
  - …..
- **Measurement standards**
  - Vaccines
  - Blood products
  - In vitro diagnostics
  - …..

WHO International Standards

Measurement Standards

- Biological materials for standardization of diagnostic assays
- Globally available
- Representative for target materials
  - analyte: species, strain
  - matrixes
- Commutable to routine test samples
  - no introduction of bias

WHO International Standards

- „High“ concentration of target
  - to cover linear range of quantitative assays
  - to enable calibration of secondary standards
  - to enable preparation of working reagents, run controls
- Lyophilization
  - worldwide shipping at ambient conditions
- Proof of suitability in international collaborative study
  - harmonisation of assays

Need for Reference Materials
Inter-assay variation in proficiency testing

Virus	International Standard	SD range of geometric mean (log10)	% of commercial assays
HIV	Y	0.17 – 0.27	> 95%
HCV	Y	0.20 – 0.30	> 95%
HBV	Y	0.30 – 0.45	~ 50%
BKV	N	0.5 – 0.6	~ 30%
HSV	N	0.6 – 0.7	< 15%
EV	N	>1.0	< 10%

Expert Committee for Biological Standardization (ECBS)

- Committee establishing WHO standards for biologicals
  - Written standards, e.g. WHO Guidelines
  - Biological reference preparations, e.g. WHO Intern. Standards
  - Blood products, in vitro diagnostics
  - Vaccines and biotherapeutics
  - Cell therapy products

66th ECBS, October 12-16, 2015

- **Report of WHO CC Meeting (July 02/03, 2015)**

WHO Collaborating Centers for Blood Products and IVDs

- FDA CBER, USA
- NIBSC, UK
- PEI, DE

Priorisation of new standardization projects,

Update on ongoing projects

Discussion of issues

66th ECBS, October 12-16, 2015

- WHO Collaborating Centers for Blood Products and IVDs

Priorisation of new standardization projects

input from...

- WHO MSs, WHO CCs
- Health organisations and projects
- IVD industry

agreed proposals presented at ECBS for endorsment

66th ECBS
New Projects endorsed

WHO International Standards for....

....Ebola RNA, antiEbola

....VZV DNA

....Plasmodium falciparum antigen

....Plasmodium vivax DNA

....Trypanosoma cruzi DNA

WHO International Reference Panels for...

.....antiHEV: HEV genotypes

.....HIV p24: HIV subtype VLPs

.....antiBabesia microtii

.....KRAS codons 12,13

WHO Repository for transfusion-relevant bacteria, eythrocyte-derived

66th ECBS, October 12-16, 2015

- WHO Collaborating Centers for Blood Products and IVDs

Update on ongoing projects

discussion of collaborative study outcomes

presentation at ECBS for establishment

66th ECBS
Biological Reference Preparations established

New WHO International Standards for....

....BK DNA, JC DNA

....Insulin C peptide

.....several replacement WHO Iss

New WHO International Reference Reagents for...

.....antiEbola

.....Ebola RNA

.....antiA, antiB

WHO Repository for transfusion-relevant bacteria, platelet-derived

.....extension by 10 further bacteria strains

66th ECBS, October 12-16, 2015

- Report of WHO CC Meeting (July 02/03, 2015)

  WHO Collaborating Centers for Blood Products and IVDs

Discussion of issues

problems encountered during standardization projects

scientific updates

66th ECBS, October 12-16, 2015

- WHO Collaborating Centers for Blood Products and IVDs

Standardization issues

varying stability of viral RNA in some preparations

HEV	stool- versus plasma derived virus; stabilizers
HCV	residual moisture

66th ECBS, October 12-16, 2015

- WHO Collaborating Centers for Blood Products and IVDs

Standardization issues

Commutability of WHO International Standards

April 2013: WHO Consultation on Commutability of WHO Biological Reference Preparations for of Infectious Markers

Evaluation of commutability part of collaborative studies and post-establishment

66th ECBS, October 12-16, 2015

- draft WHO Guideline on
  Calibration of secondary standards for IVD

  covering nucleic acids, antigens, antibodies

  advice on statistics, number of assays, matrixes etc

  further discussion by different stakeholders

  IVD manufacturers, QC material providers
  PTS organizers
  SOGAT

  adoption planned for ECBS 2016

66th ECBS, October 12-16, 2015

- **Standardization of biotherapeutics, e.g. mAbs**

  New concept for reference materials ?

  for control of the bio-assay, or

  reflecting the target material (e.g. mAb)

WHO consultations

/catalogue/en/

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Blood products and related biologicals

- Blood products and related biologicals
- Norms and standards
- Blood regulators network
- International reference materials
- Quality and safety
- Support to regulatory authorities
- Regulation of in-vitro diagnostic devices
- Good manufacturing practices
- Transmissible spongiform encephalopathies (TSE)
- Snake antivenoms

Catalogue

The catalogue of International Reference Preparations is updated following the Expert Committee on Biological Standardization meetings. See below for the listings which now include additional information and web links. The listings are in alphabetical order and by subject as well as for the distribution.

Alphabetical list
pdf, 221kb

Allergens
pdf, 53kb

Animal Sera
pdf, 63kb

Antibiotics
pdf, 44kb

Blood Products
pdf, 141kb

Blood Safety
pdf, 77kb

Coagulation Factors
pdf, 75kb

Highlights

Potential for Use of Convalescent Plasma in Management of Ebola: BRN Considerations
pdf, 142kb

– Catalogue of the WHO International Reference Preparations

Publications

WHO Biological Standardization Program
www.who.int/bloodproducts/catalogue/en/

Thank you