Orphan Drug Development Guidebook

Building Block U207

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	FDA Special Protocol Assessment (FDA-SPA)
References	https://www.fda.gov/downloads/Drugs/Guidances/UCM498793.pdf
Description	FDA-SPA is a process in which sponsors may ask to meet with FDA to reach agreement on the design and size of certain clinical trials, clinical studies, or animal studies, to determine if they adequately address scientific and regulatory requirements for a study that could support marketing approval. Specific to Pivotal Study agreement, FDA-SPA can be useful to navigate the inherent complexities of rare disease development, including assisting on the selection of the design of a trial. The procedure takes around 45 days FDA review period.
Category	Regulatory Building Block
Geographical scope	United States of America
Availability	Applicants developing medicines for rare and non-rare diseases.

Scope of use	An FDA-SPA agreement indicates concurrence by FDA with the adequacy and acceptability of specific critical elements of overall protocol design (e.g., entry criteria, dose selection, endpoints, and planned analyses) for a study intended to support a future marketing application. These elements are critical to ensuring that the trial conducted under the protocol can be considered an adequate and well-controlled study that can support marketing approval. Feedback on these issues provides the greatest benefit to sponsors in planning late-phase development strategy.
Stakeholders	• Drug developers • FDA
Enablers / Requirements	A request should be submitted to a sponsor's existing IND (Investigational New Drug) for each protocol the sponsor wants reviewed under an FDA-SPA. A request should not include more than one protocol. If there is no IND for the product, FDA will assign a pre-IND number so that a meeting to fully inform FDA of the overall development plan for the product can be scheduled. The sponsor can subsequently open an IND after the meeting and then submit a Request to the IND.
Output	Agreement between the FDA and the sponsor on the adequacy and acceptability of specific critical elements of the overall protocol design for a study intended to support a future marketing application.
Best time to apply and time window	To allow sufficient time for FDA review and comment, as well as for resolution of outstanding high-level issues before the initiation of the proposed trial.
Expert tips	An FDA-SPA submission may not be appropriate for such assessment if: • It contains a request to evaluate more than one protocol. In such a case, FDA will ask the sponsor to submit separate requests for each protocol. This process may delay the initiation of the SPA reviews. • It contains a protocol for an ongoing trial. • It contains a protocol for which evaluation and critical features are adequately described by existing guidance (e.g., conventional stability study). • It does not provide enough content and detail. Content of a Request and Submission Materials, including:

	– A detailed protocol – Specific questions for FDA to address – Adequate background documents to support the critical elements of the trial design, or to determine whether it can adequately address scientific and regulatory requirements for the purpose identified by the sponsor • Prior FDA concurrence has not been obtained for the animal model to be used in the proposed animal rule efficacy study. As stated in the PDUFA (Prescription Drug User Fee Act) and BsUFA (Biosimilar User Fee Act) goals, the sponsor has not had a meeting (e.g., end of-phase 2/pre-phase 3 meeting (or end-of-phase 1 meeting, if applicable) or a BPD (biosimilar biological product development) Type 2 or Type 3 meeting) with the review division at which the regulatory context for the study or trial that is the subject of the SPA was discussed (where the trial is intended to support efficacy or trials to prove biosimilarity and/or interchangeability). PROs: – FDA will also provide advice on other important concerns identified during review, even in the absence of a specific question. CONs: – Recently updated FDA-SPA guidance further weakened the strength of agreements with the Agency on a SPA. – Agreements made on an FDA-SPA, particularly on clinical studies are not binding by FDA.