

Biologics testing in Europe

EMA ICH Guidelines
CPMP/ICH/295/95/ICH Topic Q5A
CPMP/ICH/294/95/ICH Topic Q5D
CHMP/BWP/157653/07
EMA/CHMP/BWP/398498/05

Characterisation of MCB

3AB2A CPMP/ICH/139/95 ICH Topic Q5B
CPMP/BWP/1143/00

Master Cell Bank

- Morphology - light microscope observations
- Identity – DNA Fingerprinting
- Sterility conforming to EP 2.6.1
- Mycoplasma test which complies with EP 2.6.7
- *in vitro* adventitious virus test using Simian (Vero), Human (MRC-5) and cells of the same species and tissue type as the production cells, (14 day assay in the case of non-primate cells, 28 day assay for primate cells)
- *in vivo* adventitious virus test in adult and suckling mice and embryonate chickens eggs (may also include Guinea Pigs where appropriate)
- Species specific tests inc. Bovine and Porcine viruses (CPMP/BWP/1793/02)
- Tests for Retroviruses including PERT (following EP 2.6.21), Transmission Electron Microscopy, Infectivity assays i.e. PG4 S+L- or cocultivation

Working Cell Bank

- Morphology – light microscope observations
- Identity – DNA Fingerprinting
- Sterility conforming to EP 2.6.1
- Mycoplasma test which complies with EP 2.6.7

End of Production Bank

- Morphology – light microscopic observations
- Identity – DNA Fingerprinting
- Sterility conforming to EP 2.6.1
- Mycoplasma test (EP 2.6.7)
- *in vitro* adventitious virus test using Simian (Vero), Human (MRC-5) and cells of the same species and tissue type as the production cells
- *in vivo* test in adult and suckling mice and embryonated chickens eggs
- Tests for Retroviruses including PERT (following EP 2.6.21), Transmission Electron Microscopy, Infectivity assays i.e. PG4 S+L- or cocultivation

Characterisation of Bulk Harvests

- Sterility conforming to EP 2.6.1 or Bioburden conforming to EP 2.6.12
- Mycoplasma complies with EP 2.6.7 or EP 2.6.21
- *in vitro* adventitious virus testing – MRC-5, Vero and cell line of the same species and tissue type as the production cell line (14 day assay in the case of non-primate cells, 28 day assay for primate cells)
- Tests for Retroviruses including PERT (following EP 2.6.21), Transmission Electron Microscopy, Infectivity assays
- Tests for species specific testing i.e. *Mouse minute virus* or *Cache Valley virus*
- Once only – *in vivo* adventitious virus testing in adult and suckling mice and embryonated chickens eggs (may also include Guinea Pigs where appropriate)

Final Product Testing

CPMP/ICH/365/96 ICH Topic Q6B

- Sterility conforming to EP 2.6.1
- pH conforming to EP 2.2.3
- Visible and sub-visible particles conforming to EP 2.9.19
- Extractable volume conforming to EP 2.9.17
- Bacterial endotoxins conforming to EP 2.6.14
- Total proteins conforming to EP 2.5.33
- Residual Host cell DNA
- Residual Host cell Protein
- Characterisation of product
- Molecular distribution – SEC HPLC conforming to EP 2.2.10
- Purity – Gel Electrophoresis conforming to EP 2.2.30.
- Product Potency - *in vivo* or *in vitro* assay following EP section 5.3
- (Biological Activity per mass unit)
- (CHMP/BWP/271475/06)
- Appearance conforming to EP 2.2.2
- Osmolality conforming to EP 2.2.35
- Product specific Testing requirement