Paediatric development is a crucial part of all product development plans, with both US and EU Agencies focused on encouraging paediatric studies in parallel to development in adults. In the EU, an applicant is unable to submit a new licensing application, add a new indication, pharmaceutical form or route of administration for an already approved medicine, without agreeing a paediatric plan or waiver with the European Medicines Agency (EMA) or an EU national regulatory authority.

Applicants are encouraged to engage with the EMA and the Paediatric Committee (PDCO) at an early stage; scientific advice is offered at no charge for questions relating to paediatric development. To facilitate successful validation and assessment, there is also the possibility of having the draft Paediatric Investigation Plan (PIP) reviewed by the PDCO as part of a pre-submission meeting.

PIPs must be submitted no later than the end of healthy subject or patient pharmacokinetic studies, or the initiation of the adult phase-II studies, although many applicants do not meet this deadline.

At Emas, we have experience in developing PIPs in a wide range of conditions. We support paediatric protocol development, drawing on our network of Key Opinion Leaders (KOLs), and work with both the EMA and national regulatory authorities to design paediatric development programs which are both compliant and feasible. Our strategy for waivers and deferrals is designed to keep paediatric studies off the critical submission path for first product approval in the EU.

**Identifying the Condition**

Properly defining the paediatric condition is critical. In defining the condition, reference is made to the proposed indication in adults and/or the authorised (existing) indication, as well as the properties of the medicinal product, unmet paediatric need and a hierarchical classification of diseases / conditions (e.g. MedDRA).

**Class Waivers, Product Specific Waivers or Paediatric Studies**

- **Class Waivers**
  
The need for a paediatric development plan may be waived for some classes of medicines. According to article 11(1) of the Paediatric Regulation (No 1901/2006), a paediatric plan may be waived for classes of medicines if there is evidence showing that: (a) the class of medicinal product is likely to be in-effective or unsafe in children, or: (b) the disease or condition only affects the adult population. The list of class waivers is published on the EMA website.

- **Product-Specific Waivers**
  
  Where a class waiver does not apply, an applicant may be able to argue that a product-specific waiver is appropriate. The article 11(1)(a) and (b) grounds for waiver (see 'Class waivers') also apply here. A further ground for waiver also applies, i.e. that the product does not represent a significant benefit over existing treatments for paediatric patients (Article 11(1)(c) of the Paediatric Regulation).
EU paediatric investigation plans (PIPs) and waivers

NOTE: The grounds for granting a waiver laid down in Article 11(1) are not exhaustive. An additional implicit reason for granting, or not granting, a waiver can be derived from Article 6(2) of the Paediatric Regulation; this relates to whether or not any proposed studies can be expected to be of significant therapeutic benefit to the paediatric population and/or expected to fulfil a therapeutic need of the paediatric population. It may be possible for an applicant to argue that it is impossible (because, for example, the patient population is too small) to design studies in relation to a medicinal product which create the necessary therapeutic benefits in terms of quality, safety, and efficacy.

■ Paediatric Studies
If an applicant is unable to argue that a class or product-specific waiver applies, then the only remaining course is to agree to paediatric studies, however, these can be deferred and arguments presented in support. NOTE: A product-specific waiver may still apply to some paediatric subsets.

■ Benefits / Rewards
The Paediatric Regulation sets up a system of rewards and incentives once a product is authorised for use in paediatric patients. Benefits include:

■ a six-month extension to the supplementary protection certificate (SPC) - in effect, a six-month patent extension on the active moiety
■ an extension of the ten-year period of orphan market exclusivity to twelve years
■ the Paediatric Use Marketing Authorisation (PUMA) offers eight years of data and ten years of market exclusivity to any new off-patent product developed exclusively for use in the paediatric population and can be requested for medicines that are: already authorised; no longer covered by an SPC or patent that qualifies as an SPC; to be exclusively developed for use in children.

■ How can Emas help?
Emas, our regulatory team have extensive experience writing and filing PIP applications within the EU on behalf of our clients. We can write all sections of the application, adapt existing sponsor documents, add our independent research where needed, and provide the required regulatory formats. We will thoroughly evaluate and examine all relevant documents, including product information, scientific articles, public-domain information, disease prevalence data, etc. in order to identify the condition, and advise on whether a waiver or paediatric study (with or without a deferral) is most appropriate. We manage the entire process from beginning to end, leading to successful outcomes in nearly all cases. Key to our success is our ability to quickly understand which pathway works best for your product based on an excellent understanding of national and regional pharmaceutical law and guidelines, coupled with an ability to advance compelling scientific and clinical arguments.

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