Accelerating biopharmaceutical tech transfer to address unmet medical needs

Key activities and strategies to accelerate biopharmaceutical tech transfer, and challenges to overcome in order to support faster development and manufacturing programs

About the author

Anthony Newcombe
Senior Director of Project Management at Samsung Biologics

Diana Brown
Senior Specialist in Project Management at Samsung Biologics

Anthony Newcombe, PhD, is a Senior Director of Project Management at Samsung Biologics. Dr. Newcombe holds a PhD in Biochemistry from the MRC National Institute for Medical Research, London, UK and is a Fellow of the Royal Society of Chemistry (FRSC), UK.

Diana Brown, MBA, is a Senior Specialist in Project Management. Ms. Brown holds a Masters in Business Administration from the Kenan Flagler Business School at the University of North Carolina at Chapel Hill and a bachelors of Chemical Engineering from North Carolina State University.

Biopharmaceutical development is a long journey with uncertainties, and outsourcing the manufacturing service serves as an integral component of successful product launch. Technology Transfer is the initial step of outsourcing and well-designed tech transfer is critical for seamless scale up and robust cGMP production of biopharmaceuticals.

During bioprocess tech transfer, operational & analytical methods, technologies, and knowledge are transferred from the sending site to the receiving site, and such transfer enables the recipients to strategically plan and execute process validation and manufacturing. Timelines of tech transfer can vary widely, depending upon the scope and complexity of the projects, which are the combination of various factors such as requirements and lead-times for analytical development, equipment availability, raw materials and time needed to generate the required documentation to support GMP manufacturing. Now, how can we ensure smooth, effective tech transfer without wasting valuable time?

Proper Planning and Timely Communication

It is essential to outline all required activities as well as anticipated risks of tech transfer and then allocate resources and set milestones with priorities. Since tech transfer is not a one-way street, such plans need to be shared, agreed upon, and closely communicated with both sides along the way. The overall project plan that lays out all the activities and tasks required including a communication plan will serve as a roadmap for the joint team members involved in the process and will help the alignment in execution.

Availability of Equipment and Facility Fit

The success of an accelerated tech transfer depends on equipment availability, facility fit, and often the robustness of the process transferred. Lead times for the purchase and delivery of large scale bioprocess equipment, such as UF/DF systems, chromatography systems, and stainless steel tanks may be long, and customized equipment may also result in lengthy delays that could impact tech transfer timelines. Unless the manufacturing process is transferred to a dedicated facility, an accelerated tech transfer to a multi-product contract manufacturing organization is often better suited to typical platform manufacturing processes that fit with the facility and equipment available. Undertaking a facility fit assessment early in the process is therefore essential to determining any equipment gaps or process changes that may be required to support an accelerated tech transfer. Optimized processes that have been developed to reduce processing times and solution volumes may be problematic because of minimum volumes required due to tank and vessel sizes available at commercial scale. Therefore, where possible, process development should consider the feasibility of expedited scale up and commercial manufacture, particularly if the process is transferred to the first commercial facility. Where the purchase of new production equipment is unavoidable or equipment is transferred internally from another site or facility, a process for accelerated equipment installation and qualification can help to reduce tech transfer timelines.

Timing of Small Scale Verification Runs

Laboratory scale verification runs undertaken within process development laboratories are often included as part of a tech transfer program. Typically data from small scale studies is available prior to the start of an engineering to provide additional process understanding and support troubleshooting if required. As part of an accelerated program, laboratory scale verification runs may need to be undertaken concurrently with a large scale engineering run or may be considered optional depending on the level of process understanding and characterization undertaken prior to tech transfer. Due to the timing and availability of small scale verification runs, processes that have been extensively characterized and used for manufacture of product at commercial scale minimize the potential risk of issues and the need for technical support and troubleshooting within process development laboratories. The joint tech transfer team and the business team have to evaluate if the risk of not having the small scale laboratory verification data is acceptable before commencing accelerated tech transfer.

