ThermoFisher SCIENTIFIC

TO ERR IS HUMAN, TO CORRECTLY FORMULATE IS DIVINE

RISKY ASSUMPTIONS FOR ADDRESSING LIMITED BIOAVAILABILITY

patheon

- API
- BIOLOGICS
- VIRAL VECTOR SERVICES
- **EARLY & LATE PHASE DEVELOPMENT**
- CLINICAL TRIAL SOLUTIONS
- LOGISTICS SERVICES
- COMMERCIAL MANUFACTURING

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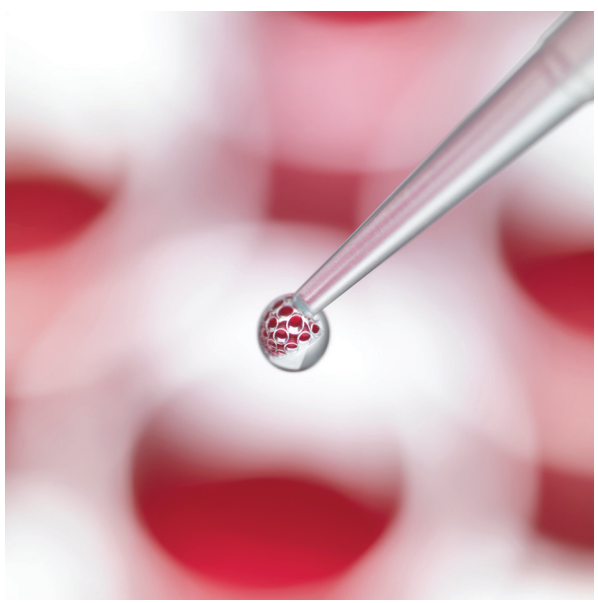
Introduction

Increasing the bioavailability of a poorly soluble drug is a challenging aspect of the drug formulation and development process. Despite best efforts, formulation challenges still need to be overcome.

An estimated 70-90% of molecules experience solubility and bioavailability challenges[1]. Some of these challenges are minor, while others are significant, and can even be detrimental to the successful clinical outcomes and eventual launch of your molecule. How can we best cope with these setbacks?

First, we must recognize and accept bioavailability challenges as an inherent part of the drug development process. Secondly, we must address some common assumptions made during the development stage that can have serious impacts on the timeline and cost of your project.

This eBook is designed to address some risky assumptions surrounding bioavailability issues during development and key ideas to consider for addressing them.



An estimated 70-90% of molecules experience solubility and bioavailability challenges[1].

[1] Source: GlobalData, Pharma Intelligence Center Drug Database

One size (solution) doesn't fit all (challenges)

Assumption you may make: We have managed bioavailability issues before and have solutions to offer

Risks: Relying on a one-size-fits-all mentality risks extended timelines and additional cost

It's critical to understand that not all molecules behave the same way, so approaching bioavailability formulation issues with a "one-size-fits-all" mentality can be detrimental to your timeline and budget. Each molecule needs a tailored strategy and could require different formulation strategies and technologies to ensure a successful outcome. The various steps in formulation enabling solutions include:

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- **In-silico**
  - Computational formulation modeling solutions
- **In-vitro followed by in-vivo**
  - Solid dispersions:
    - Spray drying
    - Holt melt extrusion
    - Amorphous
  - Particle size reduction
    - Spiral jet milling
    - Air jet milling
    - Air classifying milling
    - Pin milling
    - Hammer milling
  - Inclusion complexes
    - Cyclodextrin
  - Self-emulsifying drug delivery system (SEDDS)
    - Oil
    - Surfactant
    - Cosurfactant
  - Lipid-based delivery systems (LBDDS)
    - Self-microemulsifying
  - Lipid-based delivery systems (LBDDS)
    - Self-microemulsifying

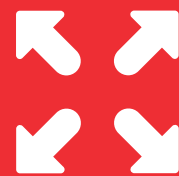
The key to success in early development is employing the right formulation technology that is tailored to each compound's unique properties. This requires a holistic understanding of the molecule–its properties, complexities, and challenges–and building a customized phase-appropriate formulation development strategy that addresses those challenges. Utilizing tailored formulation solutions will enable the molecule to have a quick and seamless transition through the development phases to clinical trials.

Key point

Remember, all molecules are unique–ensure a fast, successful transition from preclinical to clinical by using formulation enabling technologies that are tailored to each compound's unique properties rather than relying on previously successful strategies.

Need help with tailored solutions?

