Roundtable Session – Table 9 – Risk Based Approaches in CMC Filing for Biological Products

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Abstract:

Risk-based approaches to CMC development have existed as concepts for many years and are reflected in ICH and Health Authority guidance. These principles are becoming increasingly important as CMC development is expected to keep pace with innovative clinical study design and the broader acceleration of medicinal product development and approval, so that it does not become a bottleneck to bringing medicines to patients sooner.

An important enabler was the joint FDA/EMA work on risk-based CMC approaches, including the 2018 FDA/EMA workshop and the subsequent FDA/EMA joint toolbox[1] guidance. These helped frame practical opportunities to apply risk-based thinking in areas such as prior knowledge, platform knowledge, tailored validation approaches, and management of post-approval changes.

Several years on, this roundtable will provide an opportunity for an informal, collaborative discussion on how these concepts are being interpreted and applied for biological products. The session will explore current experience, perceived opportunities, and remaining challenges in the use of risk-based approaches in CMC filings.

Discussion Questions:

Roundtable Discussion Questions:

1. Are risk-based CMC approaches for biological products being applied in practice for PRIME/BT designated products and have there been successful applications for non PRIME/BT products of high unmet need globally?

- Yes we are using prime with some caveats
- When trying to apply risk based approaches organisation needs to have scientific capability to do so, the more products, experience is advance to being able to develop robust approaches
- Submission cannot be bunch of hole: need to explain the gaps, justify why they aren't an issue now, and provide an action plan to address

- (ex)Regulator view: saw really good examples setting out the data packages before and post approval e.g. 1 batch for the submission, process characterisation, tighter specs but more IPCs upfront and then post-approval to widen specs and specs, needs a PLAN!
- Non-prime in onco space – gaps in validations, decoupling (inc global success)
- Are the tools global?
    - Different on global setting for appetite for widening. Removing things post-approval could be difficult.
    - Often MOW filing come later once data available
- Use of prior knowledge important
- Unmet medical conditions/indication… focus on patient needs

2. Which of the approaches described in the guidance and toolbox have companies had most success applying for biological products, and which are proving more difficult in practice?

- Anchor point of data, can't have gaps everywhere e.g. is missing process validation, then the method should be complete
- Process validation – robust small scall data, process validation scheme
- Process characterisation – provide further data to post approval and use of prior knowledge
- Stability – using different dose formats, engineering batches that allow use of representative data, and inform when will data be available and commitment
- Potential to file PACMP as routine in the MAA a tool to implement the plan
- Launch out of IMPD site – limited experience is this being used but could be

3. What are the main barriers to broader use of risk-based CMC approaches for biological products,?

- Global angle is a blocker, reliance not necessarily all phases and difficult to know the different risk acceptance different agencies
- Factors: Agency maturity, building the trust (inc legal basis of a country)
- Factor: Type of bio newer type need more data, less likely to have trust
- Strong clinical data/safety profile need to there
- Tightened controlled strategy tricky on a global level (may delay the MOW filings)

4. What would you like to see for future developments in this space?

- More global alignment across agencies e.g. PACMP, tools acceptance differ across even the more mature agencies
- Any additional tools that could be added? More formalisation of prior knowledge via the master file
- Are all the tool used, can they be expanded what can be further explore:
    - Example: Cell pools for banks … a later homogenous cell bank (risk on the sponsor not sure if the risk is enough for the sponsor) (potential topic at next BWP-IP)
- Post-approval – reprieve early on, risk-bask thinking should stop at the MAA, PRIME extended say to first renewal, especially close to approval