# Orphan Drug Development Guidebook

## Building Block E103

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 |
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| Building Block (BB) Title | EMA Protocol Assistance (EMA-PA) |
| References | **Scientific advice and protocol assistance**<br>https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance<br><br>**European Medicines Agency Guidance for Applicants seeking scientific advice and protocol assistance**<br>https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-guidance-applicants-seeking-scientific-advice-protocol-assistance_en-0.pdf<br><br>**Decision of the Executive Director on fee reductions for designated orphan medicinal products**<br>https://www.ema.europa.eu/en/documents/other/decision-executive-director-fee-reductions-designated-orphan-medicinal-products_en.pdf |
| Description | The EMA protocol assistance is the scientific advice of the Committee for Human Medicinal Products (CHMP) along with Committee for Orphan Medicinal Products (COMP), particularly designed for products that have orphan drug designation status.<br><br>The process has a fixed procedure timelines of 40 days or 70 days (+ pre-submission, if required). |
| Category | Regulatory Building Block |
| Geographical scope | European Union |

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| Availability | Applicants developing medicines for rare diseases for which orphan drug status has been granted (i.e. only available *after* designation of orphan status), regardless of their legal entity. |
| Scope of use | All matters related to drug development discussed during scientific advice (SA), such as quality, safety, efficacy and methodology aspects. In addition to the scope of the SA, protocol assistance may relate to:<br>- The demonstration of significant benefit within the scope of the designed orphan indication<br>- Similarity/clinical superiority in cases where other potentially similar products have market exclusivity in the concerned therapeutic indication<br>The EMA protocol assistance is particularly useful to orphan medicine developers when:<br>- there appears to be no or insufficient relevant details in European Union guidelines or EMA guidance documents, or in Pharmacopoeia monographs, including draft documents or monographs released for consultation;<br>- the developer chooses to deviate from the available guidance during the development plan due to the complexity of the disease, the low prevalence of patient population, etc. |
| Stakeholders | • EMA, CHMP and COMP<br>• Orphan drug developers |
| Enablers/ Requirements | A medicinal product that has already obtained the ODD status. |
| Output | Written responses to the questions posed by the developers to the Agency on the development program. This advice is not legally binding, however has to be justified either at the subsequent PA or at the time of marketing authorisation (MA.) |
| Best time to apply and time window | The tool may be used anytime during drug development, after granted ODD and before marketing authorization. |

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| | Multiple requests (at different stages of development) are possible and in some cases a post-approval request might be possible as well. |
| Expert tips | Any assessment done on orphan exclusivity during development has to be re-evaluated at the time of Marketing Authorisation Application (MAA) it depends on which applicant obtains the MA first.<br><br>The time to prepare briefing materials and to complete the procedure can be long. It is critical for key staff to be available to answer possible questions at a Discussion Meeting.<br><br>PROs:<br><br>• As of 19 June 2020, EMA can provide protocol assistance free of charge to academic organisations developing orphan medicines.<br>• Pre-submission meetings are free of charge and very useful to minimize validation questions**.**<br>• Like Scientific Advice, an opinion from CHMP on appropriate CMC, preclinical and clinical development (i.e., tests and studies) is requested during the development of an orphan drug. If the advices are followed (or deviations justified), this should minimize objections at the time of MAA evaluation which could otherwise delay or compromise the registration.<br><br>CONs:<br><br>• As per the scientific advice, it is not legally binding, however, there is a regulatory expectation to follow it during the development and until the time of the MAA submission. |