Case Study: Experience with a PACMP to Support a Major Process Changes to a Vaccine Drug Product Registered through a Centralised Procedure.

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Presentation Overview

• Experience to Date

• Analysis of Benefits of a Post Approval Change Management Protocol

• Next steps
What is a Post Approval Change Management Protocol?

**What is a PACMP?**

- **Submitted within a new MAA or as a Type II variation**
- **Using a detailed protocol, sponsor & regulator reach prior agreement on change strategy**
- **Subsequent submission of the agreed data package as a Type IB variation (for biologicals)**
- **Offers significant opportunities for optimal data package preparation and for predictable and rapid approval of the subsequent data**
- **Introduced with the 2010 revision of the EU Classification Guideline**
Case Study: Major Process Change for a Vaccine

- Addition of a Primary Drug Product Manufacturing Site for a Vaccine
- Transfer of the Same Process not Possible due to Site Specificities
  → Major Process Changes Needed
- Approval Time on the Critical Path to Meet Commercial Demand
Comparison of a Traditional Approach and a PACMP

- Traditional Regulatory Strategy
  - B.II.b.3 Change in the manufacturing process of the finished product
  - c) The product is a biological/immunological medicinal product and the change requires an assessment of comparability
    → Type II variation
    → 60 day timetable, Procedure starts when all data are available
    → Approval 2-6 months
Comparison of a Traditional Approach and a PACMP

• Change submitted via PACMP
  – B.II.g.2 Introduction of a post approval change management protocol related to the finished product
    → Type II variation
    → 60 day timetable, independent of data
Comparison of a Tradional Approach and a PACMP

- B.V.c.1 Update of the quality dossier to implement changes, requested by the EMEA/National Competent Authority, following assessment of a change management protocol
- c) Implementation of a change for a biological/immunological medicinal product
  - IB variation
  - 30 day timetable
    - Procedure starts when all data are available
  - Approval 1-3 months
  - More Predictable as risk is leveraged upfront
  - Faster
Content of PACMP (Type II variation)

- Key components of the PACMP submitted as a Type II variation
  - **Module 2**
    - Comprehensive introduction providing the overall strategy and articulating the different development studies to accomplish the aim of the protocol
  - **Module 3**
    - Pharmaceutical Development
      - Development studies to support the modified process and to establish the process parameters and acceptance criteria.
    - Manufacturing Process Description
      - Description of the manufacturing process to be subjected to validation
  - Protocols
    - Validation Protocol
      - process parameters, acceptance criteria, specifications and additional characterisation as needed
Content of PACMP (Type II variation)

- Stability study protocol based on ICH requirements to confirm registered shelf-life
  - Studies to be undertaken, specifications and additional characterisation as needed
- Comparability protocol based on data assessment
  - Risk Assessment
    - Risk assessment according to ICH Q9 conducted with regards to the modified process
  - Regulatory Strategy
    - Commitment to provide in the Type IB variation
      - Completed validation summary
      - Completed comparability summary
      - Stability data and stability commitment to notify agency of any confirmed out of specification result or out of trends results
- Table of Contents for the subsequent Type IB variation to be submitted
Content of Type IB variation

• Key components of the Type IB variation
  – Module 2
    • Comprehensive introduction providing the overall strategy and outcome of validation, comparability and stability studies to demonstrate that the protocols were successfully executed.
  – Module 3
    • 3.2.P.3.5 Process Validation and/or Evaluation
      – Completed validation report summary
      – Completed comparability reports summary
    • 3.2.P.5.4 Batch Analyses
    • 3.3.P.8 Stability
      – Stability data (3 months) and stability commitment to notify agency of any confirmed out of specific results or out of trends results
Feedback from Regulators

- First PACMP for a biological product (Vaccine) within Pfizer
- Approach discussed with QTL and Quality reviewer
  - Agreement on the Strategy
  - Agreement on the table of contents
- PACMP approved without question
- Type IB variation approved without question
Traditional Regulatory Approach

- Manufacture PV Batches
  - December 2011

- Submit Type II variation with PV and 6 months stability data
  - July 2012

- Type II Variation Approval
  - December 2012

PACMP Approach

- PACMP filed
  - Sep 2011

- CHMP Positive Opinion obtained in
  - Nov 2011 (no RfSI) – supported PV initiation

- Type IB Variation
  - submitted May 2012

- Type IB Approved
  - June 2012

The PACMP approach secured approval about 6 months sooner than the traditional approach envisioned.
Next Steps

- PACMP approach contemplated for all Biological products
- Applicable to a large number of changes
- Valuable when
  - Strong development package
  - Data generated over a significant period
  - Timing is a key element
  ➔ Balance between resources/cost associated with a PACMP and overall benefit
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Thank you for your attention! Questions are welcome