VIROTHERAPY INSIDER

Overcoming Technical Transfer Challenges in Virotherapy Manufacturing

Technical transfer is the handover of knowledge and technical capability from one stage in the development supply chain to another and can take several forms, for example:

- The transfer of a project from one production site to another
- The transfer from a research and development (R&D) stage to a current Good Manufacturing Practice (cGMP) stage, including scale-up engineering

All technical transfer processes involve challenges that must be overcome to ensure success, and these obstacles can multiply when it involves virotherapy manufacturing, due to the unique complexities of the field.

Below we share a brief guide to navigating the technical transfer process for viral vector projects.

Technical Transfers from R&D to cGMP

Whether transferring between internal departments or to a contract development and manufacturing organization (CDMO), viral production projects must follow the same steps and processes as other biopharmaceutical projects.

It is crucial to follow Quality by Design (QbD) engineering processes from the beginning. This is vital to establishing a successful technical transfer program with the appropriate Critical Quality Attributes (CQAs), Critical Process Parameters (CPPs), Standard Operating Procedures (SOPs), which include establishing the design space, considerations defined in risk assessments, and settings mechanisms for control.

he sooner this process takes place, the easier it will be to build a robust and effective cGMP manufacturing process. The more a process has been developed with QbD principles in mind, typically the more defined a process transfer will be, contributing to overall improved success of transfer.

Another critical step is to develop manufacturing processes utilizing a scale-down model, where all equipment is a smaller scale version of production equipment intended to simulate larger or at scale operations. This model allows for the performance of USP/DSP process characterization, as well as defining robustness, and creating opportunity to design and evaluate process optimizations translatable to the pilot plant or cGMP manufacturing setting. Unlike the model used in early research processes, the scaled-down approach is designed to simplify the characterization, optimization and standardization processes needed to prepare for the scale-up to large scale cGMP manufacturing.

The scale-up should be relatively easy to execute if QbD principles have been considered and scaled down steps have been carried out effectively. During scale-up process development scientists will adjust scale-dependent operating parameters, while keeping scale-independent parameters unchanged. When scaling up viral vector processes in particular, production unit operations and equipment such as bioreactors, depth filters, chromatography, and tangential flow filtration (TFF) need to be assessed and adjusted to create a scale-up model. This is crucial to obtaining an accurate assessment of large-scale manufacturing capability and to identify potential risks in advance, so they can be mitigated appropriately.

Technical Transfer Between Different Sites

When transferring viral vector manufacturing projects between geographical sites, such as between a development facility and a CDMO partner, it is important to begin with an assessment of the new facility and its fitness for transfer. Vital to this assessment, is fully understanding the upstream and downstream processing equipment availability, the analytical instruments required, the quality systems in place, and importantly the expertise which in turn will yield security and reliability of the supplier during transfer.

For viral vector projects, it is particularly important to know the cleanroom grade and biological-control level at a facility, as well as the total number, size, and type of the critical process equipment in place equipment.

Thorough preparation prior to establishing technical transfer is vital to success. Above all, this preparation will benefit from considerations of QbD, established CQAs, CPPs, SOPs and risk assessments, as with any technical transfer from R&D to cGMP. Added to this, though, are other processes that need to be performed:

• The creation of manufacturing flow diagrams to identify the needed equipment, processes, raw material movements and operator requirements.

• Platform-based and validated assay lists for incoming, in-process, drug substance/ drug product (DS/DP) release and stability monitoring, highlighting platform-specific assays such as potency, identity, and product impurity, and considerations on a sampling plan.

• Process and test method characterization summary reports with details of processes and test methods.

• A list of essential biological materials and their specifications, such as master or working cell banks, master viral seed stock / infection or helper virus banks, plasmids, cytokines, growth factors, lipid supplements, and more.

A robust CDMO partner will evaluate these processes upon delivery of the technical transfer package, or prior-to in general consultation, focusing on gap analyses to identify any insufficiencies in terms of equipment, instrumentation, expertise, capability, and capacity.

Technical Transfer with Viral Vector Products

In addition to the above requirements, viral vector manufacturing presents unique challenges compared with other biopharmaceutical projects that need to be overcome to ensure technical transfer success.

Common virus and viral vector challenges that should be considered in the technical transfer process include:

• Infection or transfection efficiency

• Upstream titers

• Residuals and Impurities such as Residual Plasmid, Host-cell Protein or DNA levels

• Capsid integrity

• Upstream impact on downstream considerations Additionally,

the high variability of platform-specific processes in the viral vector space can make scale-down and scale-up modelling and other transfer processes highly complex.

Benefiting from Viral Manufacturing Expertise

Few CDMOs have the skills and capabilities to support virotherapy companies in addressing these technical transfer challenges. Therefore, working with an experienced CDMO specializing in virotherapy products is very important.

Whether taking on a project directly from the originator, or from another supplier, CDMOs have the expertise and experience to identify and overcome the challenges that frequently arise during technical transfer. A CDMO specializing in virotherapy development also has the dedicated technical insight to streamline process integration and incorporate key analytical method development goals for proper characterization and QC release.

About Vibalogics

Since 2003, Vibalogics has operated as a specialized global Contract Development and Manufacturing organization (CDMO) offering process and analytical development, manufacturing, testing, and fill-finish services to innovators developing transformational virotherapy products. From its headquarters and commercial facility in Boxborough, MA, USA and operations in Cuxhaven, Germany, Vibalogics supports its customers in the development and commercialization of oncolytic viruses, gene therapies and viral vaccines.

Vibalogics US Inc.
1414 Massachusetts Ave.
Boxborough, MA 01719

Vibalogics GmbH
Zeppelinstraße 2 Cuxhaven,
Germany 27472

Business Inquiries:
experts@vibalogics.com