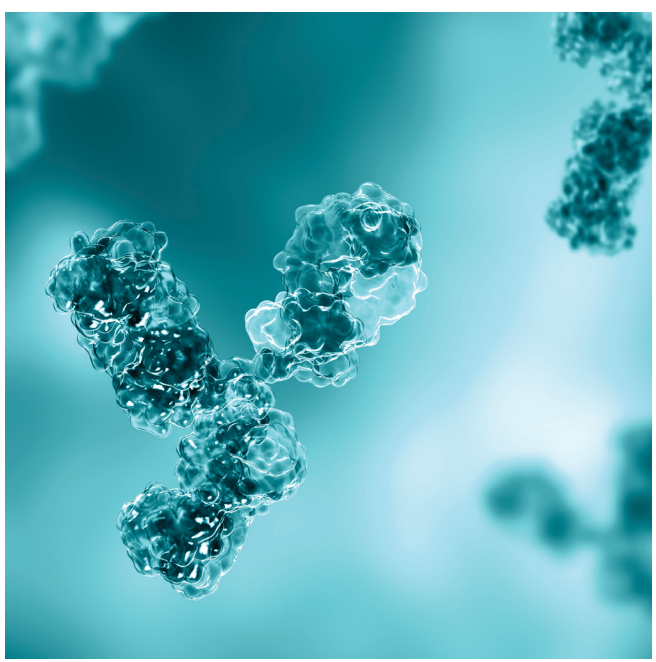
Our industry experts have the specialized technologies and industry experience to develop an optimal process that is tailored to your unique bioavailability challenges.



Understand challenges early

Assumption you may make: I can get to clinical trials faster by not worrying about formulation issues, like bioavailability, until later clinical phases

Risks: Delaying formulation development can derail timelines if you must revise your formulation after Proof of Concept.



Decisions made in early development can have severe implications in later phases that can lead to time-intensive rework and costly delays. Taking shortcuts may be tempting, especially if your molecule looks promising in early development studies, but postponing questions about formulation and manufacturability until formulation steps later in the clinical phases can result in significantly more cost and time added to your project. While aggressive timelines are commonplace in the race to market, time should always be secondary to understanding your molecules challenges early. By delaying formulation testing, you risk developing a drug that needs to be reformulated or even lack clinical efficacy once it reaches human trials - resulting in additional experimentation required to identify a more efficacious formulation.

Computational modeling can dramatically reduce the time and investment often wasted on extensive and unnecessary testing. These in-silico platforms use computer algorithms to select the most effective solubility enhancement for a compound and which excipient should be used for formulation and process development. Utilizing such predictive tools can help you understand your molecules challenges early on while minimizing experimental effort, saving time, and valuable API during product development. But be aware, not all computational modeling solutions are created equal. When vetting a partner for formulation modeling, ensure their platform can provide the highest degree of accuracy needed for a successful formulation.

Key point

Avoid the tedious and costly trial-and-error approach to formulation testing by using in-silico models that can predict the most optimal solubility enhancement technology and excipient combination that are most likely to succeed.

Interested in utilizing computational modeling?

Thermo Fisher Scientific can complete computational modeling in as little as two weeks. Our Quadrant 2® technology selection tool is more than 90% accurate and the Quadrant 2® excipient selection tool is more than 80% accurate.

Focus is key

Assumption you may make: We have a small team that manages all aspects of our projects. We can focus on formulation issues as they arise.

Risks: Limited in-house resources may not have the necessary expertise, experience, and time to properly focus on issues that arise during drug development

Outsourcing offers drug sponsors a variety of benefits including having access to a global network of cGMP facilities and highly skilled experts in a variety of fields.

Drug sponsors maintaining a small team tend to juggle multiple responsibilities at once. Key challenges often faced with limited resources are lack of time and insufficient expertise in key disciplines needed to adequately address critical issues that occur during drug development.

This disadvantage can derail timelines and create disastrous setbacks on the path to commercialization – driving more drug sponsors to outsource all or part of their projects to a CDMO. In 2021 alone, 46% of newly developed drugs were outsourced to CDMOs.

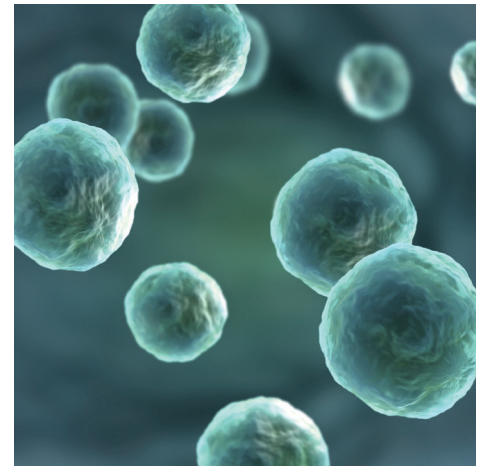
Outsourcing offers drug sponsors a variety of benefits including having access to a global network of cGMP facilities and highly skilled experts in a variety of fields. Access to such a broad range of industry knowledge and capabilities makes it easier for a project to go smoothly through the development stages, enabling faster market entry.

