Medicines & Healthcare products Regulatory Agency

NIBSC
Confidence in Biological Medicines

WS3. Facilitating development of common QA methodology and regulatory convergence

Mark Page

The National Institute for Biological Standards and Control

- UK government Institute
- 300 employees (70% scientific staff)
- WHO International Standards
- Serum, antigen, viruses, bacteria, allergens, cytokines, stem cells etc

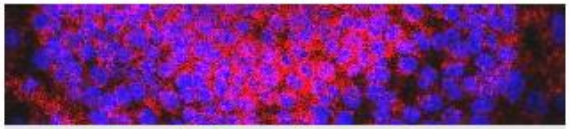
News: New strategy to end Cholera

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.

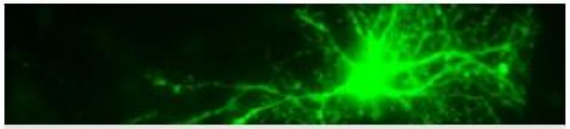
Biological reference materials

Influenza Resource Centre



UK Stem Cell Bank

Centre for AIDS Reagents



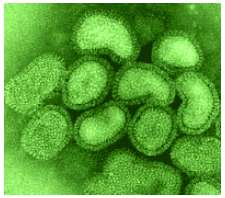
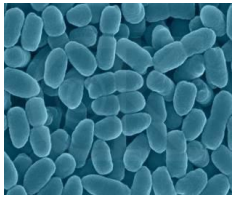
CJD Resource Centre

Biological Medicines: Why are they special?

(why does NIBSC exist?)

- Made from biological sources
- Highly complex
- Must be measured by biological effect
- Inherent variablility in product, manufacture and test methods
- Special risks (sensitive targets)



Biologicals - 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 *in vitro* assays
- Physico-chemical methods
- Imaging
- Animal models, 3Rs

Protocol review

Medicines Control

Independent regulatory testing (Europe) required for

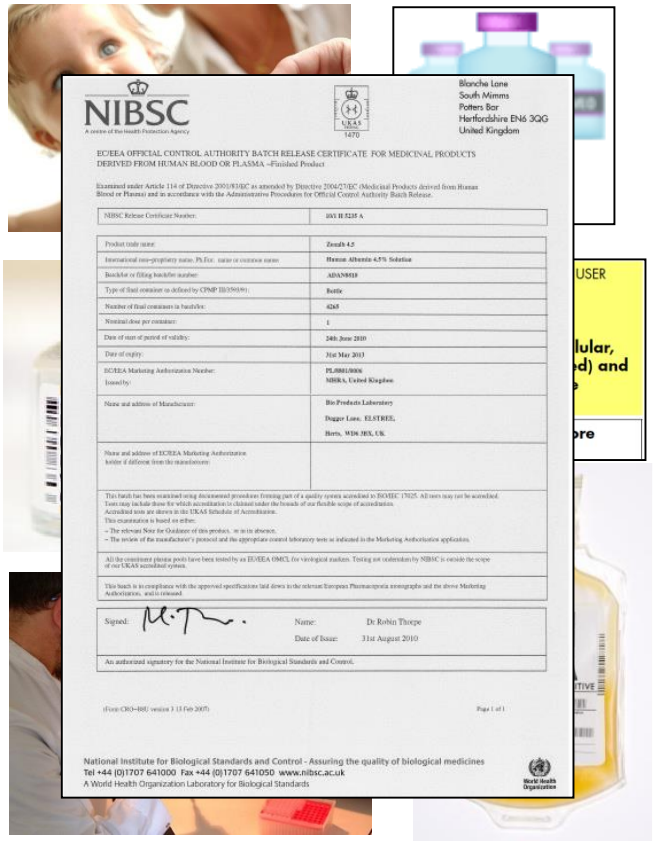
- Vaccines, Blood-derived products, Biotherapeutics

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

WIKIPEDIA
The Free Encyclopedia

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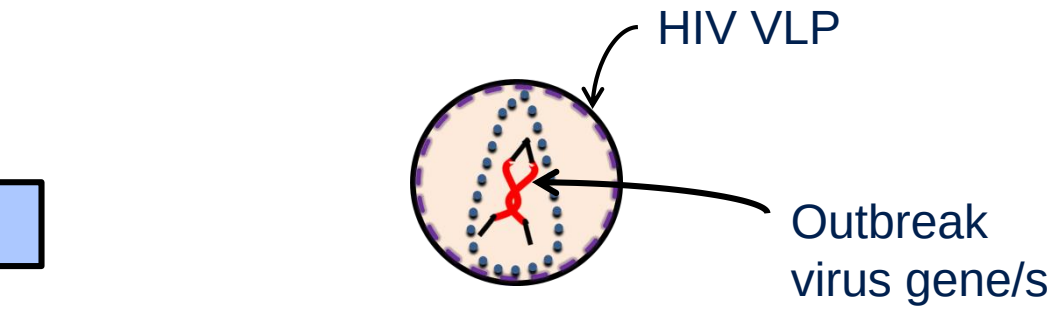
International unit

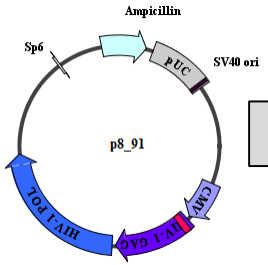
From Wikipedia, the free encyclopedia

In pharmacology, the **International Unit** is a unit of measurement for the amount of a substance, based on biological activity or effect. Italian *unità internazionale*), or **IE** (German *Internationale Einheit*, Dutch *Internationale Eenheid*, Danish *International Enhed*, Swedish *I* hormones, some medications, vaccines, blood products, and similar biologically active substances.

