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Supplementary information

A qualitative study of biosimilar manufacturer and regulator perceptions on intellectual property and abbreviated approval pathways

In the format provided by the authors and unedited

Supplementary Methods: Interview Guide

Interview introduction

- Introduction to the interviewer and the project; the context of the study (PhD project); objective of the study; the topics of the interview. Information about anonymity and confidentiality.
- Interviewer ask the interviewee to introduce their experience with biosimilars.
- Interviewer ask for permission to audio-record and for written informed consent. Asking if any questions before the interview.

INTERVIEW TOPIC 1. Establishing biosimilarity

- What aspects do you experience as challenging for companies regarding establishing biosimilarity? (e.g., quality, nonclinical, clinical, specific parts of these?)
    - Are these challenges similar for both recombinant protein products and other types of biological products? (e.g., derived from natural sources such as intestines, blood, etc.)
    - What aspect of establishing biosimilarity do you think is the most difficult?
- What aspects do you perceive as challenging for companies regarding the biosimilar manufacturing process development? (e.g., specific parts of upstream or downstream processes)
- When initiating biosimilar development, what do you think are the main pros and cons about choosing the same excipients as the originator product?

  Regulator-specific questions:
- Do you evaluate the manufacturing methods and their order when evaluating biosimilarity between the proposed biosimilar and originator products?
- For evaluating biosimilars:
    - Are the same clinical endpoints as the originator clinical trials needed for the clinical comparability exercise for biosimilars?
    - Do you prefer some analytical methods over others?
- Do you think the analytical methods need to be the same for the biosimilar application as for the full application of the reference product?

INTERVIEW TOPIC 2. Usefulness of limited disclosure to an aggregated analysis of the Quality by Design (QbD) space of the originator product.

The interviewer introduces the QbD topic, and questions follow:

- What manufacturing process parameters and their operational ranges for the originator process do you think would be useful for biosimilar developers? (parts of QbD space)
    - Which would be more helpful and why?
        - (for example, excipients variation ranges, specific process parameters ranges, critical quality attributes for the product, etc.)
    - Are there combinations of some parts that would be more useful than others?
- Are QbD usually a part of the market authorization application for originator biologics?
- Are QbD usually a part of the market authorization application for biosimilars?
- What are the regulatory advantages for a company to submit a QbD space as part of the product approval?
- If introducing a regulatory requirement for limited disclosure to part of the originator QbD space, how do you think this

would affect the innovation incentives for new biologics?

INTERVIEW TOPIC 3. Comparing the EU and the US

- Why do you think that there is a difference in number of approved biosimilars comparing EU and US? Other than the difference in year of introduction?
- Do the regulatory differences for biosimilars between EU and US affect the biosimilar development?
    - If yes, what parts get affected?
    - If no, why not?

  Company-specific question:
- Have you for product Z applied different approaches to biosimilar development depending on which of the EU/US jurisdictions you aim to apply for marketing authorization in?
    - If yes, what parts get affected?
    - If no, why not?

Outro

- What do you think is the most important that we have talked about?
- Are there other relevant aspects that we have not talked about?
- Are there any potential "landmines"/controversial aspects I need to be aware of?

Thank you so much for your participation, this has been of great help! If I at a later point have more questions, can I reach out to you for an additional interview?