

Guidance document
Project Orbis

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1 Terms, definitions, abbreviations

1.1 Abbreviations

AAid	Assessment Aid document
ANVISA	Agência Nacional de Vigilância Sanitária
FDA	U.S. Food and Drug Administration
HSA	Health Sciences Authority
MHRA	Medicines and Healthcare products Regulatory Agency
MOH	Ministry of Health
IR	Information Requests
LoQ	List of Questions
POWG	Project Orbis Working Group
RMP	Risk Management Plan
SAL	Sponsor Authorization Letter
SMC	Swissmedic
TGA	Therapeutic Goods Administration
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPLRO	Ordinance of the Swiss Agency for Therapeutic Products of 9 November 2001 on the Licensing Requirements for Therapeutic Products (SR 812.212.22)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Introduction

Project Orbis is a program coordinated by the US Food and Drug Administration (FDA) to promising cancer treatments. It provides a framework for concurrent submission and review of oncology products among international partners. It aims to deliver faster patient access to innovative cancer treatments with potential benefits over existing therapies across the globe.

It currently involves the regulatory authorities of:

- Australia (TGA)
- Brazil (ANVISA)
- Israel (MOH)
- Canada (Health Canada)
- Singapore (HSA)
- Switzerland (Swissmedic)
- United Kingdom (MHRA)

FDA serves as the primary coordinator for application selection. Initial queries have to be addressed to the FDA first.

2.1 Legal framework

The procedure for the authorisation of medicinal products with new active substances is based on the following legislative texts in particular:

TPA

- Art. 9 Marketing authorisation
- Art. 10 Conditions for granting a marketing authorisation
- Art. 11 Application for a marketing authorisation
- Art. 14 Important medicinal products for rare diseases (para. 1 f)

TPO

- Art. 7 Fast-track authorisation

TPLRO

- Art. 2 General preconditions
- Art. 3 Documentation on the analytical, chemical and pharmaceutical tests
- Art. 4 Documentation on the pharmacological and toxicology tests
- Art. 5 Documentation on clinical trials
- Art. 6 Special requirements for fixed combinations of medicinal products

The procedure for the authorisation of new indications of medicinal products is a type II major variation and based on the following legislative texts in particular:

TPO

- Art. 23 Major variations

TPLRO

- Art. 22a Classifications of the variations
- Annex 7 List of amendments according to Articles 21-24 TPO

3 Objective

This guidance document describes the marketing authorisation process for medicinal products with medical applications in oncology within the framework of Project Orbis.

Swissmedic uses this guidance document first and foremost as a resource for applying the legal provisions in a uniform and equitable manner. For applicants, the document is intended to illustrate the specific framework to comply with so that corresponding applications can be processed by Swissmedic as quickly and efficiently as possible.

4 Scope

New marketing authorisation applications (MAAs) with new active substances and new indication applications (type II variations) for oncology medicinal products are eligible for Project Orbis.

The applicant is not legally entitled to demand the use of Project Orbis without the consent of Swissmedic. Rather, the Project Orbis procedure is a voluntary special service offered by Swissmedic in collaboration with the FDA.

There are no limitations with respect to the types of procedures in Project Orbis: Applications may be submitted in the standard procedure, the “Fast Track Procedure”, “Temporary Authorisation

Procedure” or the “Procedure with prior Notification”. Applications for use of these special procedures must be submitted to Swissmedic as usual.

5 Description

5.1 Requirements

The requirements for the authorisation of medicinal products with new active substances are described in the guidance document *Authorisation of human medicinal product with new active substance HMV4*.

The requirements for the authorisation of new indications are described in the guidance document *Variations and extensions HMP HMV4*.

The following documents outline specific criteria and requirements for the procedures of the same name:

- Guidance document *Fast-track authorisation procedure HMV4*
- Guidance document *Temporary authorisation for human medicinal products HMV4*
- Guidance document *Procedure with prior notification HMV4*

5.1.1 Formal requirements

The formal requirements are based on the guidance document *Formal requirements HMV4* and the associated directory of *Documents to be submitted HMV4*.

