

A scientist in a white lab coat and safety glasses is working in a laboratory. He is using a pipette to transfer liquid into a multi-well plate. The background shows various laboratory equipment and shelves. The image has a blue tint.

Recipharm

A CONNECTED APPROACH
TO **OSD DEVELOPMENT**

Introduction

Executive summary

Successful oral solid dose (OSD) development depends on decisions that extend far beyond the immediate formulation objective. Choices made during development can shape analytical requirements and influence process robustness, scalability and readiness for commercial manufacturing. Consequently, when each stage is considered separately, risks may remain

hidden until later in the programme, increasing the potential for additional development work or delays.

By building greater continuity across development, teams can anticipate downstream requirements, make better-informed technical decisions and maintain momentum towards key milestones.

This eBook explores where risks can arise during OSD development and how greater coordination between

activities can help developers address challenges earlier and reduce uncertainty as a product progresses. It also examines how development partners can integrate formulation and process development with analytical and manufacturing expertise to overcome capacity constraints and accelerate progress, while maintaining continuity through regulatory filing and technology transfer to commercial supply.



Sections

1. Connecting science, process and manufacturing in OSD development
2. Building a science-led approach to connected OSD development
3. Recipharm Development: Progress your OSD product with greater confidence



Section 1

Connecting science, process and manufacturing in OSD development

OSD forms, particularly tablets and capsules, remain among the most established and widely used formats in pharmaceutical development. However, developing a robust OSD product requires increasingly integrated decision-making as developers navigate complex active pharmaceutical ingredients (APIs), more demanding product profiles and formulations that require tighter control of product and process performance. Poor aqueous solubility alone now affects ~70% of new chemical entities entering development¹.

Alongside these technical demands, OSD developers face growing pressure to shorten development timelines and progress products towards commercial manufacture at speed, driven by the need to reach patients sooner and maximise the commercial opportunity for new products.

Maintaining this pace depends on optimising individual development activities and recognising how they influence one another. Decisions made during formulation development, for example, can affect material requirements and downstream processes, as well as the analytical and stability studies needed to support the programme.

These interdependencies can be seen in several areas:

- ▶ Formulation decisions can influence product performance and determine the requirements for later manufacturing processes.
- ▶ Variability in API and excipient properties can affect how consistently the formulation performs and how robustly the process operates.
- ▶ Process parameters and equipment characteristics can influence material behaviour and product quality, making it important to understand which variables need to be controlled as the process is developed and scaled.
- ▶ Analytical methods need to provide the data required to guide formulation and process development while remaining suitable for later validation and transfer.
- ▶ Stability data can identify changes in product quality that require formulation, process or packaging decisions to be revisited.

These dependencies highlight why OSD development is best approached as a connected development pathway, where scientific understanding generated at each stage informs the decisions that follow.

Potential consequences when development risks are identified too late

- ▶ Repeated development iterations
- ▶ Late identification of technical issues
- ▶ Difficult analytical or technology transfer
- ▶ Delays to filing or commercialisation
- ▶ Increased development costs and resource requirements
- ▶ Potential conflicts with the selected clinical strategy
- ▶ Additional pressure on internal development teams



1. Kumari, Lakshmi et al. "Advancement in Solubilization Approaches: A Step towards Bioavailability Enhancement of Poorly Soluble Drugs." *Life (Basel, Switzerland)* vol. 13,5 1099. 27 Apr. 2023, doi:10.3390/life13051099.

Section 1. Connecting science, process and manufacturing in OSD development

Building a thorough understanding of these relationships during development is therefore critical, allowing teams to identify the variables most likely to affect performance and establish appropriate controls before moving to larger-scale equipment. Material characterisation, process knowledge and targeted experimental data can be used together to build this understanding and anticipate how the formulation and process may respond as conditions change.

How can OSD developers reduce downstream development risk?

Reducing the risk of technical issues emerging during scale-up, transfer or preparation for commercial manufacture requires early consideration of later-stage requirements, which must continue throughout development.

Development programmes need to be formed with an understanding of the impact of formulation and process on quality attributes, and with consideration of later-stage requirements from the outset, including:

- ▶ Product and process robustness
- ▶ Material variability
- ▶ Scale-up requirements
- ▶ Equipment differences
- ▶ Analytical and QC readiness
- ▶ Stability and filing requirements
- ▶ Future manufacturing needs

However, managing these considerations in isolation can make it harder to understand how a decision in one area may affect another.

