Miltenyi Bioindustry

How collaborative preparation drives optimal tech transfer execution.

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Technical (tech) transfer is one of the most critical steps in pharmaceutical development, whether transitioning from the lab to clinical production or scaling to commercial manufacturing. Any misstep in this process can compromise product quality and introduce significant risk. This pressure is compounded for drug developers – particularly startups, academic spinoffs, and other smaller organizations – who must also contend with tightly controlled funding, unforgiving timelines, and rigid regulatory expectations.

Tech transfer success is usually judged by how well the receiving unit is able to maintain quality while simultaneously optimizing for speed and efficiency. Successful tech transfers typically begin with a pharmaceutical sponsor that effectively communicates a well-developed transfer strategy to the Contract Development and Manufacturing Organization (CDMO), followed by a collaborative planning process rooted in mutual commitment to preparation and clear communication. This ensures the partners' goals and strategy remain aligned throughout planning and execution of the transfer.

Make a plan. Follow the plan. Update the plan.

Preserving product quality throughout tech transfer is generally accomplished by adhering to existing standard operating procedures (SOPs), drawing on existing process knowledge, implementing an effective control strategy, and diligently developing and executing analytics. However, reducing timelines while maintaining such high quality is an exercise in risk management and opportunism. At a minimum, the ability to expedite tech transfer without compromising document, product, or process quality relies on early cross-functional engagement between internal teams as well as between sponsor and partner teams.

Proactive planning discussions help the CDMO understand the sponsor's stated needs and goals. These initial conversations foster the establishment of clear roles and task assignments relevant to each partner's technical teams, helping to set expectations, implement systems that support open communication, and clarify where the project lies in terms of process development and product life cycle. This information is vital to performing an initial gap assessment, which enables the CDMO to explore ways they can refine process-related elements such as materials, processing methods, testing requirements, and analytical specifications.

From a project management (PM) standpoint, the CDMO and project sponsor should collaborate to build a timeline of activities and milestones needed to accomplish a successful tech transfer. This timeline acts as a shared roadmap, which ensures the appropriate subject matter experts (SMEs) from each side are engaged at exactly the right time. For example, by engaging its manufacturing, science, and technology (MSAT) team during project planning, the CDMO enables that team to observe activities during process development (PD), giving them early insight into where the process can be optimized.

To create a robust PM timeline, it is critical to ensure that all team members are aligned on potential risks by creating a risk register in which risks are identified and classified (high, medium, low). As the timeline is developed, the teams work through which risks should be mitigated or accepted, as well as the strategy for how to address each risk should it occur. It is important to keep in mind that risks may be negative (delaying an activity) or positive (condensing the timeline for an activity). Understanding the impact of both negative and positive risks on a PM roadmap is key to effectively managing a tech transfer.

Additionally, a comprehensive PM roadmap helps both sides to understand and agree upon the CDMO's scope of work, mitigating the chances of scope creep. Non-value-added activities must be identified and minimized, or eliminated, while adaptive workflows ensure necessary changes are appropriately controlled, rather than haphazard. Scope changes often become necessary as a project progresses. However, the reasons for each change should be understood and agreed upon by each partner and accompanied by an official realignment of partnership expectations and the potential impact to the timeline.

The PM roadmap generally focuses on two areas: process stream and analytical stream. The process stream comprises of process development studies, as applicable per the project goals, and the incoming process's state of development, whose outputs pass to the CDMO's MSAT team. The CDMO's MSAT team then uses this information to organize raw materials, equipment, process records, and tech transfer plans appropriate for a Good Manufacturing Practice (GMP) setting at scale, in preparation for engineering, and eventually process qualification production. In many cases, standardized systems can be applied to facilitate workflows. The analytical stream flows through development and transfer, eventually supporting quality control (QC) and QC testing.

These streams should be executed in parallel, since adjustments are typically made to each based on information obtained from the other. Waiting for information due to linear transfer steps, followed by significant unplanned changes, is a common way timelines get derailed. This fact reinforces the importance of interdisciplinary communication and a robust project timeline, which help ensure that any workflow challenges are well understood, and deliverables remain aligned between partners.

Four common pitfalls that can derail a tech transfer

Even when a sponsor engages a CDMO partner well in advance of a planned tech transfer, the partnership can still be undermined by common, and preventable, problems:

1. **Lack of a dedicated Project Manager**
   Without a dedicated PM, technical, and regulatory teams can lack interdepartmental alignment or suffer from miscommunication. Both the drug developer and the CDMO should leverage a PM to ensure their internal teams are in agreement before suggesting or requesting changes. This will prevent rework or reactive back and forth that can lead to project delays.

2. **Absence of an established CMC strategy**
   A pharmaceutical company with an established Chemistry, Manufacturing, and Controls (CMC) strategy is far less likely to be impacted by unexpected process and analytical changes, rework, and timeline extensions during tech transfer. The more a sponsor organization can build their strategy out, with an awareness of the project's current status, long-term targets, regional regulatory requirements, scale, material controls, extent of necessary testing, etc., the better a collaborative outsourcing partner can help build an executable and efficient program.

