Table 49: Combination Products / Therapies: Development of Control Strategies

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SCOPE:

Combination products, as defined in 21CFR3.2(e), are comprised of any combination of drug, device, and/or biologic product. A control strategy for combination products should ensure that a safe and effective product is manufactured and distributed to patients. At the core of this strategy is a systematic risk-based approach to product development and manufacturing - starting with the identification of the product’s critical quality attributes (CQAs) and continuing through development to understand the product functionality and manufacturing process with the detail needed to establish critical design and process specifications. This round table discussion will focus on the control strategy for device- and product-related attributes of a combination product. Specifically, the process for determining device related CQAs will be discussed. The scope of product and process characterization experiments will be reviewed, as well as the final controls implemented – including attributes controlled by suppliers, in-process controls for manufacturing, release test attributes and attributes monitored during stability. Participants are suggested to share health authority feedback on their processes and the controls they have implemented.

QUESTIONS FOR DISCUSSION:

1. The process for determining control strategy for combination products that include a device:
   a. What is the process that manufacturers follow to determine the control strategy for the device component of their combination product? Do they follow a risk-based approach and how is it integrated into their established design controls procedures?
   b. Discuss how manufacturers determine critical quality attributes (design input requirements that are critical to the safe and effective use of the product).
   c. Discuss the product characterization experiments performed to understand the critical design and manufacturing process parameters.
   d. Discuss how these parameters are controlled – are they controlled with the suppliers of those components? Are they controlled in the final assembly process or at release testing? How does a manufacturer decide where the control is needed?
   e. What health authority feedback has been received on control strategy processes?

2. The process for determining control strategy for combination therapies without a device:
   a. Discuss analytical method development challenges for combination therapies without a device – what strategies or unique approaches have been developed?
   b. Discuss approaches to setting specs for drug/biologic-related and process-related impurities.
   c. What is the process used to design the overall control strategy for the individual products as well as their combinations?