THE CLINICAL MANUFACTURING CHECKLIST

6 STEPS

to build a smart clinical filling strategy

How to plan an efficient, successful transition from preclinical to clinical development —with fewer roadblocks along the way.

VETTER

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Get your product to the clinic with confidence

The shift from preclinical to clinical development is a critical step in the development of your drug product.

During this transition, you not only have to significantly upscale production of your product, but also make many new strategic decisions that will lay important groundwork for your regulatory submission, commercial production of your product, and many other key components of your product's life cycle.

This eBook will help you build a plan that not only streamlines your product's path to the clinic but also sets you up for long-term development and market success - starting with a proven 6-step process for filling your critical clinical batch.

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6 KEY STEPS

The Clinical Manufacturing Checklist

Developed by Vetter's team of clinical development experts, this thorough approach has been used on more than 200 drug candidates across a wide range of substance classes and therapeutic areas.

Follow these 6 steps and your team will be ready to:

- Rapidly and efficiently scale production of your API
- Proactively address potential logistic, technical, and regulatory hurdles
- Identify the right CDMO partner to help you shift to the clinic

Key takeaways

Early planning makes all the difference

The decisions you make early in the process can have a significant downstream impact on your product's development. Make sure you're armed with the information you need to take smart actions that set you up for success going forward.

Continual communication is key

As your product's development advances, it's vital you have a clear chain of communication and a dedicated internal point person who can triage questions. That will eliminate roadblocks and make sure that all your internal teams and external partners stay in alignment.

Your processes are as important as your product

As you scale production of your API, establishing and documenting rigorous production methodology becomes a vital part of your product's development. Here's where implementing clear strategies and robust processes will facilitate highest possible quality in your clinical batch, as well as a strong regulatory foundation.

The right CDMO partner is a vital asset

Bringing in the right manufacturing partner - someone with deep expertise and a proven track record - will help you navigate the process, avoid unforeseen challenges, and pave the path to success.

STEP 1

Create a proactive plan

Create a clear, honest game plan that includes everything that could impact your ability to hit key trial and regulatory dates.

Have a realistic timeline

Your plan should be realistic and account for every factor that could impact your ability to hit key trial and regulatory dates like:

- Product complexity
- Required development work
- Potential risks and delays

Get regulatory guidance on your development approach

Reach out to the relevant authorities for advice on what to plan for in your product's first in-human studies so they can provide advanced guidance on:

- Filling process and timelines
- Submission requirements
- Quality parameters

Assess your clinical manufacturing needs

Confirm your team has the knowledge, resources, and support they need to scale up the production of your compound, especially:

- Compliance with good manufacturing practice
- Small-scale study results

Know your API and formulation

Make sure your team has a detailed understanding of your API and how it's produced, including:

- Your current formulation and its requirements
- Any precursors or excipients needed
- Any special physical properties or sensitivities

Map out your supply chain

Determine what resources you need and the external partners involved in obtaining them. Have clear answers to the following questions:

- Will you need any hard-to-obtain components?
- Who will you rely on to secure supply?
- What are the logistical complexities involved?

STEP 2

Select and source your primary packaging and raw materials

Stay on-schedule by identifying exactly what components you'll need now and in the future—and where and how you'll obtain them.

Understand your primary packaging options at the start

Selecting the packaging for your clinical batch is a key strategic decision in your product's life cycle. Consider critical factors such as:

- Will my product launch in a vial, syringe, or cartridge?
- Will my product need to transition to a pen or autoinjector?
- Do we need to start planning for an advanced delivery system?

Confirm materials sourcing with your CDMO

Consult with your manufacturing partner to determine the best ways to obtain the raw materials for your API and packaging. Work with them to get answers to questions such as:

- Which cGMP qualified components will they need?
- Will scaling your API product pose any sourcing or logistical challenges?

Account for all sourcing requirements

Some materials may be more challenging or time-consuming to source. You and your CDMO will need to assess the time it will take to assemble all the resources you need to fill your clinical run.

- Are you importing any of your API components?
- Do you need to export your API for manufacturing?
- What will customs wait times be? Will any materials require special clearance?

Determine whether your product may need an injection device

Will you eventually need to shift your product to an auto-injector, pen, or similar delivery device? Knowing that will help determine:

- Appropriate selection of primary packaging material
- A more efficient transition between phases of your product's life cycle
- Increase attractiveness for patients and provide a competitive advantage

STEP 3

Finalize all scopes and contracts

Ensure that your suppliers and external resources are all aligned on your team's expectations and their responsibilities in the clinical filling process.

Build in time for multiple partners

Filling a clinical batch is a collaborative, multidisciplinary process that can involve multiple internal teams and external partners. Plan for the time it takes for them all to work through contracts, establish lines of communication, and align workstreams. Finalizing these later steals time and attention from more valuable production work.

Specify the scope of work

Before beginning the filling process, thoroughly discuss and document exactly what each supplier and partner will deliver. Even small misunderstandings here can add up to potentially big delays and cost overruns later.

