Roundtable Session 1 – Table 16 – Molecule-Independent Device Bridging Approach (MIDBA) – a Novel Proposed Methodology for the Clinical Validation of Subcutaneous Device Platforms

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Abstract:

During the development of biotherapeutics, such as monoclonal antibodies and oligonucleotide therapeutics, for subcutaneous administration, the final injection device is often unavailable for use in pivotal clinical studies. As a result, pharmacokinetic comparability studies are required to bridge manual injection methods as applied in the pivotal trials with automated injection using the intended device platform. This traditional approach can lead to a sequential launch of the molecule and the device, potentially delaying the introduction of decentralized care solutions.

The Molecule-Independent Device Bridging Approach (MIDBA) proposes an alternative by leveraging existing pharmacokinetic comparability data from other monoclonal antibodies or oligonucleotide therapeutics using the same device platform. By meeting predefined criteria such as slow subcutaneous absorption, an acceptable therapeutic window, and previously qualified injection sites with manual injection, this approach could eliminate the need for dedicated pharmacokinetic studies for each molecule.

MIDBA has the potential to streamline drug-device development, reduce timelines, and accelerate access to innovative subcutaneous delivery systems. Continued refinement and validation are essential to address remaining challenges and fully realize the benefits of this framework.

Discussion Questions:

- Do you have experience with similar approaches in your institution?

- From your perspective, what are the opportunities associated with the approach?

- From your perspective, what are the challenges associated with the approach?

Notes:

Do you have experience with similar approaches in your institution?

“MIDBA” Acronym not widely used, but people have used approach in the past. Some attendees have not heard of this approach before and are here to learn. Some experience with connecting with agency on leveraging previous data.

- Typical development moves from a vial in early development to AI or PFS to AI in late stage or launch.
- The most important aspects are route of administration, time of admin and tissue you are administering into. Key parameters include location, depth and speed. Example – no clinical bridging would be required from a vial to PFS (not to be confused with clinical validation often used when describing Human Factors Studies). F
- rom PFS to AI it is a little different because elements of the AI are different and response rates of the drug between the two may be different.
- But when using the same device platform across different molecules, how can you ensure that across formulations of different drugs that PK would be the same? Differences to consider are intended user population, drug attributes (i.e., viscosity, viscosity modifiers, concentration).

From your perspective, what are the opportunities associated with the approach?

- How does one design a trial to demonstrate that regardless of the molecule that the device is appropriate – could create surrogate material. A reference study that can successfully bridge to historical PK. How do you even choose a reference molecule? You have original PK data from reference.
- Drug - How do we choose a reference molecule. What are the molecule's properties (e.g. IgG1, IgG2)
- Bucket molecule properties and bracket a PK study by formulation (i.e. location, depth, angle (device) volume, speed, concentration (drug)). Reference study for healthy volunteers using a bracketed approach. Has anyone studied PK profiles and injection parameters? You would want to choose the "worst case" most sensitive drug to injection parameters?
- There is a huge body of data available where PK data exists in vial platforms and device platforms that could be leveraged.
- Group's recommendation is to form a industry led working group to assess the availability of the PK data for "simpler" products such as IgGs in a variety of device platforms.

From your perspective, what are the challenges associated with the approach?

- Imbalance of need versus cost. Smaller biotech companies with very few products by which a bridging strategy could be employed do not have the resources or time.
- This body of data is best approached from companies with large portfolios by which bridging data and prospective reference studies could be executed. This is a challenge.

References Discussed:

FDA Guidance Bridging for Drug-Device and Biologic-Device Combination Products Draft Guidance for Industry December 2019

Bridging for Drug-Device and Biologic-Device Combination Products | FDA

https://pubmed.ncbi.nlm.nih.gov/34186147/ literature on impact of subcutaneous injection sites for a variety of drugs