A connected, science-led approach brings formulation, analytical, process and manufacturing considerations together, allowing knowledge generated throughout development to inform subsequent decisions and remain available as the programme progresses.

Building knowledge around critical material attributes (CMAs), critical process parameters (CPPs) and critical quality attributes (CQAs) is an important part of this approach. Understanding the relationships between materials, processing conditions and product quality can help OSD developers identify potential risks earlier and make more informed decisions as the process is refined and scaled. Maintaining this continuity of product and process knowledge can also support later scale-up, technology transfer and commercial manufacture.

“A more connected, science-led approach allows teams to identify risks earlier, retain product knowledge as the programme progresses and develop with scale-up, transfer and commercial manufacture in mind.”

Section 2

Building a science-led approach to connected OSD development

A science-led OSD development strategy should build product and process understanding early, then use that knowledge to guide decisions across formulation, analytical development, scale-up, filing and transfer. This approach also considers how the programme will be resourced, including where external capacity or specialist expertise can add value.

Predictive development provides the scientific foundation for a science-led OSD development strategy. By identifying and modelling potential sources of variability, teams can anticipate how formulations and processes are likely to perform under defined conditions and focus experimental work where it is most informative. Targeted experimental studies can then test those predictions against measured results, using the evidence to verify or refine the underlying models and progressively strengthen product and process understanding. This creates a more informed basis for development decisions and helps reduce uncertainty as the product moves towards scale-up and commercial manufacture.



Section 2. Building a science-led approach to connected OSD development

Figure 1. The predictive development cycle

1. Define CQAs based on quality target product profile
2. Link raw material attributes to CQAs and perform an initial RA
3. Define manufacturing process. (Link process parameters from each unit operation to CQAs RA)
4. Define appropriate CQA test method
5. Define mathematical model for manufacturing process
6. Define mathematical model for analytical test method
7. Initial risk assessment based on models to identify CPPs

8. Performing tech-trails
 9. Analyse IPO (input — process — output)
 10. Compare predicted results with measured
 11. Identify all relevant sources of variability
 12. Verify or update model for manufacturing and analytics (including power-sample size calculation)
- Iteration loop until predictable model is found**

Design of Experiments (DOE) is a systematic approach used to:

- ▶ Understand relationships between process inputs and outputs
- ▶ Evaluate the effects and interactions of multiple factors
- ▶ Develop predictive models
- ▶ Optimise process performance

Section 2. Building a science-led approach to connected OSD development

Building product and process understanding early gives development teams a stronger basis for decisions across the wider programme. Filing and commercial requirements can clarify what evidence and controls need to be established, with early insight into material and process behaviour also helping to inform preparation for changes in scale, equipment and operating conditions. Programme resourcing can also be planned around anticipated needs, with external capacity or specialist expertise added where internal resources are constrained.

The following five steps show how OSD developers can apply this science-led approach across formulation, analytics, filing, scale-up and programme resourcing.

1. Develop formulations with manufacturability in mind

Developing a successful OSD formulation requires teams to achieve the target product profile (TPP) while considering how the formulation will perform during manufacture. API and excipient characteristics, material behaviour and processing conditions can all influence how reliably the formulation performs, with limited API availability and specific release requirements potentially placing further constraints on development.

A science-led formulation strategy accounts for future manufacturing requirements from the outset. Starting with the TPP, teams should define the formulation and process characteristics needed to achieve the required performance and identify potential sources of variability in the materials, formulation and process early in development.

Quality by Design (QbD) principles can provide a framework for building this understanding systematically. Material characterisation and existing process knowledge can help determine which inputs are most likely to influence process performance and product quality, providing the basis for predictive, data-driven development.

These models can be used to assess expected formulation and process performance under defined conditions and identify areas requiring further investigation. Targeted experimental studies generate data that can be compared with model predictions to verify or refine the model and guide further experiments towards resolving the remaining uncertainties. This iterative approach helps build confidence in formulation and process performance and supports more informed scale-up and manufacturing decisions.