   For example, a drug developer's initial manufacturing process may utilize small-scale plate formats and purification columns. However, as the project moves to later phases and larger-scale production, a reactor and tangential flow filtration are more suitable to achieve the required throughput.

   Also, this shift raises critical questions: How much time and what sort of investment will be necessary to understand and implement these new unit operations, with their different process parameters, inputs, and outputs? What additional process learning and data are needed? Further, if the new production process is not comparable to the commercial-scale process, does that impugn the integrity of clinical data?

3. **Raw material sources or quality are limited**
   A process can be progressing smoothly, using justified in-use materials and producing exemplary outputs, yet the developer still encounters supply chain issues. This can occur because the materials are not available in a GMP-acceptable grade or are difficult to acquire in the necessary quantities. The need for material risk management reinforces the importance of creating a thorough risk register as part of the PM timeline.

4. **Testing methods are inadequate**
   Selecting, developing, and qualifying methods, particularly potency, is a consistent challenge across the industry. The earlier a drug developer and its partner(s) can establish appropriate assays, the better. Products can be put on hold because valid and appropriate analytical methods are not in place, or because controls surrounding the materials are insufficient.

   Mastering these common elements of preparation and communication is essential to overcoming the most common tech transfer challenges and ensuring a successful, on-time project.

Phase-appropriate tech transfer supports high product quality

Ideally, the entirety of tech transfer should be standardized: rinse and repeat within the same basic framework. However, every tech transfer is unique, requiring specific challenges to be addressed with targeted adjustments. A tech transfer may involve a product heading from the lab to the clinic, or a product transitioning into commercial production, and each situation is subject to different technical and regulatory requirements. Process knowledge documented by the developer may provide a solid foundation for tech transfer, or tech transfer, or the available information may be limited.

The journey is dynamic and demands situational adaptability. Thus, understanding where the product exists within its life cycle, and what activities are possible/necessary at that point in its evolution, is vital to taking phase-appropriate action and documenting it properly. As the partners move through different phases, it also is imperative that they have a control strategy in place that matches the sponsor's target IND filing strategy.

How Miltenyi Bioindustry's Integrated Control Strategy drives results

Miltenyi Bioindustry's Integrated Control Strategy (ICS) is the foundational framework that guides our experts throughout the product life cycle. It is an adaptable system designed to produce unique, collaboratively molded control strategies optimized for each sponsor project. The ICS is rooted in Quality by Design (QbD), following well-defined endpoints and knowing the attributes the sponsor seeks, and then working toward those goals in the context of market demand and regulatory requirements. It spans three fronts: process control strategy, product protection control strategy, and contamination control strategy, all working in tandem.

As a sponsor and its CDMO partner build process understanding, they can better identify how their process parameters influence critical quality attributes (CQAs). The datasets supporting that knowledge are vital because they guide some development studies that characterize the process. Ultimately, process characterization should form a de facto predictive model of how critical process parameters (CPPs) influence critical outputs, indicating precisely how variances or interactions in one area will impact others.

Once those variabilities are understood and controllable, process-performance-qualification activities can be executed. Thus, the project proceeds through process design, process-performance qualification, and continued process verification. The last of these stages is continuously reevaluated throughout the product life cycle, allowing for adjustments in how the process is controlled to maintain consistent end specifications in the drug product.

Prepare for success

Early, cross-functional engagement between a sponsor and its CDMO is vital to a speedy and successful tech transfer. It helps ensure that everybody understands their roles and that everybody's responsibilities have established trigger points. Otherwise, different departments with misaligned priorities can lead to many challenges. So, initial discussions should lay out a general strategy for the tech transfer, its flow, and product life cycle management.

This collaborative environment also helps non-linear workflows to thrive, streamlining the project by enabling overlapping activities. The partners can use existing information and processes as a foundation, refining and adapting them as needed for the tech transfer. For this reason, a CDMO with more experience in transfer templates, documentation, training, communication streams, etc., is likely to offer a more cohesive partnership experience.

Additionally, tech transfer always is a learning experience, so the more structure a sponsor and its CDMO partner can introduce while remaining adaptive, the smoother and more quickly it will proceed. In addition to proper planning and communication, a major element of adaptability is trust between the two teams. This seems intangible but the means to establish trust are evident. As noted above, clear communication and open collaboration between all teams is key in building a trust-based development plan and partnership.

Sponsor teams and their CDMO counterparts should work in sync, making sure they are always communicative, aligned on potential risks, aware of existingchallenges and solutions, and actively present in situations where their expertise is needed. By understanding the risks and the likelihood of success based on those risks, the team can adjust as early as possible, positioning the partners to complete a timely, well-executed tech transfer.

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