

Project ORBIS: Opportunities and Challenges from the CMC Review of Biologics at Health Canada

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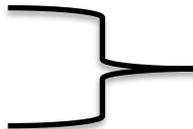
Project Orbis

- An initiative of the FDA Oncology Center of Excellence
- Review process is collaborative, but final decision is independent
- Three types of Project Orbis submissions:
 - Type A
 - Filed with Project Orbis partners within 30 days of submitting to FDA
 - Sharing of reviews
 - Exchange requests for clarification
 - Discussion amongst partners
 - Type B
 - Filed with partners more than 30 days after filing with FDA
 - Less collaboration
 - Partners receive FDA reports, in some cases
 - Discussion amongst partners
 - Type C
 - FDA has completed review and issued a decision
 - Review documents shared with partners
 - FDA reviewers available for discussion with partners, if needed

Health Canada Experience with ORBIS

- Participation by both Biologic and Radiopharmaceutical Drug Directorate (BRDD; biologics) and Therapeutic Product Directorate (TPD; small molecules)
- Products are either new active substances or new indications for previously approved drugs
- Generally required to meet one of two Health Canada priority review pathways
- BRDD received first Orbis submission in 2019; did not require CMC review
- CMC review of Orbis biologic drug submissions:
 - First review in 2021
 - Most have been Type C, from a CMC perspective
 - Still incorporate Health Canada-specific requirements

CMC Evaluation of Biologic Drug Submissions in Canada

- Biologics review in Canada uses an integrated approach to manage the risks unique to biologic drugs
 - Dossier review
 - Confirmatory laboratory testing
 - On-Site Evaluation (OSE)
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- Unique to Health
Canada
- Health Canada-specific post-authorisation requirements
 - Certified Product Information Document
 - Lot release
 - Yearly Biologic Product Review

Process Step	Regular Process	Orbis
Screening	Management begins to plan submission assignment and testing and OSE determinations	Discussions to determine whether to participate or not and what type of Orbis submission it will be (A, B, C)
Review Planning	Timelines will be determined based on target date, complexity of submission, On Site Evaluation and testing dates, availability and experience of reviewers.	Timelines dictated by FDA process; some flexibility for meetings for Type C. Separate timelines developed for On Site Evaluation and testing.
Review	Review follows review plan and is adjusted as required due to operational needs.	Timeline is driven by FDA; generally condensed. Parallel or sequential review with discussions with FDA along the way.
	Questions are issued on a rolling basis, as needed.	Questions are issued on a rolling basis, as needed, independent of FDA.
	First review is independent but may use other Agency Q&As as source of additional information. Quality review report captures first review.	FDA quality review report may replace part of first review by Health Canada.
	On Site Evaluation and testing (if conducted) are completed during review cycle	
	CPID and PM finalised at end of review.	
Second review	Second review conducted by senior evaluator. Quality review report is uploaded to dB and signed by reviewers and managers.	If quality review report is provided by other jurisdiction, it is uploaded to dB but is not signed off by Health Canada. Health Canada reviewers conduct thorough review of report from other jurisdiction (if available) and whatever supplemental information is necessary. The resulting report does not make specific reference to the content of foreign review report.

BRDD CMC Experience

Advantages

- Exchange of ideas with CMC reviewers in other regulatory agencies
 - New for BRDD
 - Help to increase regulatory harmonisation
 - Opportunity to learn about processes used by other regulatory agencies
- Reduction in workload
 - Especially noted for Type C Orbis submissions
- Quicker review times
 - For Type B and C Orbis submissions, review times can be greatly reduced
- Access to FDA pre-license/pre-approval investigation reports have aided in the risk mitigation strategy for the inability to travel during the pandemic

BRDD CMC Experience Continued...

Challenges

- Timelines can be difficult to manage
 - difficult to manage with current high workload and limited resources
 - may become an issue once travel is permitted for On-Site Evaluations
- Health Canada seems to receive many Orbis submissions after other agencies
 - an advantage in terms of having access to review reports
 - decreases utility of discussions/meetings with other regulatory agencies
- Different approaches to regulation can lead to differences in opinion on how to approach issues
 - a potential advantage to learn from other agencies

Conclusions

- Sharing of CMC information between different regulatory agencies is new
- Work-sharing via Project Orbis has several advantages
 - Increased interaction with other agencies
 - Sharing of ideas
 - Increased understanding of approaches to CMC review
 - Management of workload
 - Potential for quicker review times, especially Type C submissions
- Project Orbis is relatively new to BRDD CMC
 - Still developing approach
- Biggest challenge is coordination of timelines
 - Not as much of a challenge for Type B and Type C Orbis submissions