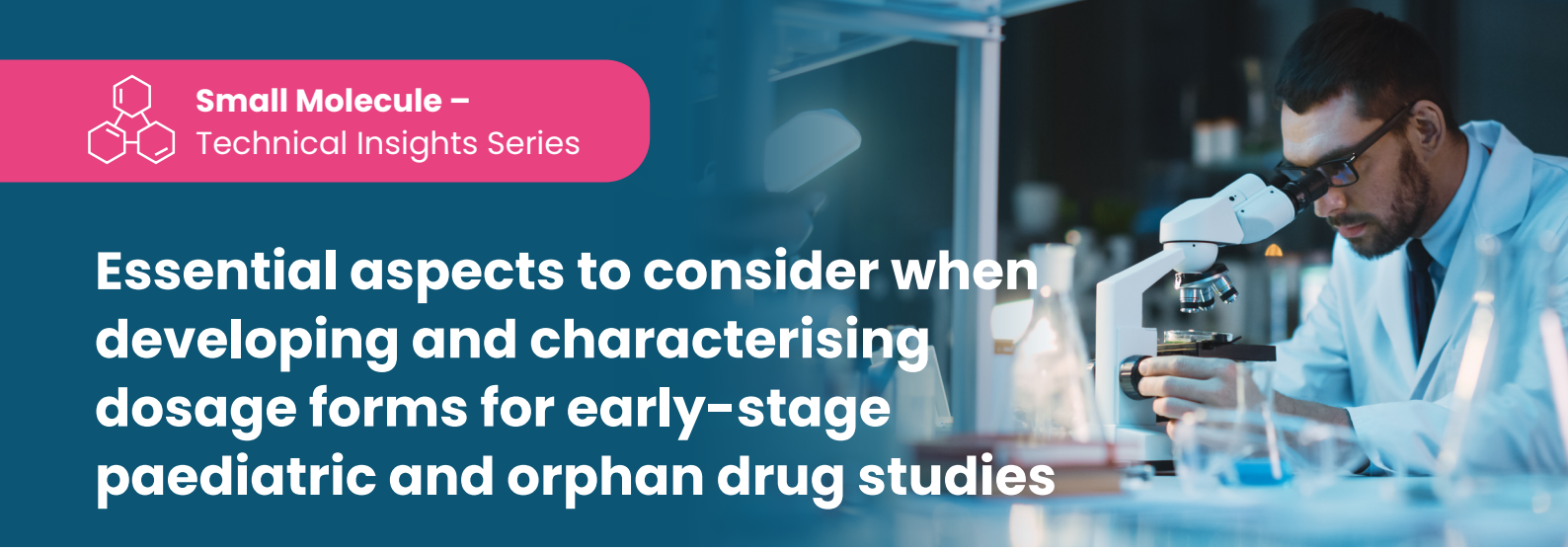
Small Molecule –
Technical Insights Series



Essential aspects to consider when developing and characterising dosage forms for early-stage paediatric and orphan drug studies

Introduction

As part of our small molecule insights interview series, we review the 'essential aspects to consider when developing and characterising dosage forms for early-stage paediatric and orphan drug studies'. Such considerations are essential when outlining a target product profile and planning the scope of development studies necessary to establish formulations for both clinical use and translation towards commercialisation.

This interview with Mandar Paratkar Technical Consultant at SGS CDMO Solutions discusses the challenges involved in small molecule paediatric/orphan drug product development activities, highlighting some of the complexities likely to be faced by companies when embarking on drug product development studies.

With over 15 years of experience in pharmaceutical product development, Mandar specialises in providing strategic guidance to organisations, steering their liquid and semisolid pharmaceutical product development projects through the early phases of clinical trials to successful commercialisation.

Background

Q1. Why do paediatric and orphan drugs require special consideration in dosage form design compared with standard medicines?

Paediatric and orphan drug development differs fundamentally from mainstream medicines because the patient populations are smaller, more heterogeneous, and often more vulnerable. For paediatric patients, developmental physiology, taste preferences, precise and flexible dosing considerations must be incorporated from the outset. For orphan drugs, the rarity of conditions often results in limited clinical data, requiring careful risk–benefit balancing and flexible formulation approaches. In both cases, patient-centricity drives success, meaning safety, acceptability, and practicality of administration are as critical as pharmacological performance.

Paediatric and orphan drug development

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Q2. What are the essential aspects you need to understand about a project from your clients to outline an appropriate development strategy?

To design the right development strategy, we need clarity on the target product profile, the clinical context, and the patient journey. Specifically:

- **Therapeutic indication & unmet needs**
- **Patient demographics** (age ranges, weight bands, comorbidities)
- **Dose range and adjustment needs**
- **Regulatory expectations,** especially for paediatric or orphan pathways
- **Formulation constraints** (API solubility, stability, taste)
- **Clinical trial supply requirements** (batch sizes, timelines). This upfront knowledge enables the tailoring of dosage forms that are both clinically viable and commercially scalable.

Patient-Centric Design

Q3. How do age, body weight, and developmental stage influence dosage form design for paediatric patients?

