Roundtable Session 1 – Table 5 - The Road to One Global CMC Dossier

Facilitator: Jane Worthington, *BioPhorum*

Scribe: Debra Barngrover, *Biologics Consulting*

Abstract:

The biopharmaceutical industry and regulators are leveraging structured data to expedite patient access to medicines. They are working towards a unified global CMC dossier to streamline regulatory reviews and eliminate redundant resources. One key initiative is using structured data for regulatory compliance, research, and development, which aims to improve submissions, data consistency, interoperability, and efficiency.

Structured data is moving the industry closer to the ideal of One Dossier, enabling error-free population of dossier modules and allowing a single dossier to be reviewed by multiple agencies. This expedites regulatory reviews and approvals, helping bring new products to market faster.

This approach requires transforming unstructured data into a format that can be easily mined and transferred between systems, standardizing terminology, ensuring appropriate software and resources, maintaining clear communication between stakeholders, and securing company buy-in. Differing global health authority requirements pose challenges, and this shift raises questions about their readiness to leverage the benefits. While beneficial, implementing structured data is challenging, and discussions aim to address these challenges and provide clarity for the industry.

Discussion Questions:

1. Adoption of Structured Data: Are health authorities prepared to adopt structured data formats? The FDA appears to be leading with innovative approaches, but what are the perspectives of other health authorities on structured data and a unified dossier?
2. Global Collaboration: Considering that drug development aims to benefit patients worldwide, how can health authorities collaborate to support a global CMC dossier? What are their expectations for future submissions and how can industry ensure alignment from health authorities?
3. Given that the FDA has posted standards for small molecules using the PQ CMC standard; What are the FDA's expectations and how should organizations submit data related to large molecules e.g. data for process characterization and method validation, given the current lack of clear guidance for large molecules?
4. Many organizations currently manage large volumes of diverse data across various formats and systems. Transitioning this data into a standardized, structured repository is a significant undertaking. How can the future benefits of structuring data be quantified to justify this effort? How can organizational buy-in be secured?

Notes:

What do you want from the session: registered products have different levels of detail depending on country, how to bring to a common ground; want to learn how leverage other company's experience to come to a global dossier.

Single dossier:

Single dossier drivers: structured data, more collaboration between agencies, convergence on requirements – ICH guidances, cloud based platforms (technology). Can industry drive this convergence by refusing to follow specific requirements when other approach can be justified?

Vision is to submit once to the cloud and open the data to all countries at once and they do their individual reviews, rapid patient access as a driver. Regulators can see each other questions in regulatory collaboration space; not seen by sponsors and thus don't need to ask same question multiple times. M1 may still be country-specific in this model. This is starting in small groups of countries (e.g., Russia and 4 others).

One company has transitioned to a single dossier for newer products, but for legacy products still have to decide if want to give information to countries which have never been seen this information before, especially information which is related to company IP. Have decided can move company IP information to 3.2.R, since can decide which country this section goes to. If do this, have to be ruthless in deciding what is IP and make sure limited to key IP.

With current model of non-simultaneous filings, divergence will continue to happen after submission, as need to answer questions and insert more information in response to these questions, how to bring back to a common dossier. Specifications are the most difficult; one possibility is to present the previous questions already asked so the new set of regulators maybe can align with this common set of specifications. But this can be difficult if file in multiple countries simultaneously, so conducting specification negotiations simultaneously. Some countries are beginning to change their regulations because industry keeps pushing back. Best practice, adhere as much as possible to ICH, leverage other approvals with strict requirements (don't say reliance), use as support for data in dossier.

One company has defaulted to having MAA as global dossier, not BLA, since more countries accept this as a reference regulatory agency. Many companies categorize countries into groups based on regulatory style and then decide dossier version that group gets. A single dossier can work to support licensure based on reliance, but still need to file changes individually, since reliance doesn't work for this.

Company affiliates in individual countries handle publishing to handle different formats from core dossier. Core dossier should meet ICH, EMA guidelines to have wide acceptance. One company has first document written is spreadsheet of controls and ranges (requested by FDA in 3.2.R), since then all other sections have to match this core list.

Stability is one area that has seems to have most differences, since some countries accept matrixing, some want 3 batches for each strength.

Countries have checklists, some of which don't actually apply to your particular product, try to educate them in most respectful way possible.

Companies see progress, some setbacks. Industry consortiums in certain areas working with their local health authorities to encourage collaboration. Also seeing more health authorities

talking to each other. Have sponsors share success stories for how they got faster approvals in several countries- what they submitted to get this approval.

Possible sources of models to follow: Global reporting of AEs – how is this being handled?

Best practice: Work closely with CMC team and have them write reports with end in mind (e.g., regulatory filing), then source data comes in format that can be dropped into dossier.

Structured Data:

Structured data requires working with many different people in company and CMOs to come up with common structure. Won't handle narratives. Regulators want story but also want data and decide themselves.

Current plans for update for M4Q – all data in Module 3; all narrative in Module 2 – similar to Japanese model. Will be easier to maintain, but long road to get there.

For structured data, terminology has to be defined in multiple languages and even alphabets (or not). Will likely happen in English first and then be translated to other countries.

What will AI be able to do?

Bring in other part of company to help justify work to go to structured data – structured data can help with mergers and acquisitions, so this brings in business development as a supporter.