Orphan Drug Development Guidebook

Building Block I417

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	Development of product specific bio-analytical assays
References	ICH M10 on bioanalytical method validation - Scientific guideline | European Medicines Agency (europa.eu): https://www.ema.europa.eu/en/ich-m10-bioanalytical-method-validation-scientific-guideline https://www.fda.gov/files/drugs/published/Bioanalytical-Method-Validation-Guidance-for-Industry.pdf https://www.nihs.go.jp/drug/BMV/index.html
Description	Measurement of drug concentrations in biological matrices (such as serum, plasma, blood, urine, and saliva) is an important aspect of drug development. These methods provide data to support the safety and effectiveness of drugs, which may be needed to support applications for new drugs in regulatory pathways. The results of animal toxicokinetic studies and of clinical trials, including bioequivalence studies are used to make critical decisions supporting the safety and efficacy of a drug. It is therefore necessary that the applied bioanalytical methods used are well characterized, fully validated and documented in order to yield reliable results, and to be used in regulatory processes. The bioanalytical assays could be chromatographic assays and ligand binding assays that quantitatively determine the levels of drugs, their metabolites, therapeutic proteins, and biomarkers in biological matrices.
Category	Development Practices Building Block
Geographical scope	International

Availability	Applicants developing medicines for rare and non-rare diseases.
Scope of use	Validating the analytical method ensures that the data are reliable by addressing certain key questions, including: • Does the method measure the intended analyte? For example, does anything interfere with the measurement, and is the method specific or selective for the analyte? • What is the variability associated with these measurements? For example, what are the accuracy and precision of the method? • What is the range in measurements that provide reliable data? For example, what is the sensitivity of the method (e.g., what is the lower limit of quantitation (LLOQ) of the method, and what is the upper limit of quantitation the method (ULOQ)?) • How do sample collection, handling, and storage affect the reliability of the data from the bioanalytical method? For example, what steps need to be followed while collecting samples? Do the samples need to be frozen during shipping? What temperatures are required to store the samples, and how long can the samples be stored?
Stakeholders	• EMA, FDA and/or MHLW • Drug developers
Enablers/ Requirements	Pivotal studies submitted in an application that requires regulatory decision making for approval, safety or labeling, such as bioequivalence or pharmacokinetic studies, should include bioanalytical methods that are fully validated. Exploratory methods that would not be used to support regulatory decision making (e.g., candidate selection) may not require such stringent validation.
Output	A well-documented, reliable, and optimized bioanalytical method, that can be used for validation and is suited for the analysis of study samples. A detailed, written description (e.g., protocol, study plan, and/or standard operating procedure (SOP)) should have been established for the bioanalytical method before initiating validation. The description should identify procedures that control critical parameters in the method (e.g., environmental, matrix, procedural variables) from the time of collection of the samples to the time of analysis to minimize their effects on the measurement of the analyte in the matrix.
Best time to apply and time window	The tool may be used at several stages during drug development; therefore an early development is recommended.
Expert tips	General and specific SOPs and good record keeping are essential to a properly validated analytical method. The data generated for bioanalytical method

	development and/or validation should be documented and available for data audit and inspection.