Each stage of paediatric development presents unique challenges: neonates have immature organ function and swallowing limitations, toddlers resist unpleasant tastes. Dosing flexibility is paramount; liquid formulations, dispersible tablets, or mini-tablets allow accurate titration by weight or age. Safety also requires avoiding harmful excipients, such as certain preservatives or solvents that are otherwise acceptable in adults. Dosage form design must therefore consider flexibility, ease of administration, bioavailability, and excipient safety to ensure efficacy and prevent toxicity in different paediatric subsets.

Q4. Is it possible to generalise about the challenges which orphan drug patients face in terms of formulation and administration?

While the diseases are highly diverse, some commonalities exist. Many orphan drug patients have comorbidities that limit routes of administration, require chronic treatment, and face accessibility issues due to limited distribution networks. The formulations must therefore be robust, stable (ideally with extended shelf life), and easy for non-specialist caregivers to administer reliably.

Q5. Irrespective of patient type, how can the expectations of dosage forms be managed if we consider the needs of patients, caregivers, and clinicians?

Early stakeholder engagement is crucial. Patients and caregivers often prioritise ease of use, palatability, and minimised treatment burden, while clinicians value accurate dosing, compliance, and safety. Aligning these perspectives requires transparent communication of trade-offs; for instance, why a liquid may be more practical despite requiring refrigeration.

At SGS, we are closely integrated with our clinical team, enabling us to gather early and ongoing feedback directly from patients and clinicians.

This feedback loop ensures that formulation development is guided not only by scientific and regulatory requirements but also by real-world usability, ultimately increasing the likelihood of successful adoption in clinical practice.

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Scientific & Technical Considerations

Q6. Palatability is obviously a challenge with administration in ensuring adherence for children, what are your preferred approaches to overcome this issue?

A combination of **taste masking** (using coatings, excipients, or microencapsulation) and **flavour optimisation** is most effective. Selection depends on the physicochemical properties of the API, some bitter compounds may be masked by addition of excipients like sweeteners or taste receptor blockers, others by lipid-based delivery. Pairing sensory science with formulation technology ensures the drug is acceptable without compromising bioavailability.

Q7. What are the main formulation challenges when developing products with small patient populations with rare diseases?

Formulation development for rare diseases is uniquely challenging due to the constraints of working with very limited resources and highly variable patient needs. A few of the key hurdles include:

- **Minimal API availability during early stages —** requiring efficient use of small quantities in pre-clinical development without compromising the robustness of studies.
- **Small-batch GMP manufacture with rapid turnaround** — essential to meet accelerated timelines while supporting early clinical evaluations.
- **Ensuring dose accuracy across diverse patient groups** — particularly where weight- or age-based dosing adjustments are critical.
- **Developing scalable yet adaptable approaches** — strategies must be designed to accommodate both the small populations of early trials and potential future expansion if indications broaden.

Q8. How does limited clinical trial data impact dosage form design for orphan drugs?

Limited data often means higher reliance on modelling and simulation. Dosage forms must therefore remain adaptable, allowing dose adjustments as evidence accumulates. At SGS, we work with the sponsors to design formulations that allow for the potential adjustments and bridging strategies, so clinical insights can be incorporated as evidence grows, while minimising rework and conserving resources.

Q9. How easy is it to develop truly innovative delivery systems to meet the challenges in paediatric delivery?

Developing innovative delivery systems for paediatrics is becoming increasingly achievable as both technology and regulatory pathways evolve. Proven approaches such as mini-tablets and orodispersible tablets are already transforming how medicines are delivered to children by making dosing simpler, more accurate, and more acceptable. These formats allow flexibility across age ranges and weight bands, helping to improve adherence while reducing treatment burden.

At SGS CDMO Solutions, we see strong opportunities to continue building on these advances. Our focus is on designing practical yet innovative dosage forms that can be manufactured efficiently at small scale, adapted as clinical needs evolve, and scaled up when patient access broadens. With greater recognition of patient-centric needs across the industry, the future of paediatric delivery is bright, and innovation is no longer the exception but an expectation.

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Q11. How can developers and manufacturers balance cost, accessibility, and innovation when developing paediatric and orphan drugs?

This balance requires risk-based prioritisation. Essential aspects like safety, stability, and usability cannot be compromised. Innovation should be pursued only if it offers a tangible patient benefit or enables future scalability. Partnerships with patient advocacy groups can also inform decisions to align affordability with access.

Future Directions & Innovation

Q12. What aspects do you find the biggest challenges in developing products for paediatric and orphan drug development? And how would you like these to be addressed over the next few years?

Paediatric and orphan drug development comes with unique challenges: very small batch sizes, complex formulation requirements, and heightened regulatory scrutiny. For paediatrics, ensuring age-appropriate dosage forms and effective taste masking is essential to achieve adherence. For orphan drugs, limited patient populations often bring supply chain and scalability concerns, as well as the need to make the most of minimal API availability.

Looking ahead, we are optimistic. Greater harmonisation of global regulatory frameworks, together with targeted incentives for innovation in paediatric and orphan medicines, could help accelerate progress even further. By combining scientific excellence with agile manufacturing and close collaboration with regulators, industry, and patient communities, we believe the future of paediatric and orphan drug development will be not only faster but also more patient focused.