Joint BWP / QWP workshop with stakeholders in relation to **prior knowledge and its use in regulatory applications**

Subteam 3. Using Prior Knowledge in Process Development & Manufacturing Strategy

London, Nov. 23, 2017

Questions

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efpia
European Federation of Pharmaceutical Industries and Associations

ebe
european biopharmaceutical enterprises

Vaccines Europe
An industry for healthy lives

medicines for europe
better access. better health.

Process Development Session

Part I (25 min)

- Regulators Viewpoint (Dr. Sean Barry)-15min
- General Considerations, including small molecules considerations -10min

Part II (30 min)

3 Case Studies: 10 min each

- Prior Knowledge to optimize process characterization approaches, mAb (Amgen)
- Prior knowledge to optimize process validation approaches , mAb (Roche)
- Prior knowledge to streamline viral safety and resin lifetime studies (mAb and vaccine, EBE viral safety consortium & MSD)

Part III (30 min)

Q&A linked to case studies – 10 min

General Q&A and discussion – 20 min

PROCESS DESIGN AND DEVELOPMENT – QUESTION

Monoclonal Antibody Case Study

Use of Prior Knowledge for small virus filters to support testing of *worst case* small virus *in lieu* of large viruses

Nano-filtration for parvovirus filters

– test *worst case* small virus; and remove product-specific large virus clearance studies

– once a nano-filter has been determined insensitive to process interruption, this parameter is not tested in later virus clearance studies

Aged Protein A resins

– measuring virus LRV using multi-cycled resin on a product-by-product basis may be obviated

Resin lifetime - Monoclonal Antibody Case Study

Use of Prior Knowledge on Affinity Capture Resins to support resin age evaluation criteria

Gain Health Authority approval based on modelling of reuse performance from existing mAbs verified through a cross validation with limited data from an actual mAb. In addition a concurrent process verification at scale under the company Pharmaceutical Quality System (PQS) is performed.

Resin lifetime - Vaccines Case Study

Use of Prior Knowledge to Support Resin Reuse Across Vaccine Serotypes (chromatography step)

Gain Health Authority approval based on the prior knowledge, supplemented with data derived from the small scale model to use resin across serotypes but, still dedicated to a specific product, and monitor the performance at scale under the company Pharmaceutical Quality System (PQS).

Can these approaches be acceptable ?

PROCESS DESIGN AND DEVELOPMENT – QUESTION Cont'd

How to leverage prior knowledge to enable accelerated and/or more efficient process validation ?

- **Use of prior process knowledge to optimize validation approach and criticalities**
  - Proposal to reduce/eliminate PV studies where assessment of variability is not important; i.e. clearance of impurities with significant excess capability
  - Apply prior knowledge and strategies to establish PV acceptance criteria, i.e. move to more generic CQA control points/sample plan, platform quality requirements and variability estimates for process validation criteria
- **Develop risk-based stage 1/2 PV strategy and leveraging post-approval stage 3 PV plans**
  - Combine phase III pivotal and PPQ campaigns
  - Assess/justify # PV lots and streamline post-validation strategy based on overall knowledge of process, technology, facility and risks
- **Extensive prior knowledge be justified as 'standard' manufacturing technology** (eg aseptic filling, leachables/extractables)