Roundtable Session 1 – Table 8 – Target Product Profiles and Quality Target Product Profiles: Product Development with the End in Mind

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Abstract:

Target Product Profile (TPP) and Quality Target Product Profile (QTPP) are both strategic, evolving development tools used to streamline drug development. The TPP focuses on the overall clinical and commercial vision whereas, QTPP is a more detailed technical subset focused on quality. Both frameworks emphasize beginning drug development with a clear end goal in mind. The TPP includes both minimum and preferred product attributes, providing innovators with a defined framework to evaluate their drug candidate throughout development. The QTPP describes the design criteria for the product and forms the basis for development of the CQAs, CPPs and control strategy needed to ensure safety and efficacy.

CGTs are complex biologics that present challenges for currently available analytical techniques, which may not fully characterize them. Unlike repeated administration of a well-characterized drug to the patient, these therapies often rely on the patient's own cells to produce a missing protein or express the appropriate receptor needed for the desired biological function. Plasmids, viral vectors, or mRNA are used to introduce the genetic material required to modify these cells. Their inherent variability and complex mechanism of action make the establishment of a clear TPP and QTPP especially important. In this roundtable, we will discuss what strategies we use to establish TPP and QTPP and how we engage regulators to seek feedback.

Discussion Questions:

1. When in development do you first discuss TPP and QTPP, how often do you revisit them, and is that driven by clinical milestones or batches?
    a. If there were any surprises that happened when you reached commercial milestone?
2. Who are the stakeholders you engage with to create the TPP and QTPP for ATMPs?
3. What are your typical sources of information to build your TPP and QTPP?

    a. How do you use this TPP and QTPP to build your technical documents?
4. What are some examples of critical changes to your TPP, QTPP and control strategies from lessons learned from other modalities that can be applied to ATMPs?
    a. What are the components and critical challenges you faced while building the QTPP?
5. How do you develop the control strategy for novel modalities with limited prior knowledge?
6. Which regulators do you typically engage with? What was some feedback received from regulators on control strategies for ATMPs?
    a. For example, being frozen or cryopreserved products, what global regulatory requirements impact your QTPPs?
7. Is there any specific challenge that differentiates the tool within ATMPs and biologics?
    a. How are you employing AI to build QTPP?

Notes:

- Target Product Profile (TPP) and Quality Target Product Profile (QTPP) are the documents which help to give appropriate direction for efficient product development. It is good to have TPP once non-clinical data forms the candidate for Phase I (First in Human dosing).
- TPP covers details related to dose, indication, target population, Placebo or comparator, storage details, formulation, container closure, mode of delivery, geographical region and device details if applicable. Quality Target Product Profile (QTPP) can be developed once TPP is finalized. It is good to have both the documents early in the stage. These two documents are live documents and can be revisited after Phase I or at least before initiating Phase 3 or Pivotal studies.
- Development of TPP and QTPP is purely cross-functional team effort. Inputs from Clinical, Non-clinical, CMC, Regulatory, research, safety/tox/discovery, supply chain, Marketing/business development/commercial help to create proper TPP and QTPP. Normally TPP development activities are led by Program team/Asset team whereas CMC team owns QTPP development
- It is not necessary to have QTPP in the filing but remains in quality systems. It depends on company culture and experience with type of products. There have been examples of BLA without it. It wouldn't be a reason for RTF

- Bigger companies see the value of setting TPP and QTPP. Some of the clinical reviewers would ask if Sponsors have QTPP, helps the reviewer guide nice to have and need to have
- It is always different situation for novel modalities in terms of setting up control strategy. Sometimes, testing details are not available in Pharmacopoeia or any standards. E.g., iPSC – strength/potency assays. Early interaction with Regulatory agencies helps to helps deciding what testing is needed.
- In terms of platform, TPP is generally unique and QTPP could be platformed. QTPP – aspirational things which are developed over the course of time and needs tweaking based on scientific results
- In terms of challenges to develop TPP or QTPP for CGT products, each type of product can have unique challenges. For example, as compared to traditional biological products, it is difficult to figure out nonclinical (animal) studies for CGT products.
- To create TPP or QTPP for frozen or cryopreserved products, learnings from other traditional products can be helpful. For examples – lessons learned from vaccine products can be helpful to create details for LNPs (Lipid nanoparticles). Early interaction or feedback from US (FDA), EU (EMEA) and Japan (PMDA) can be beneficial to carve out overall product profile.
- Use of AI (Artificial Intelligence) tool to create TPP and QTPP can be both positive and negative depending on how we use it. If the company has multiple products and it is platform-based technology then for internal programs, AI can be used to generate TPP and QTPP template or initial details based on previous program documents. AI use for external reference or details should be verified before using it. Sometimes checking online for pressure testing to use pragmatically on AI is helpful
- NIH has a tool box and FDA had a draft guidance which was withdrawn
- A-cell or A-gene are very helpful in getting started with TPP/QTPP as a new modality
- For cell therapy – cell viability, stem cell derived islets, proliferative potential, keeping those CMC principles
- First filing of LNPs are common in Australia and China as compared to US