Global Approaches to Oral Drug Administration Using Enteral Feeding Tubes:
A Review of FDA and EMA Guidance

Enteral feeding tubes (EFTs) are essential to use in cases where patients are unable to swallow oral dosage forms due to conditions such as dysphagia, neurological disorders, or critical illness. While this practice is common, it introduces significant formulation challenges that impact safety, efficacy, and outcomes in both adult and children patient populations.

An article published last year in Advanced Drug Delivery Reviews noted that medicines administered via EFTs to children, in particular, are often not licensed for use via EFTs and therefore subject to manipulation, such as crushing tablets or opening capsules, to administer.[3] This leads to a greater risk of dosing errors, tube blockage, altered bioavailability, and safety issues due to age-specific physiological differences and narrow therapeutic windows. A lack of harmonised global regulatory guidance specific to paediatric EFT administration was also noted.

Pharma and biotech sponsors increasingly need early, data-driven *in vitro* testing to support EFT administration and avoid off-label use, making formulation design and testing strategy critical upstream activities. Draft guidance issued in 2021 from the US Food and Drug Administration (FDA) provided a framework for addressing these challenges, emphasising the importance of systematic testing and clear labelling.1 The FDA guidance was the first regulator-led attempt to formalise expectations for demonstrating whether oral drug products can be administered via EFTs using *in vitro* testing.

While it laid a foundation, the FDA guidance has left much to interpretation. More recently, the European Medicines Agency (EMA) have elaborated on requirements for studies that should be performed to demonstrate feasibility of EFT administration.[2] The January 2026 guidance embeds EFT administration within broader quality and lifecycle management expectations. The EMA's guidance is less exploratory and more operational, signalling that regulators will increasingly expect EFT feasibility to be designed in early drug development and clinical testing, instead of retrofitted later.

As regulations evolve, thoughtful drug product formulation design, excipient choice, and dose flexibility must be built in early and supported by data that demonstrates real-world tube compatibility. In this article, we look at factors involved in properly administering drug products through EFTs, including factors such as:

- Chemical compatibility and integrity
- Interaction with enteral feeding tube materials
- Physical stability and enteral feeding tube patency
- Labelling and instructions for use

Drug Product Chemical Compatibility and Integrity

The administration of drug products can result in interactions with EFTs that lead to possible precipitation or degradation of the drug. To mitigate this, testing across a range of dispersion media, such as water or other vehicles, and pH conditions to confirm chemical stability is required. In addition, the number of flushes and volumes of fluid are also determined to ensure successful delivery of the oral drug product.

For modified release formulations, dissolution assessments may be necessary to ensure the release profile of the drug is as expected. Drug products requiring extended hold times once mixed in dispersion media prior to administration should have microbial assessments to support the intended shelf life; this is crucial in cases when products are held at room temperature for over four hours or refrigerated over 24 hours.

Drug Product Interactions with Enteral Feeding Tube Materials

Adsorption of lipids or active ingredients to tube surfaces can reduce delivered dose. To mitigate this, EFTs are typically made from materials such as polyurethane (for nasogastric use) and silicone (for gastrostomy). These materials are highly resistant to reaction, degradation, and adhesion.

Appropriate testing is performed to confirm the potency, impurity profile and delivered dose of the drug product. It is critical that these tests confirm the absence of interaction with EFT materials to ensure accurate dosing and prevents under-delivery of critical medications.

Quotient Sciences can formulate drug products including solutions, suspensions, minitablets, and sprinkles while considering the requirements to administer via EFTs. We support clients in selecting appropriate EFTs and developing a clear dosing regime for administration in adult, paediatric, or elderly patient populations.

Physical Stability and Enteral Feeding Tube Patency

EFT clogging remains one of the most frequent complications in enteral drug administration. High-viscosity formulations, poorly dispersed particles, or incomplete reconstitution can obstruct narrow tubes.

In vitro testing to evaluate dispersion of the drug product and flowability under "worst-case" conditions, such as small tube diameters across various tube materials, must be conducted. This ensures that oral drug products, when manipulated for enteral administration, maintain physical integrity and do not compromise EFT patency.

Labelling and Instructions for Use

An important aspect of the FDA guidance is its emphasis on labelling. The EMA's latest guidance treats EFT administration as a routine quality consideration, with even clearer expectations for data generation, documentation, and labelling.

Clear, evidence-based instructions for preparation, dispersion, and administration via enteral feeding tubes must be included in product labelling. This reduces reliance on off-label practices and enhances patient safety. Instructions should cover the tube type and size compatibility, the required dilution or dispersion steps, and flushing protocols before and administration.

At Quotient Science, we adopt a risk-based approach, selecting relevant conditions that reflect clinical practice. Through *in vitro* experiments, we assess potency and impurity profiles, determine preparation steps, dilution

requirements, and any incompatibilities to prevent adverse interactions.