5.1.2 Document protection

Information on documentation protection is provided in the guidance document *Document protection HMV4*.

5.1.3 Time limits

The time limits are based on the guidance document *Time limits for authorisation applications HMV4*.

5.1.4 Fees

The fees specified in the Ordinance on Fees Levied by the Swiss Agency for Therapeutic Products apply.

5.2 Process

5.2.1 FDA Selection Process

Clinical criteria for FDA selection of applications for Project Orbis include high-impact and clinically significant applications. Project Orbis applications are generally expected to meet the criteria for “FDA Priority Review.

Qualifying criteria for FDA priority review include:

- the drug is intended to treat a serious condition

- and if approved, would provide a significant improvement in safety or effectiveness.

FDA serves as the primary coordinator for the application review. However, each country remains fully independent on their final regulatory decision and the labelling.

5.2.2 Types of Project Orbis submissions

Type A (Regular Orbis)

Applications are submitted within 30 days after submission to the FDA. Type A Orbis Projects allow for maximal collaboration during the review phase and the possibility of concurrent action with FDA.

Type B (Modified Orbis)

Applications submitted to Swissmedic more than 30 days later than to the FDA are referred to as Type B Orbis and allow the possibility of concurrent review with FDA but no concurrent action.

Type C (Written Report Only Orbis)

In case the FDA has already approved or will shortly approve an application, they share their completed review documents with the participating Project Orbis partners. These Type C Orbis projects do not allow any concurrent review or action with FDA.

5.2.3 Selection process of Project Orbis type by Swissmedic

The applicant can submit an application for Project Orbis to the FDA once topline results are available from the registrational clinical trial(s). Project Orbis proposals cannot be submitted to Swissmedic or any other Project Orbis Partner.

Swissmedic determines the Orbis type according to the definitions above. The applicant must provide the US and Swiss submission dates to this end.

Swissmedic will accept all Type A applications as such. If the submission gap is greater than 30 days, Swissmedic will decide on the basis of available resources and the extent of the submission gap whether a Type B or C will be applied.

Once the type of Project Orbis submission has been determined by Swissmedic, the US company is informed via the FDA. The US company must subsequently inform the local Swiss applicant about the planned submission and instruct it to get in contact with Swissmedic (email:

projectorbis@swissmedic.ch). In addition, Swissmedic informs the applicant in Switzerland of the participation, provided a contact person at the FDA is listed in the global submission plan.

Swissmedic's participation is contingent on agreement with the Swiss applicant.

5.2.4 Submission of the application

Submissions should be made electronically using the Common Technical Document format (i.e. eCTD) with all documents in English, with possible exception for country-specific Module 1. Marketing applications should comply with the specific requirements for submissions to Switzerland (see also guidance document *Formal requirements H MV4*).

In order to allow the exchange of information between Swissmedic and the participating Project Orbis partners over the course of the review, the Swiss applicant has to tick the corresponding check box in the Swissmedic application form.

In addition, the FDA 'Sponsor Authorization Letter' (SAL) and the FDA 'Assessment Aid' document (AAid) have to be part of the initial application submission.

5.2.5 Swissmedic review

5.2.5.1 Type A Orbis

Marketing applications for new active substances or extensions of indications submitted to Swissmedic within 30 days after the submission to the FDA are termed Type A Orbis (Regular Orbis). This allows for maximal collaboration between the participating Project Orbis partners during the review phase and parallel assessment of the application.

For Type A Orbis applications, FDA schedules and coordinates several multi-country teleconferences to discuss various aspects of the application. These include a kickoff meeting and application-specific meetings. The kickoff meeting, which is scheduled before or within 30 days of FDA application submission, discusses the overall review strategy and review timelines. Within the Project Orbis Working Group (POWG), FDA provides for the verification of the clinical trial results by analyzing the submitted tabulation and analysis datasets. Application-specific meetings include discipline-specific meetings (e.g. efficacy, safety, clinical pharmacology) and overall benefit-risk, where relevant sections of the AAid are discussed as well as the midcycle FDA meeting where particular items of relevance to the group are discussed within the POWG.

