Roundtable Session 2 – Table 16: Raw material and critical reagent control strategies - Postapproval challenges including shortages

Facilitator: Valerie Tsang, Biogen

Scribe: Mark Schenerman, CMC Biotech-MAS Consulting

Abstract

Ensuring a consistent supply of critical raw materials is crucial for the uninterrupted production of medicinal products. Challenges such as global shortages and vendor changes can significantly affect manufacturing and regulatory compliance. This roundtable will explore strategies for managing these disruptions, including the qualification of alternative reagents and robust vendor quality management systems. While incorporating flexibility into initial regulatory filings and implementing Post-Approval Change Management Protocols (PACMPs) can alleviate some burdens, complexities persist in effectively managing raw materials to ensure a continuous and reliable supply to patients worldwide. Join us for a discussion on navigating post-approval challenges in raw material and critical reagent control strategies.

Discussion Questions

1. What is your experience with different expectations / requirements across global markets with respect to implementation of alternative and new raw materials and reagents?

2. How do you manage continuous improvement in raw materials / reagents?

3. Do you have any experience relying solely on pharmacopeial standards / monographs?

4. What is your experience with vendor cooperation / collaboration in quality investigations stemming from raw material variability?

NOTES

1. What is your experience with different expectations/requirements across global markets with respect to implementation of alternative and new raw materials and reagents?

Alternative RM qualified but not used in process validation and this was challenged by China so had to be removed. The RM was an amino acid as an example; agency disagreed that it was NOT a complex RM.

Another example for China where sponsor tried to argue it was a simple RM and failed. Even the argument that it would lead to drug shortage did not prevail.

Try to minimize specificity in submissions.

Indonesia and Vietnam may be other examples. May not have DMFs from all vendors.

2. How do you manage continuous improvement?

UF/DF filter, careful management; backup viral filter

Using two resins in PPQ campaigns, matrixed approach

Alternative Protein A?

Will MAT testing affect RMs that use endotoxin testing?

3. Do you have any experience relying solely on pharmacopeial standards/monographs?

None cited

Cell culture nutrient media was sensitive to light and vendor did not supply in light resistant packaging; met compendia standards but caused dramatic decrease in production.

4. What is your experience with cooperation/collaboration in quality investigations stemming from raw materials variability?

Vendor would not file DMF; eventually updated VHP so they agreed to file DMF.

Problem with a RM that variable amount of trace metal that met USP but caused variability in production. Tightened specs from compendia to include trace metal limit. Some vendors changed process.

Reagent change in a QC test caused a nightmare and resulted in need to change vendor and revalidate.

Different sites have different raw materials; change from USP requirements regarding sterility because of radiation sterilization (non-compendial). All sites have to meet compendia criteria; problem at CMO sites; share CoA with new vendor for TT. CMOs need to align specs with other global sites. Vendor should provide data that alternative methods for sterilization are equivalent.

How have you handled shortages? Stock and micromanagement. Find equivalent parallel RMs; not for viral filters.

Put 6 month notice in Quality Agreement so there is sufficient time to implement changes.

Challenges with Russia because of in-country testing requirements. Tests done there no longer done elsewhere.