WS3. Facilitating development of common QA methodology and regulatory convergence

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- UK government Institute
- 300 employees (70% scientific staff)
- WHO International Standards
- Serum, antigen, viruses, bacteria, allergens, cytokines, stem cells etc
News: New strategy to end Cholera

The National Institute for Biological Standards and Control (NIBSC) is a global leader in the characterisation, standardisation and control of biological medicines.

NIBSC plays a major role in assuring the quality of biological medicines worldwide through the provision of biological reference materials, by testing products and carrying out research. Our expert scientists also provide advice on a routine basis and in response to emergencies.
Biological Medicines: Why are they special? 
(why does NIBSC exist?)

• Made from biological sources
• Highly complex
• Must be measured by biological effect
• Inherent variability in product, manufacture and test methods
• Special risks (sensitive targets)
Biologics - Expertise at NIBSC

Vaccines and Toxins

Anthrax
BCG
Botulinum toxin
Cholera
Clostridium difficile
Diphtheria and Tetanus
Hepatitis A
Haemophilus influenza B
HSV
Human Papillomavirus
Influenza
Malaria
Measles, mumps, rubella
Meningococcal
Pertussis
Pneumococcal
Polio
Rotavirus

Shigella
Smallpox
Typhoid
Yellow Fever
Varicella

Blood products

Albumin
Alpha-1 Proteinase Inhibitor
Antithrombin
Factor VIII
Factor IX
Factor X
Heparin
Immunoglobulins
Virus-inactivated human plasma
Plasma Pools

Tests

Appearance
- Visual inspection
Identity and Potency
- Molecular, Cell-, Antibody-based
  \textit{in vitro} assays
- Physico-chemical methods
- Imaging
- Animal models, 3Rs

Protocol review
Medicines Control

Independent regulatory testing (Europe) required for

- Vaccines, Blood-derived products, Biotherapeutics

NIBSC is UK Official Medicines Control Laboratory (OMCL)

Importance of medicines control

- Protects the public
- Free movement of goods
- Keeps manufacturers up to the mark

NIBSC teams tested >4000 batches of medicine/plasma pools in 2016
Task 3.1 Development of unified QA approach for licensed vaccines

- Prequalification testing
  - Assay development and optimisation
  - Validation
  - Calibration to International Standards
  - Production of standards and reference materials as needed
Task 3.2 Provision of vaccine potency assays for attenuated and inactivated viral and bacterial vaccines.

- Assay transfer
- training
- Rabies
  - standards and assays available
- Chikungunya
  - Standards in production at PEI
  - Pseudotype neutralisation assays available
- Cholera
  - Standards and assays available
  - Prequalification testing undertaken
Task 3.3 Development of validated assays reference materials for emerging infections.

- Standards, assays and reagents available for exemplar vaccines
  - Rabies
  - Chikungunya
  - Cholera

- Other programmes for emerging pathogens
  - MERS CoV
  - Nipah
  - Lassa
  - Ebola
  - Zika
  - CCHF
Standardisation

In pharmacology, the International Unit is a unit of measurement for the amount of a substance, based on biological activity or effect. It is used for hormones, some medications, vaccines, blood products, and similar biologically active substances.
Chimaeric HIV-outbreak virus RNA particles

Advantages:
- Safe: non-replicative HIV VLP, non-infectious (lack of Env) no expression of outbreak virus genes (no promoter and added stop codons)
- Easy and fast production
- HIV-1 ΔU3 LTR allows for genome quantification

Mattiuzzo et al., PLoS One, 2015
PV production in 48 hr

T.3.5 QA and regulatory knowledge dissemination

- Early contact advised
- Free
- NIBSC met with vaccine manufacturers for CMC of Ebola vaccines
- WHO link with NRLs in LMICs