For Type A submissions, Swissmedic evaluation phases I and II are combined. Information Requests (IRs) are issued during initial review in a 'rolling questions' approach. IRs from Swissmedic are shared with the POWG and sent to the applicant in Switzerland. Questions are sent in English with a response deadline of 10 calendar days as a rule. For IRs that concern the medicinal product information texts, Swissmedic can also send the revised manuscripts. Responses to IRs are forwarded to all participating Project Orbis partners via their local companies. Exceptions include FDA IRs on raw data analyses and IRs on country-specific labelling. These do not have to be submitted to Swissmedic.

For Switzerland, answers to the IRs have to be uploaded as "communication" to the Swissmedic eGov Portal. A cover letter that references the relevant IR(s) and mentions that the application will be reviewed in the Orbis framework should be enclosed with the submission. The responses must be submitted to all authorities involved with the application with minimal delay. The responsible Regulatory Manager and projectorbis@swissmedic.ch should be informed about the upload to ensure an expedited distribution to the assessment team.

After completion of the initial assessment, Swissmedic issues the pre-decision letter (right to be heard) directly to the Swiss applicant. A consolidated eCTD sequence including the answers to all outstanding IRs must be submitted in the response to the Swissmedic pre-decision.

Throughout the process, Swissmedic will inform the applicant in Switzerland about any upcoming milestones and decisions as far in advance as possible.

5.2.5.2 Type B Orbis

Marketing authorisation applications submitted to Swissmedic more than 30 days later than to the FDA are referred to as Type B Orbis (Modified Orbis).

For Type B Orbis applications, FDA schedules and coordinates several multi-country teleconferences to discuss various aspects of the application. These include a kickoff meeting and application-specific meetings. The kickoff meeting, which is scheduled before or within 30 days of FDA application submission, discusses key aspects of the application within the POWG. Additional application-specific

meetings include discipline-specific meetings (e.g. efficacy, safety, clinical pharmacology) and overall benefit-risk, where relevant sections of the AAid are discussed.

For Type B submissions, Swissmedic can issue a consolidated formal LoQ or IRs with 'rolling questions' depending on the submission gap between FDA and Swissmedic and the resulting differences in the status of the review processes. IRs from Swissmedic are shared with the POWG and sent to the applicant in Switzerland. Questions are sent in English with a response deadline of 10 calendar days as a rule. For IRs that concern the medicinal product information texts, Swissmedic can also send the revised manuscripts. Responses to IRs are forwarded to all participating Project Orbis partners via their local companies. Exceptions include FDA IRs on raw data analyses and IRs on country-specific labelling. These do not have to be submitted to Swissmedic.

For Switzerland, answers to the IRs have to be uploaded as "communication" to the Swissmedic eGov Portal. A cover letter that references the relevant IR(s) and mentions that the application will be reviewed in the Orbis framework should be enclosed with the submission. The responses must be submitted to all authorities involved with the application with minimal delay. The responsible Regulatory Manager and projectorbis@swissmedic.ch should be informed about the upload via email to ensure an expedited distribution to the assessment team.

After completion of the initial assessment, the applicant in Switzerland receives either the consolidated formal LoQ or the pre-decision letter. A consolidated eCTD sequence including all answers to information requests must be submitted at the stage of "response to pre-decision" if IRs with 'rolling questions' were issued.

