White Paper

Drug Development 2022

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Guideline on Orphan Drugs for US Pharmaceutical Companies willing to enter the EU Market

Introduction

An orphan drug designation is a status delivered by FDA (US) or EMA (Europe) for a pharmaceutical drug that has been developed specifically to treat an ultra-rare disease (affecting less than 200,000 patients in the United States and/or 500,000 patients in the European Union).

Orphan Drug Designation provides many potential benefits to pharmaceutical companies developing drugs for the treatment of rare diseases or conditions (defined as those affecting fewer than 200,000 people in the United States). The process is initiated by an interested party (for example, a patient group) requesting that the U.S. Food and Drug Administration (FDA) grant the drug candidate orphan drug designation. The FDA will then determine whether the regulatory criteria are met and if so, grant orphan drug designation.

Orphan Drug Designation in Europe follows similar pathways. Initially, the drug is assessed by the EMA through its scientific advice procedure to determine whether or not it fulfills the criteria for orphan designation.

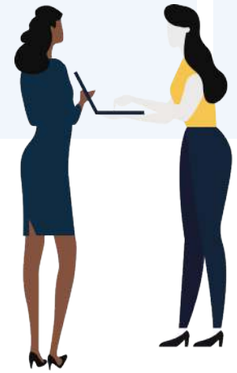
Here we will be presenting 5 tables that will help you better understand the differences in ODDs regulation between the EU and the US.

Orphan Drug Designation - Legal basis

What is the legal basis?

- US as a pioneer in Orphan drug regulation
- Complex and multiple documents, particularly for EU
- Differences between US & EU

	USA	EU
AGENCIES / COMMITTEES	FDA / OOPD	EMA / COMP
LEGISLATION	• Orphan Drug Act (1983) condified in 21 CFR Part 316 • Orphan Drug Regulations Final Rule 6/12/2013	• Regulation (EC) No 141/2000 of the European Parliament and of the Council on Orphan Medicinal Proeducts of 16 December 1999 • Commission Regulation (EC) No 847/2000 of 27 April 2000 • Commission notice November 2016 (2016/C 424/03) • Commission Regulation (EU) No 2018/781 of 29 May 2018 amending Regulation (EC) No 847/2000 as regards the definition of the concept 'similar medicinal product'



References: https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation/legal-framework-orphan-designation ; https://www.fda.gov/industry/developing-products-rare-diseases conditions/designating-orphan-product-drugs-and-biological-products

Orphan Drug Designation - Guidance

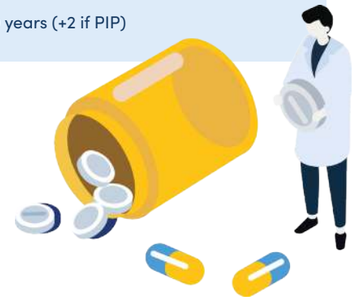
Guidance

Numerous publications covering all aspects of orphan drug development, registration, maintenance and incentives

USA	EU
Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases Guidance for Industry	Points to consider on the estimation and reporting on the prevalence of a condition for the purpose of orphan designation EMA/COMP/436/01 Rev. 1 (June 2019)
Meetings with the Office of Orphan Products Development - Guidance for Industry, Researchers, Patient Groups, and Food and Drug Administration Staff	Recommendation on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation EMA/COMP/15893/2009 Final. (March 2010)
FDA Webpages • Developing Products for Rare Diseases & Conditions • Public Identification of Orphan Drug Designation - Notice to Certain Orphan-Drug Designation Holders • Designating an Orphan Product : Drugs and Biological Products • Frequently Asked Questions (FAQ) About Designating an Orphan Product • Orphan Drug Designation : Disease Considerations	Decision of the Executive Director on fee reductions for designated orphan medicinal products EMA/135645/2020
	European Medicines Agency Guidance for Applicants seeking scientific advice and protocol assistance EMA/4260/2001 Rev. 14 (Oct. 2022)
	Procedural advice for orphan medicinal product designation EMA/420706/2018 Rev. 11 (Sept. 2021)
	IRIS Guide to registration and RPIs - Preliminary requirements for all IRIS submissions, including substance and Research Product Identifier registration EMA/31242/2019 v.2.9 (Sept. 2022)
	Procedural advice for post-orphan medicinal product designation activities EMA/469917/2018 Rev. 13 (Sept. 2022)
	Guideline on aspect of the application of Article 8(2) of Regulation (EC) No 141/2000 of the European Parliament and the Council : Review of the period of market exclusivity of orphan medicinal products (2008/C242/07)
	Guideline on aspects of the application of Article 8(1) and (3) of Regulation (EC) No 141/2000 : Assessing similarity of medicinal products versus authorisez orphan medicinal products benefiting from market exclusivity and applying derogations from that market exclusivity (2008/C 242/08)