Conclusions

Oral drug product delivery via EFTs involves physical, chemical, and microbiological considerations. A regulatory convergence toward proactive, data-driven support of enteral feeding tube administration is happening. While the 2021 FDA guidance remains influential, the EMA has now set a more explicit benchmark, signalling where global regulatory expectations are heading.

Mitigating risks of EFT administration can be accomplished through rigorous in-vitro testing, transparent drug product labelling, and instructions for administration ensures the successful dosing of oral products via EFTs to patients. Sponsors that address challenges proactively, with support of a CDMO that is familiar in best practices in this area, are better positioned to reduce off-label use, improve patient safety, and strengthen regulatory and clinical acceptance of paediatric medicines.

Choosing a CDMO with expertise in risk-based *in vitro* testing, age-appropriate formulation strategies, and device–formulation co-development is critical. Quotient Sciences' approach de-risks development and supports regulatory submissions, understanding that drug products that are supported by robust data enable clearer and differentiated labelling, strengthen our clients' regulatory and commercial position, and ensure patient safety.

REFERENCES

1. Food and Drug Administration (FDA), "Oral Drug Products Administered Via Enteral Feeding Tube: *In Vitro* Testing and Labelling Recommendations" (June 2021)
2. European Medicines Agency (EMA), "Quality of Medicines Questions and Answers: Part 2" (Updated January 2026)
3. Hu S, Nieto González N, Walsh J, Hermans E, Rassu G, Salunke S. Paediatric formulation challenges for enteral feeding tube administration – Current understanding and future directions. Adv Drug Deliv Rev. 2025; 227: 1-17

International Pharmaceutical Industry Journal speaks with Quotient Sciences

How does Quotient Sciences support early-phase drug development when medicines may need to be given through EFT?

Quotient Sciences is a CRDMO integrating drug product formulation, manufacturing, and early clinical testing. We support EFT administration by designing suitable formulations, evaluating tube compatibility and dose clearance, and generating clinical data to meet regulatory expectations. Above all, we work with our customers to understand the goals for their programme, including the target age groups (paediatrics/neonates), dose volumes and the types of EFTs intended to be used in clinical practice, so that we can design relevant *in vitro* studies with the proposed EFTs to assure safe, effective dosing when oral administration is not feasible.

What makes enteral administration particularly challenging from a formulation development perspective?

Enteral administration is challenging because formulations must remain stable and safe when delivered via feeding tubes, avoiding clogging, dose loss, or altered absorption. Variability in tube types, patient physiology, and preparation methods further complicates achieving consistent, reliable drug delivery and regulatory compliance.

What advantages does an integrated CRO/CDMO model offer when developing medicines intended for enteral administration?

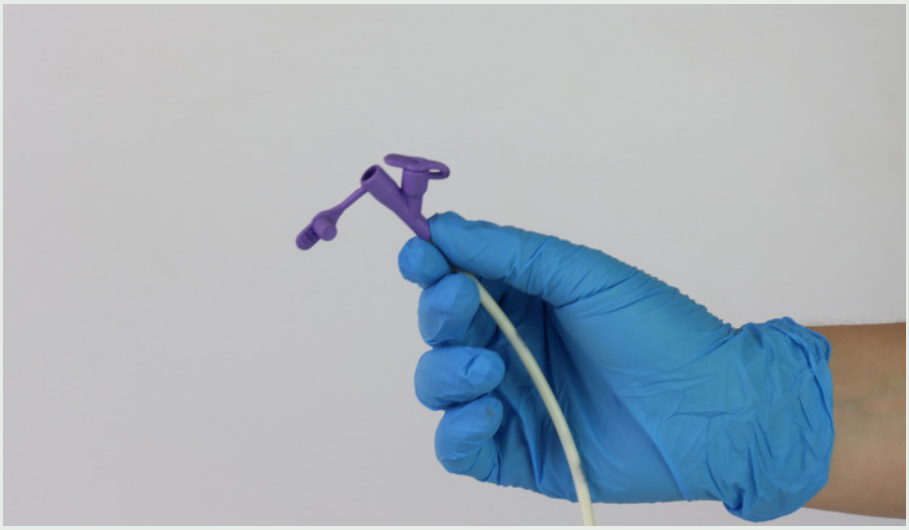
An integrated CRO/CDMO model enables seamless coordination between formulation, manufacturing, and early clinical studies. This allows us to greatly reduce risk and timelines for our clients.

In practice, what types of *in vitro* data are most valuable when assessing suitability for enteral administration?

It is important to ensure that the *in vitro* data collected demonstrates the suitability of a formulation to be adequately administered via EFTs. As such critical *in vitro* data includes confirming the potency of the drug being administered, determining the required number of flushes to deliver the full dose and ensure no blockages, and ensuring compatibility with the EFT from a drug chemical perspective.

Where do you typically see gaps between *in vitro* testing outcomes and real-world administration performance?