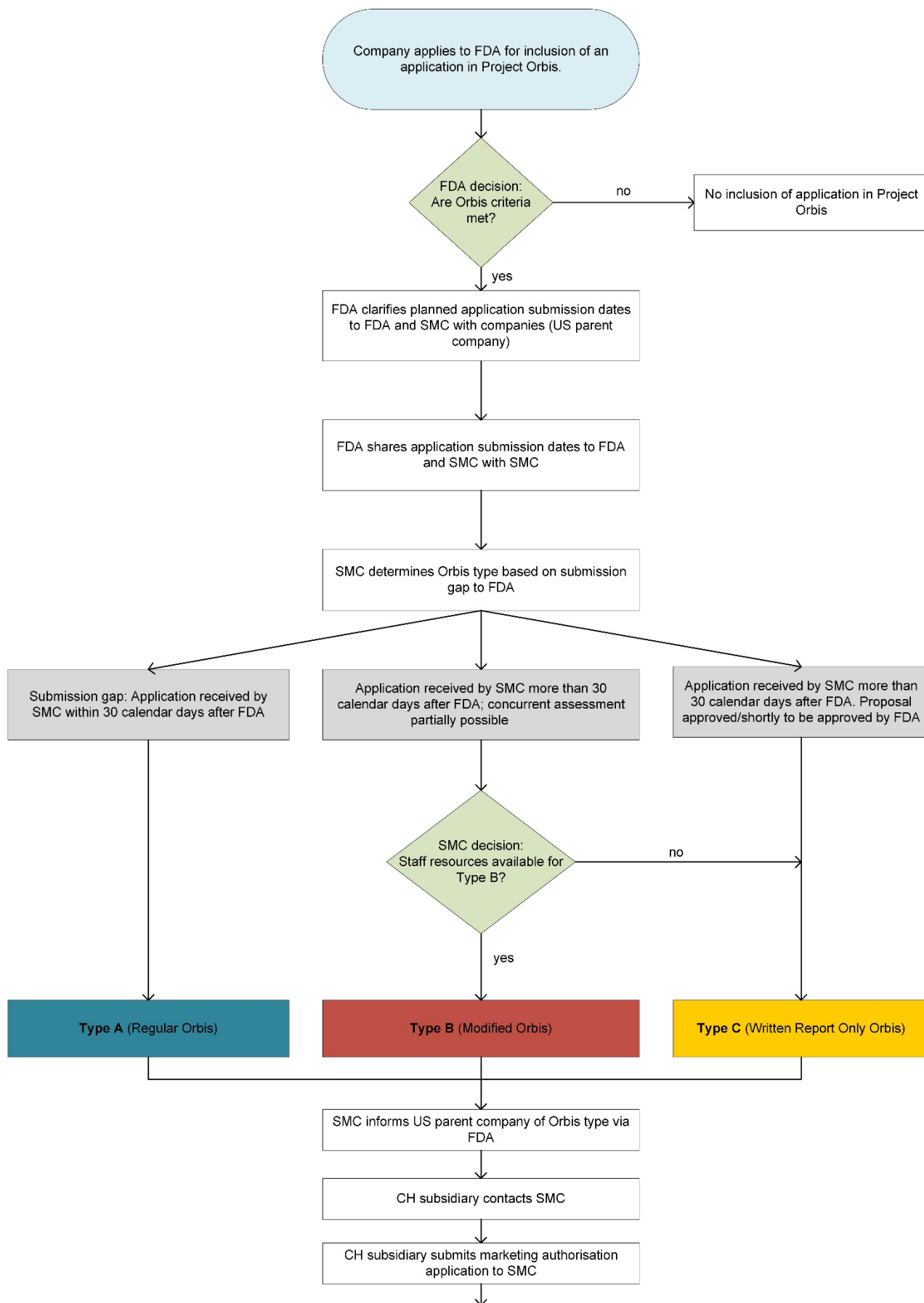
Throughout the process, Swissmedic will inform the applicant in Switzerland about any upcoming milestones and decisions as far in advance as possible.

