IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Orphan Drug Development Guidebook

Building Block I401

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	Joint EMA – FDA Scientific Advice (Parallel Scientific Advice – PSA)
References	http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2017/11/WC500239158.pdf https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/OfficeofInternationalPrograms/UCM557100.pdf
Description	The European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services have a program to provide parallel scientific advice (PSA) to sponsors. The goal of the PSA program is to provide a mechanism for EMA assessors and FDA reviewers to concurrently exchange with sponsors their views on scientific issues during the development phase of new medicinal products (i.e., new human drugs and biologics). Due to clinical particularities of rare diseases, the development plan of new treatments may deviate substantially from conventional methods and approaches and this may result in issues on acceptability of data at the time of marketing authorization assessment. Regulatory scientific advice may avoid such issues if done early in the development process, but criteria may diverge between FDA and EMA. Scarcity of populations do not allow for separate developments for each region to satisfy different criteria. Joint FDA-EMA scientific advice allows coordination of the procedure and joint discussion, so that a mutually recognized position acceptable in both regions is obtained.

Category	Regulatory Building Block
Geographical scope	European Union and United States of America
Availability	Applicants developing medicines for rare and non-rare diseases lacking development guidelines, or if guidelines do exist, those for which EMA's and FDA's guidelines differ significantly.
Scope of use	The PSA procedures should focus on sharing information and perspectives. Achieving harmonization and increased convergence is a potential beneficial outcome of the PSA process. Following PSA meetings, sponsors should have a clearer understanding of the agencies' respective requirements and perspectives regarding the development program discussed, and if divergent, the reasons for the divergence. The best candidates for PSA include important medicinal products, especially those being developed for indications lacking development guidelines, or if guidelines do exist, those for which EMA's and FDA's guidelines differ significantly. In addition, biosimilars, products with significant clinical safety, animal toxicology, or unique manufacturing concerns that could impede further product development are appropriate PSA candidates. Previous PSAs have involved medicinal products for oncology, anti-infectives, rare diseases, the pediatric population, and cardiovascular disease, as well as post-licensure commitment clinical trials. PSA requests should focus primarily on specific questions or issues involving the development of a medicinal product intended to be commercialized in both the EU and the USA, and especially if the scarcity of the target population makes it difficult to conduct conventional developments or replicate data to satisfy divergent regional requirements, and thus those for which the sponsor desires to have further scientific input from both EMA and FDA.
Stakeholders	• Applicants of the PSA program • EMA • FDA
Enablers / Require	Sponsors wishing to nominate a product for PSA should address one single "Request for PSA" letter to both emainternational@ema.europa.eu at EMA and OC-OIPEurope@fda.hhs.gov at FDA. In this letter, the sponsor should provide the following information: (1) the product in development, (2) why a discussion with the assessors

ments	(reviewers) of EMA and FDA would be beneficial to the product's development, (3) specific questions requiring clarification, (4) the desired goals for the meeting, and (5) an explicit authorization for the agencies' comprehensive exchange of all information relevant to the product, including trade secret information (as defined by U.S. statute). Pursuant to legally established authorities, both agencies will maintain the confidentiality of all such information.
Output	Advices from both agencies. The advice of each agency may still differ after the joint discussion. However, both agencies will strive to provide PSA responses that are convergent.
Best time to apply and time window	The tool can be used starting at the beginning of the clinical development until market authorization being the optimal time to apply after human PoC.
Expert tips	PROs: Joint FDA-EMA scientific advice allows coordination of the procedure and joint discussion, so that a mutually recognized position acceptable in both regions is obtained, or clear reasons for divergence and ways to approach the development if the former is not achieved. CONs: The development requirements in case of substantial divergence in criteria may be overall increased to reach mutually acceptable positions, and these may not be feasible to comply without substantial resources, which may not be available.