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Project Orbis – New Regulatory Pathway for Innovative Oncology Therapies

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1. Introduction

Project Orbis is an initiative of the U.S. Food and Drug Administration (FDA) Oncology Center of Excellence (OCE). Project Orbis provides a framework for concurrent submission and review of innovative oncology drugs among the FDA's multiple international partners[1].

The aim of that program for marketing application of oncology drugs is to facilitate faster access to promising cancer treatments with potential benefits over existing therapies across the world.

2. Results and Discussions

The Project Orbis Partners (POP) of FDA are the various national health authorities. Each participating health authority remains fully independent on their final regulatory decision and labeling negotiation. Under this collaborative framework the selection of marketing authorisation applications coordinated by the FDA. Initial queries received by the regulatory authorities are referred to the FDA. FDA requests the applicant to submit the global submission timing and plan. FDA provides the topline results and the submission plan to the participating regulatory authorities, to confirm their availability.

After confirmation from participating countries, the FDA confirms the Orbis submission plan with the applicant.

In that project, applicants may select the international regulatory authorities and simultaneously to submit the marketing authorisation applications to these authorities in addition to the FDA, once topline results are available from the clinical trials. The applications are evaluated by the other authorities in cooperation with the FDA, so that the timeframe needs for the approval is decreased. Consequently, the cancer patients can be given faster access to innovative treatments in the participating countries.

Prerequisities for participation in Project Orbis

Project Orbis started with new indication applications for previously approved therapies and now extended to new drug applications (NDA) or original biologics license applications (BLA).

Currently only oncology products are eligible for Project Orbis.

The FDA must agree that the drug meets criteria for Project Orbis and at least one other regulatory agency (Project Orbis Partner) must agree to participate. The applicant may inform the FDA and/or other Project Orbis Partners to pursue Project Orbis.

The initial marketing authorization application has to be submitted to the FDA first.

The clinical criteria for FDA selection for Project Orbis are high-impact and clinically significant applications. It is generally expected to meet the criteria for „FDA Priority review".

Qualifying criteria for FDA priority review are the followings: the drug is intended to treat a serious condition and if approved, it would provide a significant improvement in safety or effectiveness[2].

POPs may also have their own qualifying criteria for a product to be included in Project Orbis e.g. in UK qualifying criteria for the Innovation Passport[3].

Project Orbis implementation

Project Orbis, a global collaborative review program was launched in May 2019. In the first Project Orbis the combination therapy of pembrolizumab (KEYTRUDA, Merck) plus lenvatinib (LENVIMA, Eisai) for the treatment of advanced endometrial carcinoma received simultaneous approvals by the FDA, Health Canada (HC) and the Australian Ther-

Table 1 *Types of Project Orbis Submissions*

Project Orbis Type		Sharing of FDA Reviews	Multi-country meetings	Concurrent review with FDA	Concurrent action with FDA
Type A	Regular	Yes	Yes	Yes	Possible
Type B	Modified	Yes	Yes	Possible	No
Type C	Written Report Only	Yes	No	No	No

apeutic Goods Administration (TGA) in all three countries. The joint decision by the three participating regulatory authorities was a direct result of the first collaborative review process of the FDA and the two international Project Orbis Partners, HC and TGA for two oncology drugs, despite regulatory divergence. This application was approved three months prior to the FDA goal date[4].

As the Project Orbis expands, the FDA looks forward to welcoming further international partners (regulatory authorities) to collaborate with them in that important pathway. Since launching that project 5 more countries have joined to the international collaboration.

The current Project Orbis Partners (POP) include the regulatory health authorization of Australia (since May 2019), Canada (since May 2019), Switzerland (since December 2019), Singapore (since December 2019), Brazil (since May 2020), United Kingdom (since January 2021) and most recently, in July 2021 Israel joined the project.

Submission

To facilitate the review process of the same marketing application in the participating countries, the application should be submitted electronically to each authority using the Common Technical Document format (eCTD). All documents should be written in English, with possible exception for Module 1 including country-specific data. Each application should also conform to the respective national submission requirements.

With Project Orbis the FDA coordinates quarterly meetings with the POPs (internal, no applicants representation) to review the program status and facilitate scientific and regulatory discussions about core review document and applications under review. All communications as part of Project Orbis, are subject to the confidentiality agreement with all participating authorities.

Types of Project Orbis submissions

There are three types of Project Orbis submissions which are dependent on the timelines between the FDA and the POPs (Table 1)[2,5].

Type A (Regular Orbis): Submissions are concurrently or near-concurrently, within 30 days to FDA and POPs.

Type B (Modified Orbis): Submitted with a greater than 30-day delay or a regulatory action greater than 3 months of the FDA action are termed as Type B Orbis.

Type C (Written Report Only Orbis): FDA has already taken regulatory action, which allows FDA to share their completed review documents with POPs but there is no concurrent review or action with the FDA.

3. Conclusions

In the first year of implementation, Project Orbis received 60 marketing application submissions. 38 oncology marketing applications were approved working with Australia, Brazil, Canada, Singapore, Switzerland and the United Kingdom. The median number of POP was 2. TGA and HC were the most often applied POPs, with receipt of 14 and 12 submissions, respectively. The median time-to-approval was between FDA 4.2 months and the POP 4.4 months[2].

The FDA and the participating countries have strong interest to continue collaborations through Project Orbis and potentially extend the project to include additional countries and more versatile drug applications, such as advanced cellular and gene therapies. EMA is not involved due to entire review/approval process. Project Orbis has demonstrated that global regulatory collaboration can serve patients with earlier access to innovative cancer therapy in the participating countries.

References

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