Project Management: The Secret Weapon in Effective Tech Transfer

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There are many reasons behind the success, or failure, of a technology transfer. The transferring of knowledge, experience, documents, and processes involved in developing a drug product from the sponsor to the contract manufacturing organization (CMO) is complex. But at the center of this complexity is one critical role: project management in the tech transfer.

Project managers oversee the cross-functional teams that onboard and scale a client's drug product. Throughout the tech transfer process, project management must not only orchestrate the CMO's expertise, capacity, compliance, and communication – but also drive the innovative thinking that successfully delivers the project on time and on budget.

Effective project management creates and executes a plan that meets the client's needs, while making it possible for all stakeholders to understand the issues and goals of the transfer.

What makes tech transfer so challenging?

When outsourcing sterile injectable manufacturing, the detailed knowledge of aseptically filled and terminally sterilized product development is transferred from the sponsor to the CMO. This includes knowledge of the product's composition, development, and manufacturing processes. It also requires a delicate collaboration that carries multiple technical, financial, business, and quality risks if not executed properly. Transfers often also translate those processes to a larger scale for commercial production. The product's Critical Process Parameters (CPP) must be well understood and maintained to avoid impacting the product's Critical Quality Attributes (CQA) and product profile during sterile fill finish manufacturing.

Jubliant HollisterStier's project management team led innovative solutions for the tech transfer of five COVID-19 vaccine and therapeutic fill finish manufacturing projects during a period of intense pressure and uncertainty.

Real-world examples of innovative tech transfer

The COVID-19 pandemic demonstrated the pharmaceutical industry's capabilities in the face of dire need. Jubilant HollisterStier's agility, flexibility, creative problem-solving, and project management successfully transferred a number of COVID vaccine and therapeutic projects during a period of abnormal, stressful conditions.

These practices continue today, maintaining our technology transfer results in efficient and timely sterile injectable manufacturing of consistently high-quality clinical and commercial drug products – including small molecules, biologics, liquids and lyophilized products, liposomes, oligonucleotides, cold kits for radiopharmaceuticals, and vaccines.

CASE STUDY 1

Re-engineering a complex process for FDA compliance

JHS acquired the tech transfer for a COVID-19 liquid suspension vaccine product that was approved for use internationally, but not within the United States. This transfer was completed in less than half the time typically required. The challenge was developing a process to produce the vaccine in the US that did not compromise the sterility, or homogeneity, of the product.

Traditionally, this requires several experiments to perfect the process. Given the high value and low volume of the drug substance, JHS developed an aseptic compounding process with only one compounding R&D batch, rather than several. This demonstrated they could maintain sterility during bulk formulation and recirculation throughout filling, ensuring each vial received a homogeneous suspension. JHS technical services and subject matter experts collaborated to create a design of experiment (DOE) in under five months.

Prior experience with complex processing formulations and approved products expedited results. This incorporated the design and validation of multiple complex transfer assemblies, including two different filtration assemblies.

Ultimately, JHS achieved a robust, sterile transfer of material in an ISO 8 environment during compounding of the sterile bulk product. By working step-by-step with the client through the process redesign, JHS guaranteed the mutual approval of each change.

JHS conducted extensive development work to maintain the sterile handling and delivery of the various excipients and active pharmaceutical ingredients. The validation strategy developed by the JHS technical team for engineering batches included execution of a non-sterile compounding-only batch first, followed by a filled, sterile engineering run. This approach saved the innovator time and expense by delivering the maximum yield from a single compounding run. Development and process validation for the project were completed on a compressed timeline. This demonstrated agility and expertise in delivering nimble engineering solutions for a complex manufacturing process.

CASE STUDY 2

Expediting cold chain supply resources

A COVID-19 therapeutic product required a very large quantity of compounding materials to be stored under refrigerated conditions. The need was far greater than JHS' existing capacity for cold storage given the scale of the pandemic. The JHS supply chain team quickly developed an inventive solution to acquire cold storage and qualify it for use within three months, compared to the typical 18-month timeline.

Strengths of Jubilant HollisterStier in Technology Transfer

EXPERTISE JHS employees are highly experienced technical and project management professionals with the skill and talent to execute innovative solutions with rapid turnaround to meet client needs.

