EU orphan drug applications

1. Introduction
To qualify as an orphan drug, a medicinal product must meet certain criteria as laid down in EU Regulation (EC) 141/2000 (Orphan Drug Regulation). Principally, a product will qualify as an orphan drug where the sponsor (= applicant) can show that:

- **The Condition:**
The medicinal product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; and

- **Prevalence or Return on Investment:**
The condition affects no more than five in 10 thousand persons in the Community or alternatively marketing of the product would generate insufficient returns to justify the investment needed for its development; and

- **Satisfactory methods or Significant Benefit:**
There is no satisfactory method for diagnosing, preventing or treating the condition or, if such a method exists, the product will be of significant benefit to those affected by the condition.

2. Why seek orphan drug designation?
Applications for orphan drug designation (ODD) are free of charge. In addition, substantial financial incentives are offered for sponsors to develop drugs for orphan indications, including:

- Ten years of protection from market competition; extended by 2 years for products which have complied with a paediatric investigation plan.
- Fee reductions for regulatory activities including protocol assistance, marketing-authorisation applications (MAA), pre-authorisation inspections, and annual fees.
- Wider access to EU grants to help fund research.
- Wider access to a number of Agency programme including the PRIority MEdicines (PRIME) scheme.

Micro, small and medium-sized enterprises (SMEs) receive additional incentives. These include administrative and procedural assistance from the Agency's SME office as well as free protocol assistance and fee deferrals.

3. When to come for EU ODD
Sponsors can apply for ODD at any time during the product's development cycle but before the application for marketing authorisation is submitted. Many applicants apply as early as during the preclinical development phase.

4. Things to think about when preparing an orphan application
In general, a recognised distinct medical entity is considered a valid orphan condition – different degrees of severity or stages of a disease is not considered a distinct condition and is frequently rejected by the Committee for Orphan Medicinal Products. Sub-setting is generally not permitted.

Prevalence estimates should include data from the EU28 Member States plus Iceland, Norway and Liechtenstein, whenever possible.
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When arguing ‘insufficient return on investment’, all development costs should be taken into account including the cost of early preclinical development, formulation and stability studies and relevant marketing costs.

’Satisfactory methods’ includes both authorised medicinal products as well as those routinely used in clinical practice e.g. surgery, medical devices.

When arguing ‘significant benefit’ it is important to draw on the scientific evidence relevant to the product in question. In general, most applicants argue significant benefit based on potentially greater efficacy, an improved safety profile, and/or more favourable pharmacokinetics.

5. EU orphan procedure
Requests for ODD are reviewed and determined by one of the European Medicines Agency’s (EMA’s) scientific committee’s (i.e. the Committee for Orphan Medicinal Products). In most cases a determination is made within 90 days although rarely, a positive opinion is received after a 60 day review period. All COMP decisions are made public in line with EU transparency provisions.

6. How Emas can help
At Emas, our regulatory team has extensive experience writing and filing orphan applications within the EU on behalf of our clients. We prepare all sections of the application, drawing on data presented in other documents including the product’s Investigator Brochure. We conduct independent research where needed. We thoroughly examine and evaluate all relevant documents, including product information, scientific articles, public-domain information, disease prevalence data, etc.

Key to our success is our ability to quickly understand your product coupled with an ability to advance compelling scientific and clinical arguments. We manage the entire process from beginning to end, leading to successful outcomes in nearly all cases.

Contact one of our experts to find out how we can support you.