However, when considering outsourcing a project it is critical to weigh the pros and cons of a single source vs multi-vendor approach. For drug sponsors who lack experience managing CDMO relationships, a single vendor who can provide expertise across a range of services can simplify the process. The entire project journey can be easily managed and if there is a delay in one phase because timelines can be easily adjusted to stay on track. Additionally, partnering with a single CDMO early allows for seamless transition into later stages of drug commercialization when scale up, packaging, and distribution services are needed. This gets more complicated with a multi-vendor approach where the drug developers must communicate with and adjust timelines across multiple outsourced partners to keep the project on track.

Key point

Keep the bigger picture of drug development in mind and consider freeing up your limited in-house resources and simplifying the process by outsourcing to a CDMO who can manage every aspect of your drug development journey from development to commercialization.

Conclusion



Finding a safe and effective compound to bring to market is challenging and costly enough – avoid risking additional expense, be it time or money, by not making these assumptions about the importance of a well planned and executed formulation development strategy. Whether you're just starting out with drug development or are an industry veteran, being aware of your strengths and limitations when it comes to the formulation and manufacturability of your molecule can prevent serious delays before they become long-term issues affecting your entry to market.

Remember these key points when addressing formulation issues regarding your molecule's bioavailability

One size (solution) doesn't fit all (challenges)

Tailoring your formulation strategies to each molecule reduces the risk of rework and lost time.

Understand challenges early

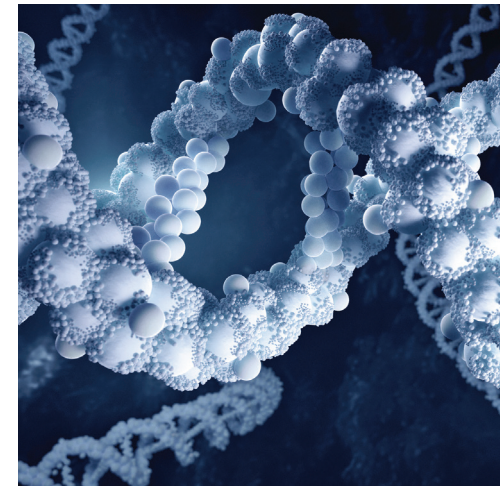
Utilizing a highly accurate computational modeling platform–such as Quadrant 2–quickly identifies the optimal solubility enhancement technology for your molecule.

Focus is key

Partnering with an experienced CDMO preserves both your internal resources and timelines.

About Thermo Fisher Scientific

Thermo Fisher Scientific Inc. (NYSE: TMO) is the world leader in serving science, with annual revenue exceeding $25 billion. Our Mission is to enable our customers to make the world healthier, cleaner and safer. Whether our customers are accelerating life sciences research, solving complex analytical challenges, improving patient diagnostics and therapies or increasing productivity in their laboratories, we are here to support them. Our global team of more than 75,000 colleagues delivers an unrivaled combination of innovative technologies, purchasing convenience and pharmaceutical services through our industry-leading brands, including Thermo Scientific, Applied Biosystems, Invitrogen, Fisher Scientific, Unity Lab Services and Patheon.



About Patheon

Thermo Fisher Scientific provides industry-leading solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With unwavering commitment to service, science and process engineering, our clinical services team is powered by people with an exceptional commitment to quality and unrivaled expertise. We are exclusively focused on serving the packaging and distribution requirements of clinical trials across the world. Whether planning, packaging, labeling,storing, or distributing the important supplies needed to perform clinical research, we are committed to delivering the highest level of quality, performance, reliability and sustainability standards through our Patheon Fisher Clinical Services[SM] offerings.

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 40 locations around the world, the company can provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vector services, early development, clinical trials solutions, logistics services and commercial manufacturing. We give all sizes of pharma and biotech companies instant access to a fully integrated global network of facilities across North America, Europe, Asia and Australia. Our global leadership is built on a reputation for scientific and technical excellence. This includes specialized capabilities for highly potent and controlled substances, aseptic filling and lyophilization, complex formulations, solubility enhancementand difficult-to-manufacture APIs. We also offer integrated services for drug development that aligns development of drug substance and drug product in a coordinated drive toward proof of concept that can reduce development timelines. We have more than 17,000 scientific and professional staff and over 40 years of experience. As a leading global CDMO, we deliver unrivaled quality, reliability and compliance. Together with our clients, we're rapidly turning pharmaceutical possibilities into realities. Contact us to discuss your upcoming development or manufacturing project with our experts.

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