Orphan Drug Development Guidebook

Building Block E102

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	European Orphan Drug Designation (EU-ODD)
References	**EMA orphan drug information** https://www.ema.europa.eu/en/human-regulatory/research-development/orphan-designation/applying-orphan-designation **EC regulation** https://ec.europa.eu/health/human-use/orphan-medicines_en **EC guideline on ophan applications (for designation and transfer):** https://health.ec.europa.eu/latest-updates/eu-guideline-orphan-applications-designation-and-transfer-2022c-44002-2022-12-19_en **IMT tutorial 'How to apply and benefit from an orphan drug designation':** https://imt.ejprarediseases.org/use_case/how-to-apply-and-benefit-from-an-orphan-drug-designation/
Description	EU orphan legislation offers important incentives to encourage the development of medicinal products for rare diseases and the success of the legislation has been demonstrated. Developers from a pharmaceutical company or an academic unit or an individual may benefit from fee reductions/waivers, specific scientific advice called protocol assistance from the EMA and protection from competition once the medicine is placed on the market (10 years of market exclusivity). The process will last 90 Days from validation date (+ pre-submission, if requested). Process details: (Pre-submission meeting, if required); Application for ODD to EMA checks validation of the application; COMP Rapporteur assesses submitted data and generates a report with EMA orphan office colleague; COMP provide a decision / opinion within 90 days; EMA forwards the opinion to the European Commission; Decision made within 30 days.

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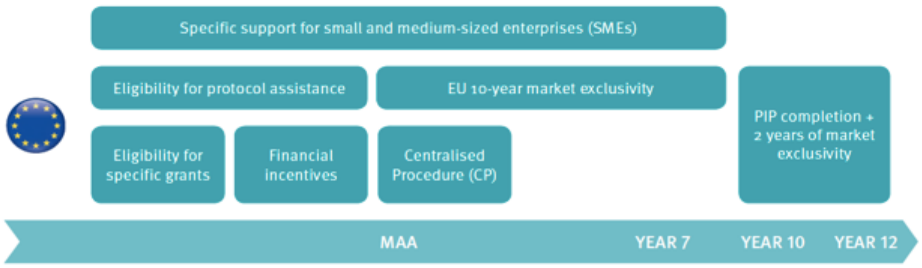
	Appeal process for negative opinions exists.
Category	Regulatory Building Block
Geographical scope	European Union
Availability	Applicants developing medicines for rare diseases
Scope of use	A formal recognition by the EMA of the need of incentives, such as fee reduction and protection from competition once the drug is placed on the market, to develop the drug.  *Modified from Regulatory Rapporteur – Vol 13, No 7/8, July/August 2016* Orphan designation provides a degree of validation of the development programme, specific grants are available for orphan designated medicines, scientific advice is an important element to aid the development of the drug and the 10 years of market exclusivity and fee reductions are important incentives.

Stakeholders	• EMA
	  ○ Committee for Orphan Medicinal Products (COMP)
	  ○ Committee for Advanced Therapies Medicinal Products (CAT), in case of ATMPs
	  ○ Paediatric Committee (PDCO)
	• European Commission
	• Medicinal product developers

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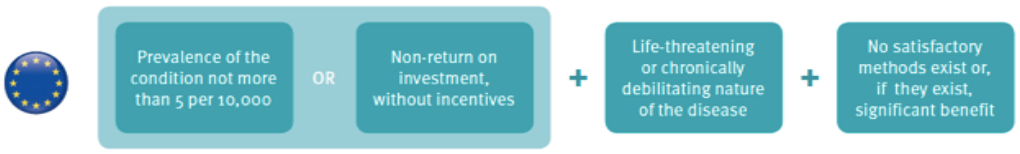
Enablers/ Requirements	For European designation, the drug must meet all the three following criteria (orphan EC Regulation 141/2000): 1. the prevalence of the condition in the EU must not be more than 5 in 10,000 ***or*** it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development; 2. it must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating; 3. no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorised, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.  *Modified from Regulatory Rapporteur – Vol 13, No 7/8, July/August 2016*
Output	The output is the orphan drug designation status, an official legally binding recognition recorded in the European Commission orphan drug designation database and will have to be reconfirmed at the time of market authorisation.
Best time to apply and time window	The tool has its use any time after obtaining non-clinical proof-of-principle data, until before Marketing Authorization Application submission. In most cases, the best time is when you enter clinical phase. ODD granted during development is re-evaluated and confirmed at the time of the MAA submission.
Expert tips	A pre-submission meeting is offered free of charge, and it could be very valuable for academia/SME to pre-validate the package and minimize the validation questions. In order to promote success, the sponsor should consult the relevant guidance documents to ensure that the content and format of the application is optimised and the submitted references are current and relevant. The published minutes can provide useful background information for similar products / disease conditions All claims should be clearly supported by relevant data (in house or published). The company must submit an annual report to the EMA, for the orphan drug that

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	was granted ODD, until it undergoes the marketing authorization process EU- ODD benefits - during drug development: Protocol assistance from EMA providing scientific and regulatory expertise into the development program (Building Block FORM_PA) The importance of requesting and adhering to scientific advice cannot be understated - For academic organisations developing orphan medicines, EMA can provide protocol assistance free of charge (as of June 2020). - For SME (small and medium size companies), exemption of fees (protocol assistance, authorization procedures) - For NON-SME, reduction fees (i.e., protocol assistance reduction up to 75%, initial marketing authorization application reduction fees up to 10%, etc) - Once ODD granted, access to specific EU funds (i.e., Horizon 2020, National grants) EU- ODD benefits – if confirmed at the time of MAA registration: - 10 years Market Exclusivity for the entire European Union + additional 2 years if PIP completed EU- ODD disadvantages - Unlike US, no ODD specific funds are provided by EU Commission - No specific ODD for pediatrics or for devices