Table 13: Introducing a New Biologic into your Commercial Facility: Best Practices

FACILITATOR:  Lou Antinori, Pfizer, Inc.
SCRIBE: Gerald DiDonato, Bristol-Myers Squibb Company

SCOPE:
The FDA requires notification of new product introduction into a facility providing commercial biologics. This session will discuss best practices, what is required, what should facilities do to meet requirements and how this could or should be reported.

“Manufacture of an additional product in a previously approved multiple product manufacturing area using the same equipment and/or personnel, if there have been no changes to the approved and validated cleaning and changeover procedures and there are no additional containment requirements.”

QUESTIONS FOR DISCUSSION:

1. Typical content could include therapeutic class, product and process description, shared equipment lists, studies demonstrating that the current cleaning procedures are still valid (worst case approach) a revised Risk Analysis and possibly revised Flow Diagrams. Anything else? What is the Best Practice content?

2. This change is typically a CBE-30 submission. Does anyone have any experience with FDA requiring, or allowing, a different submission category if all conditions are met? If all conditions are not met, has anyone tried to still submit as a CBE-30?

3. Has the filing category changed for anyone based on the particular type of product currently being manufactured in the facility or the type of new product being introduced? Has there been any regulatory relief for adding further products in the same therapeutic class?

4. Biologics facilities are typically dedicated to biologics manufacturing. Does anyone have experience where a different type of product is introduced into the facility, such as a diagnostic product, and are the filing requirements different?

5. Contracted drug product manufacturers may have many products entering and exiting their facility. Have there been additional challenges obtaining or maintaining information from contract drug product manufacturing facilities? Would a DMF approach work? What’s the best practice when many licenses are affected?
6. What filing category should this change be if all conditions are met? Are the conditions reasonable or should these be revisited?

7. Have there been any comments during inspections regarding submission content for multiproduct facilities?

NOTES:

1. Typical content could include therapeutic class, product and process description, shared equipment lists, studies demonstrating that the current cleaning procedures are still valid (worst case approach) a revised Risk Analysis and possibly revised Flow Diagrams. Anything else? What is the Best Practice content?

Participants generally agreed with proposed content. FDA reviewer did mention that aside from the requirements for introduction of a new product, establishment of an appropriate ID test was also critical in a multiproduct facility.

2. This change is typically a CBE-30 submission. Does anyone have any experience with FDA requiring, or allowing, a different submission category if all conditions are met? One company manufacturing diagnostics had to submit 20/year.

After negotiation, the firm was able to submit 4 times per year. Another company indicated that the FDA came to them and said new product introductions to an established facility could be done for a particular product without notification, while two other companies indicated successful submission and acceptance of a comparability protocol that allowed any new product introductions into an already established multiproduct facility could be filed as an annual reportable update.

3. Has the filing category changed for anyone based on the particular type of product currently being manufactured in the facility or the type of new product being introduced? Has there been any regulatory relief for adding further products in the same therapeutic class?

No experience with this aside from the regulatory relief cited above in question 2. There was an ancillary discussion on sampling upon shipment and the use of satellite samples (re: Annex 16 in EU GMPs) to do the ID test. QPs have agreed to this for importation testing but provided a risk assessment which is kept on file in case of inspection. There is a strong preference not to sample the entire shipping container if possible due to risk to bioburden, etc.
4. Biologics facilities are typically dedicated to biologics manufacturing. Does anyone have experience where a different type of product is introduced into the facility, such as a diagnostic product, and are the filing requirements different?

   FDA participant indicated that in two instances, peptide and nucleic acid introduction into an already approved biologics manufacturing facility required a regulatory filing.

   ANVISA had issue with Veterinary vaccine manufacturing facility now manufacturing mAb.

Anyone receive question during an inspection? One sponsor received questions regarding their ADC re: cleaning and segregation. FDA indicated this was to be expected given the potency/toxicity of most conjugates used in ADCs.

What about bundling filings for multiple products? Yes, this was a successful strategy using cross referencing and individual letters to each BLA.

To what countries to companies generally file? Generally file only to CA and US. Someone mentioned affiliate in BR indicated ANVISA was considering requiring this.

5. Contracted drug product manufacturers may have many products entering and exiting their facility. Have there been additional challenges obtaining or maintaining information from contract drug product manufacturing facilities?

   Participants agreed it was important that CMOs engaged in multi-product manufacture be aware of the reporting requirements and that updates to the sponsor were part of the quality agreement. One company did have issues with timely reporting by a CMO.

6. What filing category should this change be if all conditions are met? Are the conditions reasonable or should these be revisited?

   Everyone agreed when all conditions are met that it should be managed under GMP; AR worst case.