Accelerated Preparation of Documentation

As part of an accelerated tech transfer, expedited preparation of documents should be considered. To permit time for review and approval of documents at the receiving site, controlled documents required to support performance qualification (PPQ) batches (e.g., SOPs, batch records, process validation master plan) may need to be prepared concurrently with an engineering run. Due to an urgent need for clinical or commercial material, there may be limited time between an engineering run and a subsequent PPQ campaign, and therefore accelerated tech transfer is better suited to commercial products manufactured at large scale using a platform process and are likely to require minimal process or documentation changes between an engineering run and PPQ campaign. Although there may be a critical need to provide material for the clinic, this strategy does however require careful evaluation, because tech transfer typically involves different production equipment, utilities, and site documentation; and engineering runs provide an opportunity to test equipment, documentation, and systems prior to the

manufacture of GMP material for human use. Again, the joint tech transfer and business development teams have to evaluate if higher risk of clinical run or PPQ run is acceptable before deciding to skip the Engineering Run. Face-to- face or virtual meetings may need to be considered to expedite review of manufacturing documents and process data, and this may need to be undertaken after completion of individual unit operations during an engineering run to minimize any delays and identify any document or potential process changes required.

Sourcing & Management of Raw Materials (RM)

Obtaining the required raw materials for manufacturing campaigns is often on the critical path. Stocks of common raw materials may be readily available to support other production activities (for example, NaCl or NaOH) or sourced from other qualified suppliers, but specialized raw materials, such as cell culture media and chromatography resins are often sourced from a single supplier and typically cannot be easily substituted. Raw materials that are considered critical, such as excipients sourced from a specific vendor, may need to be evaluated and supply lead times as well as options for expedited procurement should be assessed as soon as possible. Additionally, critical reagents containing animal-derived components may also be long lead-time items, subject to more stringent import restrictions. An alternative option is to ship purchased raw materials from another site or facility. Shipment of research cell banks may be considered under quarantine with mycoplasma and sterility test results whilst awaiting further analysis, and shipment of reference standards and critical raw materials for QC laboratories may be split into multiple deliveries to minimize the risk of customs delays impacting the project. Strategies for sufficient inventory buffer or multi-sourcing of critical raw material may also need to be evaluated to minimize risk to GMP manufacturing activities.

Comprehensive, yet Prioritized Analytical Method Transfer

Transfer and validation of analytical methods and know-how to a receiving site are often part of the critical path for the tech transfer timeline. Analytical methods for in-process and release testing are typically transferred to the receiving site as part of an analytical tech transfer program. Transfer and validation of some analytical methods may require several months to complete, particularly for cell based or potency assays that may require several days for each test to obtain a result. To support an accelerated tech transfer timeline, analytical transfer should focus on the qualification of methods that are needed for in-process control (IPC) testing which provide data needed to continue manufacturing and specific tests that will provide product quality data to identify any potential process or product issues as soon as possible. Compendial methods (for example, pH, and conductivity measurements) typically do not require an assay transfer and can be qualified relatively quickly. Samples may be shipped for release testing at an existing (sending site) laboratory until method transfer is complete. As part of an accelerated tech transfer program, completion of all method transfer activities may not be completed until after completion of performance qualification (PPQ) batches. This requires shipping of selected samples to the sending site for testing until method qualification or validation is completed at the receiving site.

Importation Requirements for Cell Banks (if applicable)

To support an expedited tech transfer, shipment of cell banks is one of the first tech transfer activities to coordinate, and an understanding of the incoming process for receipt of cell banks (WCB / MCB) at the receiving site is needed. Importation of vials of cell banks may be required to undertake small scale laboratory studies, and documents such as a manufacturing health certificate (MHC), export certificate, and a certificate of analysis may be required for importation of required cell banks, depending on the cell bank exporter and country of manufacture. For importation of cell banks for GMP use, additional information is typically required, such as TSE / BSE statement and details of cell bank qualification status and several weeks may be required to coordinate the documentation needed. Time required to obtain temperature data from data loggers used during shipping of cell banks may also need to be considered, as verification of the shipping temperature is usually a requirement for release of the cells for use in GMP manufacturing.

Tech transfer of biopharmaceutical processes is particularly challenging and should be accurately planned and executed by an experienced team with proven success in transferring processes from laboratory or pilot-scale to commercial GMP operations. Aggressive timelines associated with biopharmaceutical tech transfer have been historically associated with challenges due to limited tolerance within the production schedule to address unexpected issues related to critical path activities. To support the development and manufacture of potential therapies for the global COVID-19 pandemic, accelerated technology transfer with more innovative strategies should be adopted to allow for rapid engagement and utilization of cross-functional teams to coordinate faster tech transfer programs and manage critical path activities. Whilst a number of factors need to be carefully considered, with the appropriate knowledge and experience, it is possible to accelerate tech transfer activities while avoiding common pitfalls. It is important to understand that some additional risks will follow with such rapid tech transfer. Setting expectations and tolerance of these additional risks to the joint tech transfer team will enable efficient decision making and successful tech transfer within the shortest time possible.