Table 13: Raw Materials

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SCOPE:
Raw materials used in the manufacturing process for both small molecules and biologics are typically purchased from vendors, rather than made in-house. As such, it may be challenging to ensure the quality and reproducibility of the raw materials being utilized. Furthermore, determining the amount and types of testing to be done to release raw materials for use may be phase dependent which can add further complications to the overall raw materials strategy. This roundtable aims to discuss the challenges associated with raw materials and the strategic elements for overcoming these challenges.

QUESTIONS FOR DISCUSSION:
1. Do you face issues with consistent quality of raw materials from vendors (If so, what type(s))? 

2. How does your raw material strategy differ between phases? What is the strategy for performing reduced testing (as opposed to repeating vendor CofA tests)? What challenges do you face in qualifying raw materials to meet different pharmacopoeial requirements?

3. For compendial excipients, do you frequently have additional specifications in place with the vendor or with regulatory agencies to ensure quality?

4. How do you ensure consistent performance of your raw materials from batch to batch? What challenges do you face regarding controlling the levels of trace materials in your raw materials? Is there a difference in how materials are handled upstream versus downstream (i.e. reagents versus excipients)?

5. Oftentimes with biologics, purchased media and resins can be proprietary and vendor information is limited. What types of challenges do you have with these types of materials (is vendor generally helpful or not with information requests?) How do you establish an ID test method for these types of materials?

DISCUSSION NOTES:
• In some instances, companies have had issues with consistent quality of raw materials. These issues can be related to the lack of clear understanding of how different quality attributes of the raw materials can affect product quality. Some companies do make an effort to look at lot-to-lot consistency and the impact on final product quality. In some cases, sponsors have internal controls for a particular quality attribute of a raw material, but do not have this control listed per se in the marketing application.

• It can be a challenge to ‘plug into’ the quality system of a CMO and ensure specific quality attributes for raw materials. In some cases there does need to be a specification in
place for a particular raw material, with the vendor. One company indicated that they purchased the raw material and provided it to the CMO to ensure product quality.

- In general, material used in early stages is released by review of a vendor COA and an ID test. The testing requirement increases upon marketing authorization and can include full testing on a limited number of batches or limited testing on select batches. In general, ID testing consists of a few tests and generally is not limited to a single test to confirm ID.

- In general, for compendial raw materials, sponsors do not have additional tests in place beyond the pharmacopoeial requirements. One company noted an exception where a bioburden limit was included. Sponsors do face challenges where the supplier does not test to a specific monograph, but guarantees the material would meet all compendia. In those cases, sponsor has to do the additional tests (e.g. to show material would meet JP).

- Some sponsors do list raw materials as critical or non-critical, and base testing requirements upon a risk assessment. One company used the risk assessment to drive the testing strategy; thus for some raw materials a simple COA review was all that was necessary for release while for a critical raw material, full testing was applied.

- One company pre-tested lots prior to shipment from the vendor. In one instance, the vendor was making material for the food industry and the material might not meet an endotoxin specification required for a biologic.

- Most sponsors agree that trace metals are critical to product quality. Some companies test raw materials for trace metals and impurities and trend the data.

- Testing chemically defined media, which is often purchased from CMOs and is proprietary information, can be challenging. A combination of tests can be used which could include pH, osmolality and solubility. NIR can also be used.