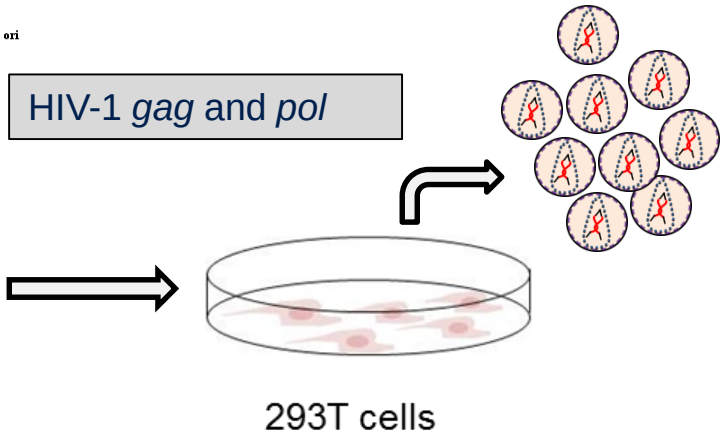
Chimaeric HIV-outbreak virus RNA particles

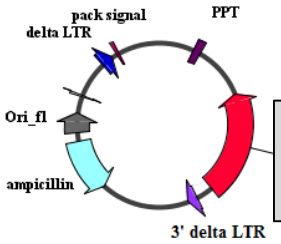


Production



HIV-1 *gag* and *pol*





Outbreak RNA virus genes

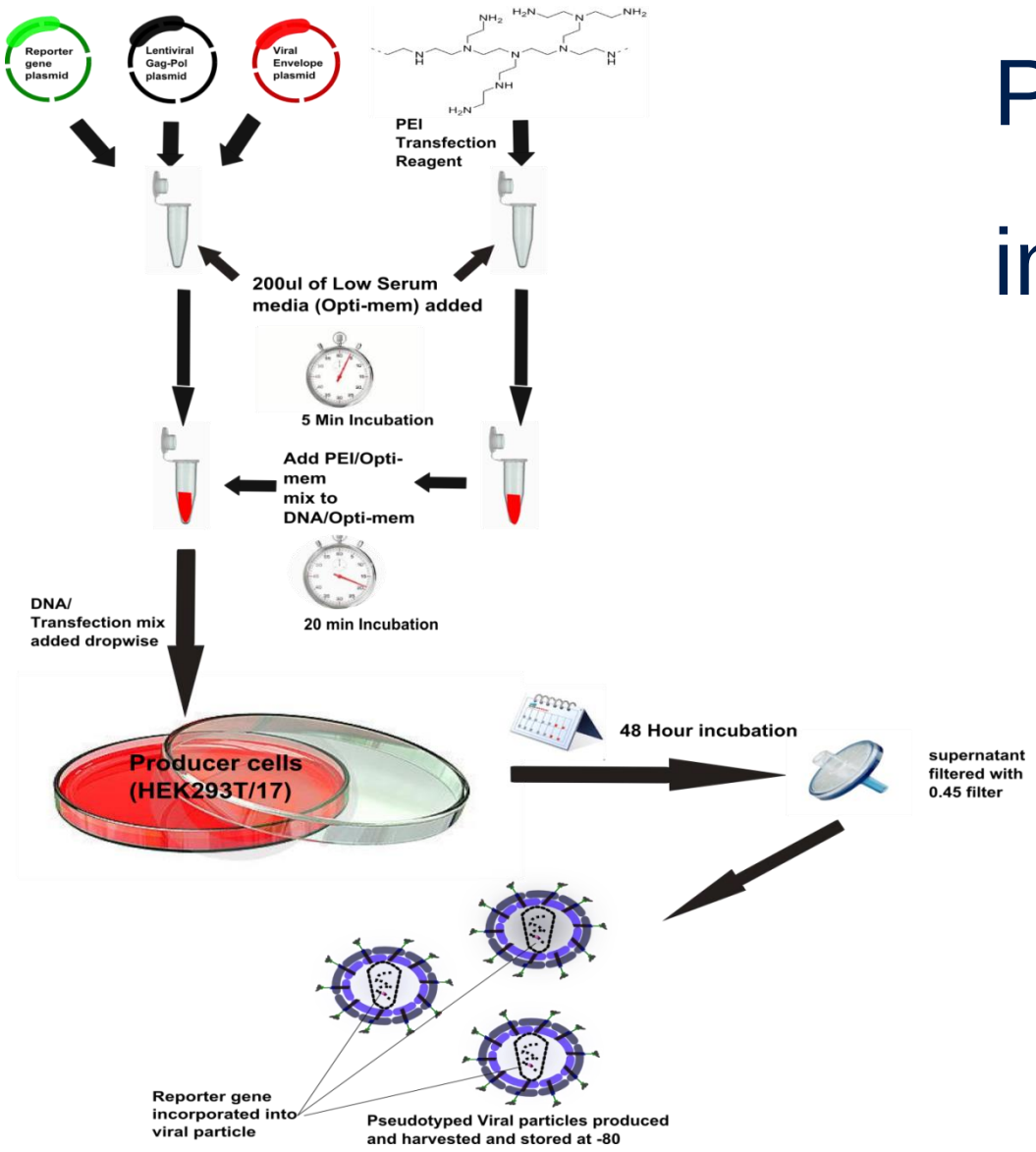
Advantages:

- 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



Graphical Abstract: Grehan *et al*. MethodsX, 2015

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

NIBSC

Celebrating 40 years of excellence