5.2.5.3 Type C Orbis

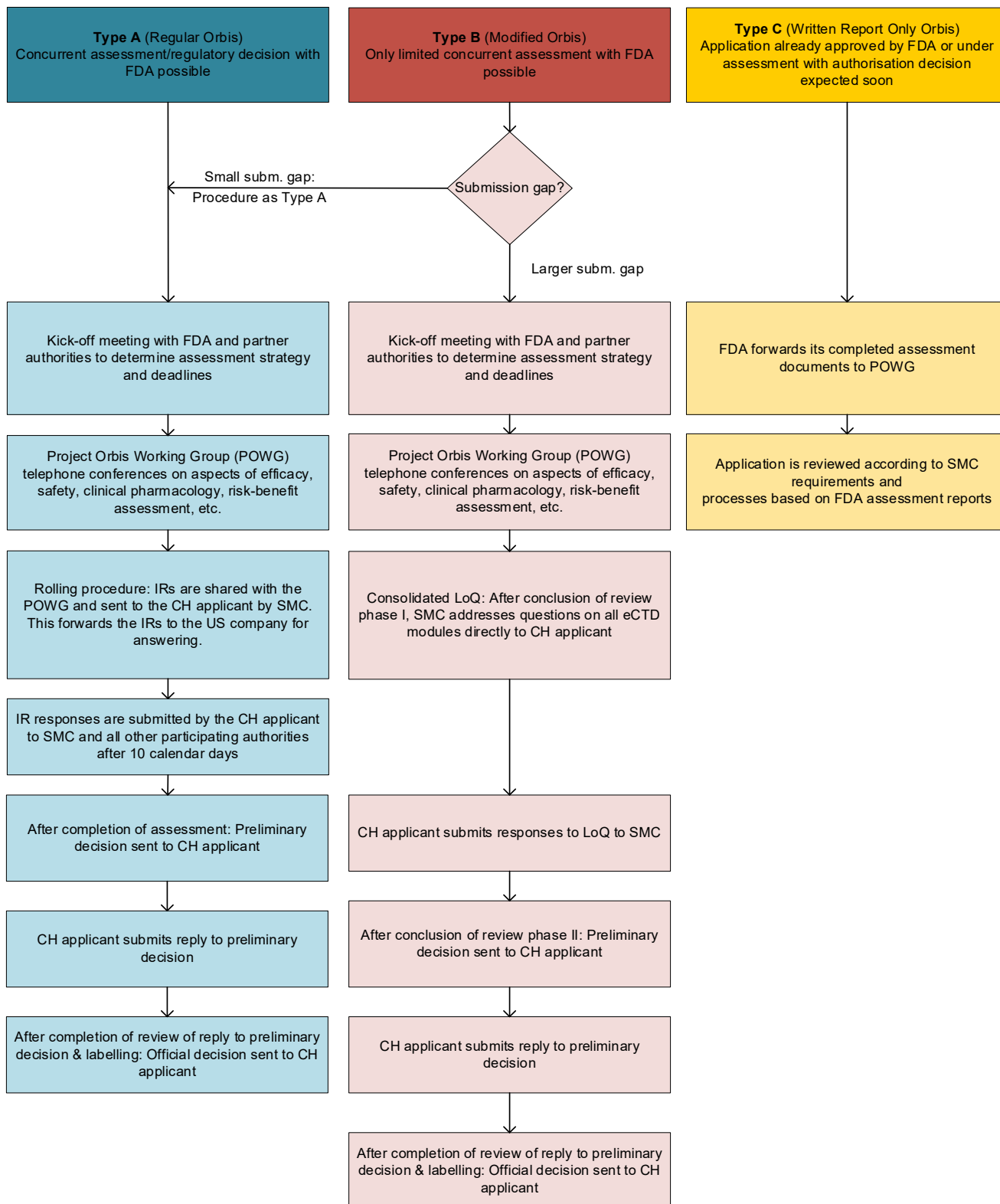
For applications already approved or to be approved shortly by the FDA, there is Type C Orbis (Written Report Only Orbis) which allows FDA to share their completed review documents with the participating Project Orbis partners. These must be provided to Swissmedic before review phase I. For Type C submissions, the above-mentioned meetings for Type A or B do not occur because FDA scientific assessment had already been completed.

Unredacted FDA assessment reports support Swissmedic's assessment and might accelerate the review procedure. If necessary, a consolidated formal LoQ is issued after phase I followed by the pre-decision letter after phase II. Throughout the process, Swissmedic will inform the applicant in Switzerland about any upcoming milestones and decisions as far in advance as possible.

Annex 1 – Flow Chart



Process steps after application submission



Change history

Version	Change	sig
3.1	New layout, no content adjustments to the previous version.	dei
3.0	Clarification in section 6.2: Notification of the Information Request directly to the applicant in Switzerland	rim, ru, wph, fg
2.0	Section 2: Israel new partner authority in Project Orbis Linguistic clarifications New Annex 1 with flow chart	rim, ru, dts
1.0	New document	rim, ru, wph, dts