WHITE-GLOVE CUSTOMER SERVICE JHS prides itself on providing a customer-focused, full-service "white-glove" experience. They work with every client collaboratively from the pre-transfer evaluation through the commercial manufacturing phase.

PARTNERSHIP JHS focuses on partnership and collaboration, working with the client to create solutions. Clients have access to JHS leadership and SMEs throughout the project.

INNOVATION JHS teams are innovative, imaginative, and creative when envisioning solutions for clients' tech transfer.

AGILITY AND FLEXIBILITY JHS has the speedy response clients need when on a tight timeframe to complete a tech transfer.

THOROUGH JHS has the expertise to help prepare regulatory documents for approval as smoothly and seamlessly as possible.

TEAM APPROACH Multiple teams work together at JHS to complete a high-quality, professional tech transfer to produce the highest quality product.

BEST PRACTICES IN TECHNOLOGY TRANSFER

Jubilant HollisterStier has developed a proven, yet flexible, approach to technology transfer. Acknowledging the uniqueness of each client and their sterile injectable, ophthalmic, or liquid, ointment, and cream drug product, JHS project managers oversee a rigorous process to onboard and lead projects to a successful conclusion.

Pre-transfer evaluation: This first step involves determining the feasibility of the transfer, while scoping critical steps and potential challenges. During this phase, JHS evaluates the manufacturing processes necessary to verify they are within its sites' capabilities. Primary packaging and other critical manufacturing components are identified to support the transfer.

Technology transfer plan: A kickoff meeting led by project management is held to develop the technical transfer plan. Experts from JHS' functional departments – i.e., manufacturing, validation, analytical/microbial methods, process development, supply chain, quality, and regulatory – participate to consider:

- The client's current process and areas of concern or improvement
- Existing facilities and equipment
- Technical and validation gaps
- Available or acquired process technology
- Critical Process Parameters, Critical Quality Attributes
- Data to support manufacturing process efficiency

The meeting results in a detailed project schedule and process walk-throughs in which manufacturing instructions are translated to the batch record.

JHS functional experts are onsite while the batch record is developed, as well as during all initial execution activities – from engineering batches to process validation batches. This establishes that all steps are correctly defined and followed, and that the product meets its CQAs.

Engineering/development batches: After the walk-throughs, an engineering or development batch goes through the live process.

JHS works with the client to develop a sampling plan that collects data to demonstrate process capability or efficacy to execute this batch. Certain process development work may need to happen during this phase to support the scale up of the product. For example, sampling and testing may be designed to ensure the right fill volume is delivered or that the bulk mixing parameters are appropriate. If new equipment has been introduced, its function will be evaluated and analyzed during this batch. Concurrent paths can be evaluated at the same time during the engineering batch. Occasionally more than one engineering batch will be produced, but JHS strives for right-the-first-time batches to avoid unexpected results during registration and qualification phases.

Clients are encouraged to be onsite during execution of the engineering batch to facilitate faster decision-making and oversee process performance.

Clinical trial product/registration batches: Depending on the client filling strategy and scope, a Process Performance Qualification (PPQ) is executed to qualify the manufacturing process. These PPQ validation batches are for human use and made following JHS' standard operating procedures (SOPs) and current Good Manufacturing Processes (cGMP). The batches are validated by the same technicians who will manufacture the product for clinical or commercial use.

BEST PRACTICES (cont.)

JHS' project management and technical experts oversee the execution of the clinical trial or commercial registration batches and perform sampling as needed to collect process data during compounding, fill, and finish. These additional samples are used to demonstrate the manufacturing works as intended, producing product within the stated CQA and product profile. Additional data is gathered to demonstrate that all aspects of the manufacturing process – including lyophilization, mixing, and sterilization – are operating within specifications.

JHS is flexible in meeting client needs for ICH-compliant stability studies on the registration batch, as well as final container testing and in-process testing.

Clinical trial and registration batch data is transferred to the client. JHS may aid in the production and submission of registration/submission packages for various regulatory agencies. They are also available to respond to time-sensitive process-relevant queries from regulators during the approval process.

