



Meeting Minutes: CMC Comparability Workshop
28 of September 2020

Actions:

Action	Responsible	Date
Share link to articles that provide additional detail on possible analytical strategies in accelerated scenarios (Analytical Target Profile for right- first-time selection of assays and to support changing assays during development)	Cristiana	Complete (see below) USP Chapter relevant links: <ul style="list-style-type: none"> • Chapter description • USP site access (after free registration to USP site, search doc #1220) • Analytical Chemistry paper
Capture Svein’s question regarding use of clinical batches which differ to allow more flexibility for comparability	Cristiana and team	October 7 th
Analyze feedback and questions of the chat when putting together comparability question for the RAG	Mike, Cristiana, and team	Before submitting to the RAG
Reach out to Julia.Kuhn@gatesfoundation.org if you are interested in receiving a link to the meeting recording	All	Ongoing
Send workshop recommendations to Ingrid, David, Nicolas, Julia	All	Ongoing

Decisions:

Future discussion points

- Impact of changing assays during development (changing both the manufacturing process and analytical method and its impact on comparability)
- Matrix and bracketing approaches for DS from multiple sites filled in multiple DP sites.

ITEM 1iii: [Notes]

Brief overview of structure, interactions, and goals of COVAX facility/SWAT (manufacturing)/RAG-regulators

Mike Thien laid out the purpose of this workshop.

1. to provide a baseline understanding of issues regarding comparability as applied to the case of the ultra-rapid development and supply of COVID-19 vaccines
2. to review for COVID-19 vaccines the potential risk-based strategies that could be used to perform comparability assessments in the absence of data one would typically generate during the course of normal vaccine development

3. to seek alignment on which comparability strategies are both scientifically justifiable and of the greatest utility to developers so that regulators around the world can be asked to harmonize on the acceptance of these strategies for COVID-19 vaccines.

David Robinson gave an overview of the most recent COVAX goals

- There are currently more than 160 countries that are part of the COVAX facility and 13 manufacturers across Asia, Europe and S. America making this the largest actively managed portfolio of COVID-19 vaccines.
- Regulatory questions can be sent to David, Ingrid, Nicolas to be prioritized for approx. monthly submissions to the RAG.

Rationale for Request Regarding Comparability: Complexity, Concerns, Urgency

Cristiana Campa presented on this topic and the content was prepared by a group of experts from different companies, members of IFPMA, Vaccines Europe

- Comparability “ ... does not necessarily mean that the quality attributes of the pre-change and post-change products are identical, but that they are highly similar and that the existing knowledge is sufficiently predictive to ensure that **any differences in quality attributes have no adverse impact upon safety or efficacy of the drug product.**” [ICH Q5E]
- References to region specific guidelines are at the end of the following article: [Alignment in post-approval changes \(PAC\) guidelines in emerging countries may increase timely access to vaccines: An illustrative assessment by manufacturers](#)
- Carmen clarified that WHO guidelines presented are for existing “normal vaccines” and are not specific to emergency vaccines which will need to be addressed at the country level

During a Q&A session Cristiana recapped audience feedback on the problem statement and issues:

- More reflection on deferral of the activities (e.g., level of assay validation could be extended to other elements and analytical)
- Relevance of non-clinical vs. clinical considerations
- Importance of clarifying difference between specifications testing and comparability exercise (focused on impact of process changes)
- Importance in some situations to consider more than one assay/test per attribute for additional characterization

Potential Approaches and Agreement Requested

The following list of potential approaches was put together by the comparability expert team that put together meeting materials and document

Meeting participants voted to rank the potential approaches to demonstration of comparability in the following order:

1. Risk-based analytical comparability assessments of the subset of CQAs that are impacted by the proposed changes
2. Early feedback from regulatory authorities for comparability approaches in advance of obtaining efficacy data from Phase 3 to help confirm requirements and ensure alignment on product specific approaches.

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3. In cases where prior knowledge is limited, and when there is no statistical basis for acceptance criteria due to limited number of lots, use of approaches to comparability focused on product quality expectations
4. Global Use of general/ broader PACMP for routine changes/ introduction of multiple manufacturing processes & A harmonized single approach to comparability amongst nations
5. Use of release, forced degradation and/or characterization data to demonstrate comparability
6. Use of post-change lots to be compared to lots used in pivotal clinical studies