Plan for audits

Regulatory authorities routinely request opportunities to inspect facilities, examine processes, and assess both your and your partners' compliance. Book the resources you need in advance to avoid manufacturing delays. A surprise audit can throw everything off course, pushing back crucial deadlines and adding unnecessary costs.

Secure quality agreements

Make sure everyone knows which cGMP responsibilities are whose. Start by establishing clear communications between your quality organization and your partners' to promote openness and transparency going forward.

Put all your service contracts in place

Make sure all your partners are clear on your business objectives and the know-how they need to work together. This provides a single source of truth and will help you handle any issues that arise.

STEP 4

Implement good development best practices

Confirm your filling strategy includes a robust process development approach, data capture and sharing methods, and standardized knowledge transfer procedures.

Align your production processes with relevant guidelines

Ensure they all conform to ICH Q8/Q9/Q10 to protect quality and transferability. Effective, consistent implementation of these guidelines will streamline both your clinical filling run and your future transition to commercial filling facilities and processes.

Leverage quality by design methodology

Build quality into your product by defining Critical Quality Attributes (CQAs) and Critical Process Parameters (CPPs) at the beginning of your filling project. Clearly establishing these key factors in your product's quality profile will help ensure consistent adherence to shared development targets across your teams and partners.

Know where you need more data

Identify any attributes of your product or process that need further evaluation and measurement before you scale production. An early understanding of your needs allows you to address them sooner and find proactive solutions before you begin your clinical batch fill.

Know what to share with your CDMO

Identify the product, process, and quality data that your CDMO will need to start your clinical run, and when they'll need that information. Delivering the right information at the right time will help your manufacturing partner confirm filling processes, equipment, and analytics are appropriately optimized for your product.

Map your analytical method transfer

Put robust standard operating procedures (SOPs) in place to confirm your partners' analytical methods are consistent with yours. Ensure you are both using aligned approaches to validating all inputs and outputs, including bulk solutions, in-process materials, and finished products

STEP 5

Align with cGMP across your teams and partners

As your team begins to start the clinical manufacturing process, ensure everyone involved is clear on the quality practices they need to follow.

Know how much API you need

Make sure you have enough product for your clinical sites by accounting for typical manufacturing factors like:

- Line losses
- Filling overages
- Typical rejection rates
- Destructive sampling

Factor in technical runs

Before filling your clinical batch, your CDMO will want to confirm all filling processes have been thoroughly tested, optimized for efficiency, and evaluated for quality. This involves initial technical runs to determine elements like mixing parameters and fill volume tolerance.

Determine processing times

Work with your CDMO to understand their cycle times and how long they'll require to execute your clinical filling run. Your product's stability at different temperatures is a key consideration at this point. Always verify that it will maintain its stability throughout the filling process under the manufacturing conditions that will be required.

Specify batch release times

Once your clinical batch has been filled, any delay in delivery to your trial site can become extremely costly. Work with your CDMO to get answers to questions like:

- How long will it take to release a clinical batch to trial sites?
- What resources and documentation are involved in releasing the batch?

Consider the future impact of frozen formulations

Frozen vials can be a quick, efficient clinical filling solution, but the complex storage and shipping processes they require can also become burdensome once you scale up to commercial manufacturing. Consider whether reformulating or lyophilizing your product now may be a smarter long-term approach.

STEP 6

Select the right CDMO partner

Bring in the right manufacturing partner to help you achieve your goals and pave the path to success.

How to know your CDMO meets your needs

The right CDMO partner will have the right combination of know-how, technical capabilities, and resources. To find that partner, see how their answers align to these questions:

- Can they safely handle your compound?
- Do they have experience handling your specific product type?
- Do they have a Quality Management System aligned with your Quality Assurance team's expectations?
- Have they run your desired packaging configuration?
- Can they source your desired packaging now?
- Can they perform all your necessary test methods?
- Do they have available fill slots at the times you need?
- Can they deliver on time and as promised?

SUMMARY

Follow these 6 steps

to a successful first clinical batch

Transitioning to clinical development is a complex process. But one you can complete with confidence through proactive planning, smart guidance, and the right manufacturing partner.

These proven steps will help you streamline that process from start to finish, while protecting your product's quality and value at every step.

ABOUT VETTER

Your CDMO partner

from preclinical through Phase III

Our expert clinical development services are backed by 40+ years of experience. We built this checklist based on many years of experience with a wide variety of drug sponsors and product types - so we are confident we can help you get to the clinic with confidence.

Accelerating your products to market

We offer a comprehensive range of clinical development solutions for high-value injectable product candidates:

- Formulation support
- Process development
- Clinical manufacturing
- Drug delivery systems
- Regulatory support

250+
clinical development experts at facilities in the US, Germany, and Austria

12
new customer product launches in 2020 alone

80%
of current customer projects are complex, sensitive, biologics

160+
active customer projects in preclinical through Phase III*

*Projects as of 2020

Take the next step with us.

Contact Vetter to learn more about how we can support you, your product, and your success in transitioning to clinical trials. Follow **#GettingtotheClinic** on LinkedIn for more clinical development insights like these.

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