Project Orbis – What you need to know

Summary

Project Orbis might be a regulatory game changer. A global dossier approach, global labelling procedure and a global regulatory pharmacovigilance network may become best practice for start-ups and small to medium sized companies. Collaborative international agency initiatives will change the regulatory landscape, providing new innovative therapies to patients with unmet needs.

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In May 2019, the Oncology Centre of Excellence of FDA launched the Project Orbis initiative. The initiative provides a framework to enable near concurrent submission and review by international Project Orbis Partners (POPs). The key purpose of Project Orbis is to provide faster patient access to innovative cancer therapies in multiple countries. In this webinar, Claudia Reichle walks you through the basics on this new and successful pathway.

As of January 2021, Project Orbis has six participating regulatory agencies: Australia (TGA), Canada (Health Canada), United Kingdom (MHRA), Singapore (HSA), Switzerland (Swissmedic) and Brazil (ANVISA). During the first operational year of Project Orbis (June 2019-June 2020), a total of 60 oncology marketing applications were received, representing 16 unique projects, resulting in 38 approvals. The numbers indicate a large interest among both agencies and sponsors. New active substances comprised 28% of the received marketing applications.

The program initially accepted supplemental applications, also known as variations or indication extensions, that added new oncology indications to previously approved drugs. In December 2019, new molecular entities, also known as new active substances, were accepted into the program, and the pilot program is evolving quickly. The rapid development of Project Orbis makes it a steep learning curve for everyone involved: Agencies, sponsors and consultancies who support the projects. This became evident to NDA Group through the support of several Project Orbis submissions to date.

Why Project Orbis?

The most important benefits are the shortened timelines. As an example, lenvatinib in combination with pembrolizumab was approved by three agencies through the coordinated review between FDA, Australia's TGA and Health Canada, with a timeline shortened by three months1. Another important advantage is early access to the market in the involved countries, for example in Switzerland, NDA has seen a significant reduction of the review timeline versus non-Orbis projects. The third advantage is based on the coordinated and collaborative agency review, which is built on common Modules 2-5, and shared agency evaluation questions and answers.

Interested pharma companies cannot apply for Project Orbis but will be invited by FDA, which is a big difference to the common regulatory routes. There are three main qualifiers for Project Orbis:

1. Meet the criteria for FDA priority review, which reduces the standard FDA review time from 10 months to approximately six months. To qualify, the new therapy must treat a serious condition (e.g., oncological diseases), prove that the product is a significant improvement in safety and or effectiveness versus existing therapies. This can be achieved by:
    - Evidence of increased effectiveness in treatment, prevention, or diagnosis of the condition.
    - A substantial reduction of treatment-limiting drug reactions.
    - Documented proof of patient compliance that is expected to lead to an improvement in serious outcomes.
    - Evidence of safety and effectiveness in a new subpopulation.
2. High-impact and clinically significant oncology therapy.
3. Meet criteria for local accelerated program.

The FDA will identify a viable applicant and regulatory pathway for each jurisdiction and subsequently reach out to the POPs and to the applicant. A prompt decision on participation is needed and the applicant must ensure their ability to conduct simultaneous submissions to the countries involved.

There are different types of Project Orbis submissions which are dependent on the timelines between the FDA and POPs. The agency interactions vary depending on the type of submission. For Type A and certain Type B Orbis applications, FDA schedules and coordinates several multi-country teleconferences with the POPs to discuss various aspects of the application.

Type A (Regular Orbis): Submissions are concurrent or near-concurrent (within 30 days) to FDA and POPs and allow for maximum 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 them to share their completed review documents with POP but without concurrent review or action with FDA.

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 clarifi-

cation from the applicant throughout the review process. As an integral assessment tool for Project Orbis, it is shared between FDA and POPs and serves as the core document for discussions between the agencies.

As the key objective of the AAid is to focus the agencies' review upon 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.

Each country remains fully independent of the final regulatory decision, it is therefore necessary to acknowledge the national licensing requirements and to prepare a region-specific module 1. This includes all the pharmacovigilance information, such as risk management. National labelling needs to be prepared, and bear in mind that the approved indication could differ between the countries.

Claudia's recommendations:

Ensure that sufficient and capable resources are in place. To handle not only the simultaneous submissions but also the parallel review and related actions.

Advanced project management. To keep an oversight on overlapping timelines and workstreams.

Establish local regulatory partners. Not only for Module 1 but also to handle national actions, e.g., the pre-submission meetings with all the agencies.

Early engagement of support for Project Orbis. As the time frame is tight (2-4 months between 1st contact and filings), there is an urgent need of either internal support, e.g., by affiliates, or an experienced regulatory consultancy with the required network and capacity.

Create a Company Core Data Sheet (CCDS)/global labelling process. The CCDS is an ideal source document on which you can build on a global labelling process, which is most helpful when handling the different labels in the various countries.

References:

[1] *Mulchan and Allison: Project Orbis: Maximizing patient access to new medicines, regulatoryfocus.org, Feb 2021, pp1-8*

About the host

Claudia Reichle has been with NDA since 2014 and is the lead for our strategic initiative to support clients through Project Orbis. Her broad regulatory experience successfully supports clients throughout the development and licensing of their medicines, including post-approval and launch. Claudia leads and contributes to a multitude of key meetings with regulatory agencies and successful milestone submissions in Europe and the US. Her ability to think-out-of-the-box is a great asset to our clients, especially for the optimization of their regulatory strategies.