Commercial manufacturing: Once the product has been approved by all required regulatory agencies, commercial manufacturing of the product can begin and the technology transfer process is deemed complete. Each transfer is unique. Therefore, project management must coordinate a range of activities and decisions. This includes identifying new equipment, conducting boundary studies to identify CPPs, addressing technical and engineering challenges, or supply chain issues. Project management owns the transparent, collaborative, and open communication required for client satisfaction and project success.

Additional self-contained freezer units were procured and situated in temporary locations across the site to meet demand and increase available storage. JHS accomplished this without compromising cGMP and chain-of-custody requirements. Generating the solution under time pressure required adaptability and creativity from the project management, engineering, and inventory teams. This collaboration between groups was key to successful implementation on a tight timeline. Most of all, JHS' ability to drive this mitigation allowed for ongoing site production of these critical drugs to meet the high demand.

CASE STUDY 3

Meeting raw material needs

Supply chain issues have plagued nearly every industry since the COVID-19 pandemic. As a CMO that has delivered hundreds of projects for clients, the JHS project management and tech transfer teams leveraged an in-depth knowledge of a broad range of equipment, filters, components, and excipients from its project portfolio. This insight alleviates certain material shortages. Knowledge of in-facility materials that are suitable alternatives allowed JHS to recommend and plan for the use of site-qualified components, excipients, and manufacturing equipment.

In addition, JHS' relationship with well-known industry vendors offered solutions to material shortages. JHS worked with one large vendor to resolve production-loss risk due to unusually long stopper lead times. While exploring stopper materials numbers, it was found that in some cases an equivalent stopper existed under a different vendor part number. This limited the need for additional validation for its use. Pivoting kept these high-priority COVID-19 projects on track during the most challenging period for the supply chain.

CASE STUDY 4

Adapting equipment to keep pace with demand

COVID impacted the ability to acquire new or custom equipment in real time. JHS applied innovative thinking here, as well. The CMO rapidly identified alternatives, such as previously owned equipment that could adapt and qualify for manufacturing. JHS project managers and the tech transfer team also designed alternative solutions. For example, they designed a three-vessel compounding process using single-use compounding bags that met the requirements of this Emergency Use Authorization (EUA) project.

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Because of the diversity of processes run at JHS, the team quickly recognized they could use existing autoclave loads and pre-designed, validated bioburden filtration-reduction assemblies to complete the complex process on a compressed timeline. The utilization of existing assemblies reduced the validation work needed to support the project.

The tech transfer and manufacturing teams met the client often in the initial weeks of the project to ensure the complex process met all the required critical parameters for the client. This high level of collaboration, coordinated by the project manager, confirmed the successful manufacture of dozens of EUA batches for this client.

CASE STUDY 5

Zero deviations on an expedited timeline

JHS successfully and rapidly produced a clinical trial batch and three process validation batches for a client working under US Operation Warp Speed producing COVID-19 vaccines. During the clinical batch, the tech transfer team identified multiple process changes that reduced the risk of potential deviations in subsequent process validation batches. For example, the addition of a proposed component was determined to be high-risk for potential error, and the cleaning process suggested by the customer required improvements.

The knowledge and skill of the project manager enabled swift and competent performance that delivered production batches without a single deviation. This is extremely rare, even at a normal production pace. Despite the compressed timeline and a compounding process that involved multiple vessels and three separate material transfers, JHS implemented all updates and the process validation batches were produced without error and within the required timeline.

Conclusion

Effective project management brings all stakeholders together, shares critical information, and drives shared objectives. Consequently, it unleashes creative, out-of-the-box thinking that smooths the tech transfer. This yields faster, smarter, high-quality fill finish manufacturing that meets patient needs for sterile injectables, no matter the circumstance.

WANT TO DIVE DEEPER?

To learn more about efficient technology transfer at Jubilant HollisterStier, email us at info@jublhs.com.

JUBILANT HOLLISTERSTIER

STERILE INJECTABLE | LYOPHILIZATION | OPHTHALMIC BOTTLES | OPHTHALMIC STERILE OINTMENTS

Jubilant HollisterStier LLC is an integrated contract manufacturer of sterile injectables, ophthalmics, otics and sterile and non-sterile topicals and liquids. Our facilities in North America provide specialized manufacturing for the pharmaceutical and biopharmaceutical industries. We provide a full-range of support and services to streamline the manufacturing process such as on-site assistance from process qualifications through product release.