Project Orbis – What a pharmaceutical company needs to know

Claudia Reichle, Project Orbis lead at NDA

At the end of 2020, the FDA Oncology Center of Excellence (OCE) published summary data for the first full year of Project Orbis.[1] From June 2019 to June 2020, a total of 60 oncology marketing applications were received, representing 16 unique projects, and resulting in 38 approvals. New active substances comprised 28% of the received marketing applications.

In 2019, the OCE launched Project Orbis, a framework for near-concurrent submission and review of oncology products across multiple countries. This leverage of the regulatory partnerships between international agencies provides a faster patient access to innovative cancer therapies with a high medical need across multiple countries. So far, Australia, Canada, the UK, Singapore, Switzerland, and Brazil are involved.

Project Orbis applications must meet the criteria for FDA priority review. Qualifying criteria for review includes that the drug is intended to treat a serious condition and if approved, would provide a significant improvement in safety or effectiveness. Project Orbis submissions should also meet the qualifying criteria for the local accelerated regulatory programmes.[2,3]

There are several types of Project Orbis submissions which are dependent on the timelines between the FDA and Participating Orbis Partners (POP).

- **Type A (Regular Orbis):** Submissions are concurrently or near-concurrently (within 30 days) to FDA and POP and allow for maximal collaboration during the review phase and the possibility of concurrent action with FDA
- **Type B (Modified Orbis):** Applications are submitted with a >30-day delay or a regulatory action >3 months of the FDA action, with the possibility of concurrent review with FDA but no concurrent action
- **Type C (Written Report Only Orbis):** FDA has already taken regulatory action, allowing FDA to share their completed review documents with POP but without concurrent review or action with FDA[1]

Project Orbis is not a regulatory route that can be chosen by the sponsor, it is the drug programme that gets selected by the FDA based on its innovative and clinically significant attributes. And when this happens, the sponsor needs to take prompt action.

So far, NDA Group has been involved in four multinational filings under the lead of NDA Switzerland, one of these is approved and the other three are in progress. As a sponsor, you have two to three weeks to make the decision if you can undertake the work that is required.[1]

Claudia Reichle, Project Orbis Lead at NDA at NDA Group explains: "This means you need to ensure that you have well-established project management with enough capacity in place from day one, either in-house or through subcontractors".

Even if being selected for Project Orbis might come as a surprise for the sponsor, it is a much-valued opportunity and NDA Group has seen that companies tend to prioritise Project Orbis to EMA filings. "The reason for this might be that the majority of pharmaceutical innovations are developed in the US and the FDA is the coordinating agency", Reichle clarifies.

Even though Project Orbis guidance has been published recently by some authorities, the concurrent filings are a 'learning on the job' experience as there is no best practice articulated, so far.

For Type A or B Orbis submissions, an Assessment Aid (AAid) is requested by the applicants. The AAid was originally intended to streamline the FDA review, increase review efficiency, and reduce the need to seek clarification from the applicant throughout the review. Now an integral assessment tool for Project Orbis, it is shared between POP and serves as the core document for discussions between the agencies.[4] As the key objective of the AAid is to focus the agencies' review on the most critical aspects of the dossier and to decrease review time, it is important to get the content right. Applicants need additional resources for the preparation of a scientific, factual, and technical AAid, without the inclusion of any promotional or interpretive language.[1,5]

For the FDA, the review process remains the same, irrespective of whether it is under Project Orbis, and the FDA conducts its own usual review of the drug application. An important aspect of the process is that each POP ultimately determines whether to approve a therapy in its country, as well as the pathway used for the approval. The applications are examined by these authorities in cooperation and – depending on the Project Orbis type – in parallel with the FDA, so that the lead time for a possible authorisation is expected to be shortened. Regulatory decisions may occur as simultaneous actions across all Project Orbis partners, if resources permit, but it is not mandated.

To facilitate the practical process, the regulatory authorities must be able to accept the ICH Common Technical Document (CTD). As specified in the CTD, Module 1 the dossier should contain region-specific administrative and product information, therefore a substantial amount of the additional work is located to this module. The FDA Modules 2, 3, 4, and 5 are the basis for the concurrent agencies' review.

Overall, it is essential for the sponsor to have the regulatory knowledge to be able to fulfil the national requirements for Module 1 and specific national procedural aspects in the Project Orbis countries. For smaller pharma companies, without local affiliates in those countries, access to an existing regulatory network via a consultancy can be a solution.

In addition, the labelling of the drug and package design is done independently within each regulatory agency which could lead, for example, to a different wording of the approved indication. Each country has its own format for the drug label. Consequently, it can be a challenge to efficiently map the different regional labelling requirements. To ensure that the needed data is available in time, strict time periods for serious adverse events must be considered by the applicant upfront. To facilitate these parts of the licensing, a Company Core Data Sheet (CCDS) is very helpful. The CCDS is a sponsor owned, central document containing safety information, material relating to indications, dosing, pharmacology, and other information concerning the product.[6] It is the ideal source document upon which you can build a global labelling process.

The key challenge for a pharma company to manoeuvre a Project Orbis filing from start to finish is to have the capacity and capability for a project of this magnitude. Having a firm overview of the entire process and being well equipped in regards of expertise and resources is needed through the fast-moving process.

"I think the Project Orbis experience may change pharma companies' licensing strategies. A global regulatory/pharmacovigilance network as well as global dossiers and labelling strategies may become best practice, for start-ups and small and medium-sized pharma. As a pharmaceutical company working on Project Orbis submissions, I would have the EU MAA preparations in mind in order to streamline my licensing efforts", Reichle concludes.

For questions on Project Orbis, please contact project-orbis@ndareg.com

References

1. *de Claro* et al *Project Orbis: Global Collaborative Review Program,* Clin Cancer res *2020, Dec 15;26(24):pp6412-6416*
2. *Visit: https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis*
3. *Visit: https://www.fda.gov/news-events/fda-voices/project-orbis-strengthening-international-collaboration-oncology-product-reviews-faster-patient*
4. *Visit: https://www.fda.gov/drugs/real-time-review-drug-applications-now-reality-september-20-2018-issue*
5. *Visit: https://www.fda.gov/about-fda/oncology-center-excellence/assessment-aid*
6. *Annex IV, ICH-E2C(R2) Guideline*