Joint BWP/QWP/GMDP IWG – Industry
European Workshop on Lifecycle Management

Change Management Protocols
Small Molecule, Generic Experience

- Small molecules often require routine changes throughout a product's lifecycle.
- Manufacturers would like to use change management protocols to reduce the review and approval time of variations, not reduce the requirements to support variations.
- Change management protocols will reduce the variation classification and potentially reduce review and approval timelines up to 8 months.

Objective: to ensure uninterrupted product supply to the patient.

Case Description

Product: lypholysed powder in a vial

Seven change management protocols were prepared for different anticipated changes that are normally classified as Type II:

- manufacturer of active substance
- manufacturing site of active substance
- manufacturing site of drug product
- update of Active Substance Master File
- immediate packaging of the drug product
- manufacturing process of drug product
- batch size of drug product.

The approach appears aggressive with the number of protocols; however.....

- each change is routine through a product's lifecycle
- supporting data is required which impacts the timeline for the variation submission, review, approval and implementation
- concept is consistent with post approval change management plan/strategy.

Change management protocols were decided as a pragmatic solution to address the implementation timelines.

Experience

DAY 70

RMS refused to assess the content.

Applicant appealed that the protocols should be assessed based on the CHMP Questions and answers on post approval change management protocols.

DAY 120

RMS Assessor comment:

"The provided change management protocols are much too general and vague and not in line with that Q&A. The applicant more or less requests carte blanche to perform variations according the Guideline on Variations without review of competent authorities as described in that Guideline."

DAY 160 Response

Drug product manufacturing site change management protocol updated to include new information aiming to address the requested level of detail by the assessor.

The other six protocols were withdrawn due to lack of details.

Expectation/Benefit

Introduction of drug product manufacturing site as 1B variation after MA approval rather than as a type II variation.

Observations

Industry does not understand the level of detail required in a change management protocol.

•The level of detail required in a change management protocol is seen as a demanding burden by industry.

•Industry must adjust to providing the variation details earlier and focus on the time saved during the review of the re-classified variation.

Authorities are comfortable evaluating variations rather than change management protocols.

•A culture shift within the authorities is required to consider routine, lifecycle variations not as a weakness in the development but as the natural evolution of a product.

Potential Solutions

Examples of change management protocols with sufficient level of detail for evaluation.

Closer interaction of the regulatory authority and inspectorates to differentiate GMP criteria from submission criteria.

•For example, collaboration between the two authority responsibilities can address concerns about additional manufacturing sites (drug substance and drug product).

AESGP
APIC Active Pharmaceutical Ingredients Committee
ebe european biopharmaceutical enterprises
efpia European Federation of Pharmaceutical Industries and Associations
EGA Making Medicines Affordable
EUCOPE European Confederation of Pharmaceutical Entrepreneurs AISBL
EuropaBio The European Association for Bioindustries
Vaccines Europe An industry for healthy lives