There are many variables between *in vitro* testing outcomes and real-world administration



performance which can lead to a sub optimal dosing procedure. Many formulations that are tablets require crushing prior to being used in conjunction with EFTs, and insufficient crushing may lead to blockages or clogging during administration. Changes in the syringe size and void volumes in the syringe tip can affect the accuracy of the dosing procedure, and unfortunately the risk of medication error is significantly higher in patients with EFTs compared to patients without, due to inadequate flushing of the tubes.

In addition, there may be a need to dose certain formulations with vehicles other than water which may not have been assessed as part of the stability and dose clearance *in vitro* studies.

How are evolving FDA and EMA expectations changing the way companies approach enteral administration studies?

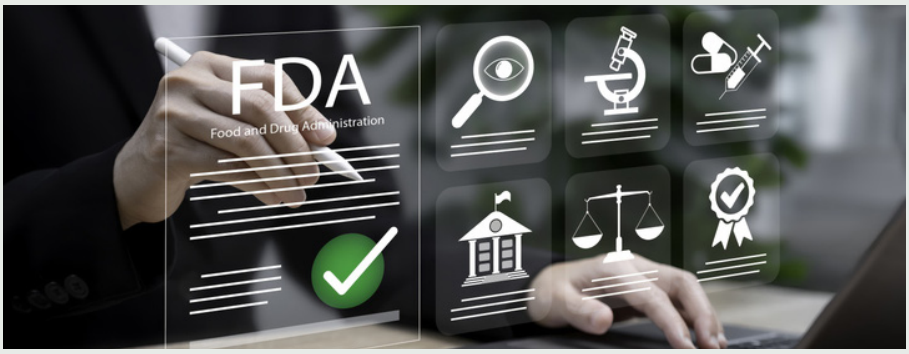
Recently, we see that evolving FDA and EMA expectations are driving more rigorous, clinically relevant enteral administration studies. We expect to see other regulatory bodies follow suit in the years to come. Sponsors must now generate robust data earlier to demonstrate safe, reliable delivery through feeding tubes. This includes more attention being paid to *in vitro* compatibility, dose recovery, and *in vivo* performance.

What formulation characteristics are most difficult to optimise for administration via enteral feeding tubes?

Key challenges include maintaining solubility and physical stability, preventing tube blockage, ensuring accurate dose recovery, and controlling particle size and viscosity. Formulations must also withstand preparation and administration steps without altering bioavailability, making it difficult to balance performance, safety, and consistency for enteral delivery.

Looking ahead, how do you see approaches to enteral administration evolving within early-phase drug development?

The FDA has already signalled a major shift with its draft guidance on "Oral Drug Products Administered via Enteral Feeding tubes", which emphasises consistent testing



methodologies to demonstrate drug product and bioequivalence after tube administration. Going forward harmonisation between the FDA and EMA and the testing requirements is likely.

Drug labels rarely mention tube material to be used or pharmacokinetic impact, therefore going forward risk-based frameworks are likely to be developed that take into account drug physicochemical properties, tube material and geometry, and clinical use scenarios. This would make the *in vitro* testing more efficient, targeted and clinically meaningful.

Finally, what do you think sponsors most value about working with Quotient Sciences?

We often hear that our clients value our ability to integrate formulation development, manufacturing, and early clinical testing within a single programme through our Translational Pharmaceutics® platform. We've applied Translational Pharmaceutics® across more than 500 programmes for nearly 20 years now, as a proven approach integrating activities that a sponsor would traditionally do through working with separate CDMO and CRO partners.

With Translational Pharmaceutics®, sponsors benefit from the ability to generate clinically-relevant data early that helps them make decisions about a programme with greater confidence. That's particularly important for complex delivery routes and dosage forms, like enteral administration but also modified-release dosage forms and oral peptides, which we've often seen.

Generally, though, we are looking to understand and meet a customer wherever they are in development. We bring extensive expertise in drug product formulation, process development, scale-up, and GMP manufacturing as the client progresses into later clinical and commercial development, too. As a molecule progresses from the clinic to commercial, our focus always remains phase-appropriate and on what the customer needs to successfully achieve their next milestone.

Nazim Kanji

Nazim Kanji, Executive Director, Pediatric Services, has more than 25 years of experience in the pharmaceutical and consumer healthcare sectors, spanning product development, formulation, and commercialisation. As a pediatric formulation expert at Quotient Sciences, he supports clients in designing pediatric development programs and advises internal teams. Previously, he co-owned Co-Formulate, acquired by Quotient Sciences in 2015. Nazim holds a Bachelor of Pharmacy from the University of Nottingham.

Justin Holland

Justin Holland, Executive Director, Analytical, has more than 20 years of experience in pharmaceutical testing across all stages of drug product development, from preclinical studies to commercial release. As Head of Analytical Development and Quality Control at Quotient Sciences' Nottingham site, he supports early phase clinical programs. His expertise includes poorly soluble molecules, modified-release formulations, and pediatric drug products. Justin holds an MChem in Chemistry from Nottingham Trent University.