Section 2. Building a science-led approach to connected OSD development

2. Use analytical insight to guide development decisions

Analytical development is fundamental to building product and process understanding throughout OSD development. Dissolution behaviour, impurity profiles, stability performance and other analytical data provide evidence of whether a formulation or process is performing as intended. It also supports teams in identifying how formulation composition, material attributes and processing conditions influence critical quality attributes (CQAs). For generic programmes, this understanding can also help teams assess potential bioequivalence (BE) risks, identify critical variables and determine where further formulation, process or analytical investigation may be required. When analytical data are integrated with formulation and process knowledge, they can support earlier, more informed development decisions and reduce uncertainty as the product progresses towards scale-up and regulatory submission.

When analytical work is treated primarily as a testing function, much of that insight can be lost. An unexpected result may show that a product has moved outside the expected parameters; understanding the underlying cause requires analytical evidence to be considered

alongside formulation and process knowledge. Without that connection, investigations can take longer, development decisions may be delayed additional testing or development work may be required.

Problems can also arise if analytical methods are developed only around the immediate needs of the programme, without considering what will be required at later stages. A method that is suitable for a development study may require significant optimisation before it can be validated or transferred into a QC environment. Identifying these requirements early can minimise rework and help avoid delays to technology transfer, regulatory submission and commercial readiness.

Turning analytical evidence into development insight

A science-led analytical strategy integrates analytical activities with formulation and process development so that measured data can build understanding of how material attributes and process parameters influence product quality and performance. Rather than waiting for an unexpected result to determine what needs to be investigated, the predictive development cycle allows teams to identify potential sources of variability and assess their likely impact before targeted experimental work begins.

Developers can then compare measured analytical data with predicted outcomes to challenge and refine the underlying understanding. Where differences remain, further targeted studies can refine and assess the underlying model, progressively strengthening understanding of the formulation and manufacturing process. This iterative approach helps focus analytical and experimental effort where it can provide the greatest development value, while reducing uncertainty as the product progresses towards scale-up and commercial manufacture.



Section 2. Building a science-led approach to connected OSD development

3. Keep filing and commercial requirements in view

Development work also needs to prepare the product for filing and registration, and, where applicable, commercial manufacture. Gaps in stability data, analytical readiness or registration-batch planning can delay filing, and insufficient process robustness or documentation can make technology transfer more difficult.

Managing these requirements can become increasingly challenging when development activities are spread across multiple suppliers or teams. Each additional handoff creates another point where product and process knowledge must be transferred and where responsibilities, timelines and technical decisions need to remain aligned. Maintaining continuity across these activities can reduce information gaps, minimise rework and support a smoother transition from development through filing, technology transfer and commercial manufacture.

Plan backwards from key milestones

A practical way to manage this is to define what needs to be in place for filing, registration batch manufacture and technology transfer, then use these requirements to inform the development plan. This can help establish when

stability data will be needed, when analytical methods need to be validated and when the process needs to reach the required level of robustness.

Regular 'readiness reviews' can be used to assess progress against these requirements and identify outstanding activities before they affect the critical path. For programmes involving multiple suppliers, they can also establish clear ownership of remaining activities and confirm that the required data and documentation will be available for the next milestone.

Taking this approach gives OSD developers a clearer view of whether the programme is genuinely ready to progress and where further work is required before committing to filing, registration batches or transfer.

4. Build scale-up and transfer readiness into development

A process that performs reliably during development cannot be assumed to behave the same way at a larger scale. Changes in batch size and equipment can alter mixing, granulation, feeding and compression conditions. Material behaviour that appears consistent at development scale may change within a commercial manufacturing environment. These scale-dependent

effects can influence critical process parameters and product quality, meaning variability sources less apparent during early development may become more significant during scale-up.

Building scale-up considerations into development from the outset helps teams identify these risks earlier, establish appropriate process understanding and generate the knowledge needed for a more predictable transition to commercial manufacturing.

Considering scale-up only once development is substantially complete can limit the options available to address these issues, with teams possibly needing to adjust process parameters or conduct additional development work. More significant problems may require aspects of the formulation itself to be revisited. Addressing scale-up risks earlier can help reduce rework and preserve more options for optimisation.



Section 2. Building a science-led approach to connected OSD development

Preparing for scale-up during development requires teams to understand why a process performs successfully at its current scale and which aspects must remain controlled as scale, equipment and operating conditions change. Bringing formulation, analytical, process development and manufacturing expertise together can help teams identify scale-sensitive aspects of the product and process, anticipate potential challenges and determine where further development or process understanding is required before transfer.