Orphan Drug Advantages

		USA	EU
Financial incentives	Fee	Fee waivers (NDA/BLA)	Fee reductions / waivers (SMEs) (PA, MA, PV, ...)
	Tax credits	Yes, 50% on clinical research costs	No (EMA)
	Grants for research	FDA Orphan Products Grant Program NIH grants	EC Framework Programmes (Horizon Europe : EU Framework Programme for Research & Innovation) ; EJP RD
Scientific advice		Yes	Yes, Protocol assistance
Regulatory tools to accelerate approval		• Fast-track approval • Breakthrough designation • Accelerated approval pathway • Priority review designation	• Priority medecines (PRIME) • Mandatory access to the Centralised Procedure • Conditionnal approval • Approval under exceptional circumstances • Faciliated access to accelerated assessment
Marketing exclusivity		7 years	10 years (+2 if PIP)



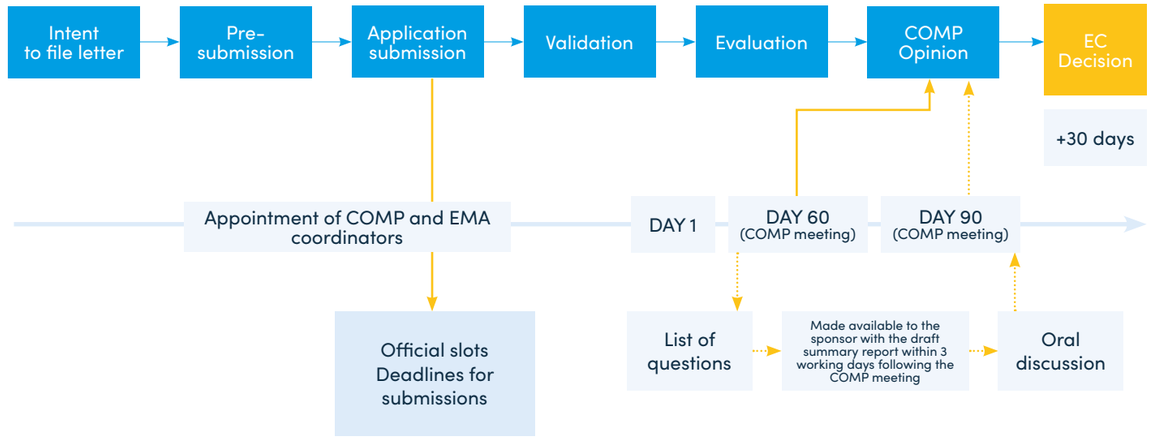
References: Recommended Tips for Creating an Orphan Drug Designation Application - A Webinar by the Office of Orphan Products Development (OOPD) 2018 https://www.fda.gov/media/111762/download ; Decision of the Executive Director on fee reductions for designated orphan medicinal products EMA/135645/2020 https://www.ema.europa.eu/en/documents/other/decision-executive-director-fee-reductions-designated-orphan-medicinal-products_en.pdf

Orphan Drug Designation – Eligibility

EU	USA
Rarity (prevalence) Medical condition affecting not more than 5 in 10,000 persons in the community	A drug/biologic may be «designated» by the Office of Orphan Products Development if it is to prevent, treat, or diagnose a disease/condition that occurs in <200,000 people in U.S
OR	OR
Seriousness / return of investment • Life - threatening or chronically debilitating • Without incentives it is unlikely that the marketing of the product would generate sufficient return to justify the necessary investment	Drugs that will not be profitable within 7 years following approval by the FDA
AND	
Seriousness / return of investment • Alternative methods authorized • If satisfactory methods exist, the sponsor should establish that the product will be of significant benefit	

References: Recommended Tips for Creating an Orphan Drug Designation Application - A Webinar by the Office of Orphan Products Development (OOPD) 2018 https://www.fda.gov/media/111762/download ; EMA website: Applying for orphan designation https://www.ema.europa.eu/en/human-regulatory/research-development/orphan-designation/applying-orphan-designation

ODD Application – Regulatory Procedure – EU



COMP meetings timetable for valid applications
(available on https://www.ema.europa.eu/en/committees/comp/comp-meetings)

Conclusion

ODD status and the related incentives will be key to the viability of your Orphan medicinal product (OMP) program by reducing the R&D costs and leading to a reasonable return on investment. It is a major milestone in your journey to bring the OMP to the patients.

A lot of pharmaceutical companies are outsourcing these activities to a European specialized consultancy in order to :

- Take advantage of European Knowledge & Expertise to optimize EU development and secure compliance
- Secure access to all the incentives you are eligible for
- Ensure your product reaches the patient at the earliest opportunity

Feel free to contact us to discuss how we can help you achieve your European ambition for your orphan medicinal product.

References: Recommended Tips for Creating an Orphan Drug Designation Application - A Webinar by the Office of Orphan Products Development (OOPD) 2018 https://www.fda.gov/media/111762/download ; EMA website: Applying for orphan designation https://www.ema.europa.eu/en/human-regulatory/research-development/orphan-designation/applying-orphan-designation
Procedural advice for orphan medicinal product designation: Guidance for sponsors EMA/420706/2018 Rev. 11 (Sept. 2021) https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/procedural-advice-orphan-medicinal-product-designation-guidance-sponsors_en.pdf

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Any questions? Contact-us!

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