Build It Right

Optimizing the Design of a Viral-Vector CDMO Manufacturing Facility

with Chris Berger

The design and build of a facility to support clinical and commercial manufacturing of advanced therapies is fundamentally important to the success of those projects. In many cases, retrofitting an existing biomanufacturing facility (e.g., for traditional biologics manufacturing operations) can introduce significant risk to manufacturing processes for advanced therapies. Chris Berger (executive director, quality viral vector at Avid Bioservices) discussed the advantages of Avid's Build It Right design philosophy for viral-vector contract development and manufacturing organization (CDMO) facilities.

Berger's Presentation

Berger emphasized the importance of envisioning an entire project, start to finish, early in the life cycle to increase its chance of success and minimize rework. Project leaders should consider the scope of the work for the projects in the facility. That can include the type and scale of cell lines they are using and whether the facility will make drug products in addition to drug substances.

It is important to define both your core project team and an extended team that can help provide additional insight and perspective. The core team should include professionals from manufacturing, quality, engineering, and information technology (IT). The extended team should include experts from facilities, automation, manufacturing science and technology (MSAT), business development, and validation. Defining roles and responsibilities can ensure that the team is empowered throughout a project.

Minimum considerations for a good manufacturing practice (GMP) production facility include lighting, temperature, humidity, ventilation, insect and animal protection, access control, and proper room classifications and differential pressure cascades. For viral vector and CDMO-specific considerations, you must ensure that your overall segregation approach, heating, ventilation, and air conditioning (HVAC) design is tailored to your needs. Avid's cleanroom is 15,000 ft² and has fully redundant air handlers serving different areas. Nonviral spaces use recirculated air and viral spaces use single pass outside air. Consideration must be given to how personnel and materials will move through a facility and how you will tour the premises. Consider any restrictions necessary and what kind of training is required.

Berger explained that safety requirements differ based on the biosafety level (BSL), and that for cell and gene therapy applications, a BSL-2 level is appropriate. The company has installed borders that restrict spills to designated BSL-2 rooms. For facility decontamination, Avid uses SteraMist decontamination technology (TOMI Environmental Solutions) based on ionized hydrogen peroxide to decontaminate viral-positive suites after each viral run.

Equipment standardization is important for CDMOs. Avid seeks to use industry-standard equipment that can meet all data integrity requirements and is well known to prospective clients. However, when equipment fails, the ability to pivot to new equipment quickly is important.

Berger said that Avid designed its facility to have two upstream production lines feeding into a central downstream processing suite. Avid utilizes the principles of both segregation in place and separation in time to handle multiple campaigns simultaneously. It's important to have robust changeover and clearance procedures within a facility. By examining risks of cross-contamination and layers of protection analysis and understanding local regulatory requirements, you can develop robust standard operating procedures (SOPs) to enable multiproduct manufacturing. Once planning and design is completed, you can then focus on managing construction efforts, qualifying finished builds, and maintaining compliance.

Avid performed pressure tests for each design layout according to company requirements and performed hazard analyses to ensure compliance. Berger emphasized the importance of having clearly documented communication lines among team personnel to ensure that all parties agree on project details before they are undertaken. Staff should use comprehensive risk assessments to implement risk mitigation strategies and regularly monitor and evaluate risk. Finally, it is important to implement a control contamination strategy (CCS) when manufacturing sterile products. That requires continuous monitoring of facilities and having procedures to control hazards and eliminate microbial ingress.

Question and Answer

How do you manage waste materials from the production suites? Waste materials are decontaminated and disposed of at our facility. Solid waste goes through a waste handler, and liquid waste goes through waste neutralization before entering the municipal waste system. All suites are unidirectional, and materials move in and out through an airlock.