Preparing for scale-up and transfer requires consideration of:

- ▶ CMAs
- ▶ CPPs
- ▶ CQAs
- ▶ Equipment requirements
- ▶ Batch scale
- ▶ Process operating ranges
- ▶ QC method readiness
- ▶ Transfer documentation

Building this understanding throughout development allows process robustness to be established before validation or manufacturing, rather than discovering the limits of the process once the product has already progressed.

Carrying scientific knowledge into technology transfer

Technology transfer introduces an additional consideration when development and manufacturing are handled by different teams or organisations. Successful transfer depends on transferring the scientific knowledge behind the process alongside the process itself, so the receiving manufacturing team understands what has been investigated, what has been learned and where important sources of variability lie.

When development and future manufacturing capabilities are connected, this knowledge can remain within the wider programme as the product progresses. The manufacturing team receives the process rationale alongside the operating instructions, providing greater context around the parameters that influence performance and the controls established during development. Maintaining that continuity can support a more predictable technology transfer and give teams greater confidence as the product progresses towards larger-scale manufacture.



Section 2. Building a science-led approach to connected OSD development



5. Match external support to the needs of the programme

Even companies with strong internal development capabilities may not have the resources or specialist expertise available for every programme. Large generic and pharmaceutical companies, for example, can have extensive portfolios competing for the same scientists, laboratory space and equipment. Smaller biotech companies may operate with leaner internal teams, while particular NCE or 505(b)(2) programmes may require specialist formulation, analytical or manufacturing expertise at specific stages.

External development support should address specific gaps in a programme's capacity or expertise. Clearly defining these requirements helps establish the scope of the partnership, allowing internal teams to retain programme ownership and focus their resources where they are most needed.

A development partner should act as a flexible extension of the internal team, with support adapted as programme needs change. This may include:

- ▶ Overflow development capacity
- ▶ Support for priority or time-sensitive products
- ▶ Specialist formulation and analytical problem-solving
- ▶ Reverse engineering and reference-product characterisation
- ▶ BE and filing-readiness support
- ▶ Clinical or registration batches
- ▶ Technology-transfer and commercial pathway planning

The scope of support should also be able to change as the programme progresses. A partner may initially address a specific capacity or technical need, then provide additional support at later stages where required, including technology transfer and manufacturing. This allows companies to access the right level of support at each stage without committing to unnecessary services or introducing additional suppliers.

Section 3

Recipharm Development: Progress your OSD product with greater confidence

Reducing development and transfer risk requires formulation, analytical and manufacturing considerations to remain connected, with the scientific expertise and capacity to address issues as they arise.

Recipharm Development applies this connected approach to small-molecule OSD products, bringing formulation and analytical process and manufacturing expertise together to build product and process understanding throughout development. As the programme advances, the same development pathway can incorporate stability and specialist testing, clinical or registration batch support and technology transfer, with access to commercial OSD manufacturing through the wider Recipharm network when required.

Support is shaped around each customer and programme. Teams can draw on Recipharm for targeted scientific expertise, additional development capacity or broader programme support, with direct access to the specialists carrying out the work. This gives customers the flexibility to complement their internal teams and maintain scientific continuity as the product progresses towards commercial manufacture.

Supporting different OSD development pathways

► Generic and portfolio programmes

For generic and portfolio programmes, Recipharm Development can act as a flexible extension of internal R&D, providing overflow or priority-product support, reverse engineering and reference-product characterisation, specialist formulation and analytical development and registration-batch support. Its predictive development approach is designed to improve efficiency through smart modelling and targeted experimental work, with the current generic offering including development timelines up to 12 weeks faster, lower API consumption and greater than 90% BE prediction success. The offering also includes a commercial commitment linked to BE prediction, with repeat

development work covered at no additional cost if the agreed BE prediction is unsuccessful. Technology transfer and commercial manufacturing can then provide continuity for suitable products as they move towards launch.

► OSD NCE and 505(b)(2) programmes

For selected OSD NCE and 505(b)(2) programmes, support can begin with early formulation and process development and extend through analytical and stability activities, clinical or registration batches and manufacturability assessment. Scale-up, technology transfer and future commercial requirements can then be incorporated as the product advances, creating a clearer pathway towards commercial supply.

Discuss your OSD development programme

Speak with Recipharm about additional portfolio capacity, specialist formulation or analytical support, and a connected development-to-commercial pathway. [Contact us today](#)



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