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Using a Risk-Based Approach to Manufacturing in a Multi-Product Facility

Manufacturing in multi-product facilities affords numerous advantages, but also presents significant challenges. At its Halle/Westfalen, Germany, plant, Baxter BioPharma Solutions has implemented a risk-based approach to addressing those challenges, providing customers with the benefits of multi-product manufacturing.

Multiple Advantages

The biopharmaceutical industry is continually challenged to reduce costs and time needed to produce advanced drug products. Drug manufacturers are consequently pursuing numerous approaches to achieving gains in efficiency and productivity.

Manufacturing in a multi-product facility offers one approach to reaching greater efficiencies and quicker time to market. Multi-product facilities offer manufacturing flexibility combined with efficiency and cost reductions. In such plants, the equipment is continuously used rather than being operated intermittently, leading to improved capacity utilization. Equipment is typically better maintained because it does not sit idle for extended periods of time. Perhaps the most important advantage is the consistency of processes on standardized equipment instead of having to build dedicated manufacturing facilities. With respect to cost benefits, one multi-product facility can replace multiple dedicated facilities, eliminating the need to invest in duplicate equipment, utilities, etc. Personnel requirements are also reduced, as is the need for auditing, inspections and compliance activities.

The Cross-Contamination Challenge

The greatest challenge in multi-product facilities is the prevention of cross-contamination. The facility itself, including product and non-product contact surfaces, is viewed as a potential source of contamination; therefore, facility, equipment design and cleaning are critical areas of focus. It is of particular concern when highly potent, cytotoxic active pharmaceutical ingredients are involved. Cross-contamination can occur if the same equipment is used to manufacture different products and is not subject to adequate cleaning. It can also occur from human interactions with open processes, which means it is essential in a multi-product facility to demonstrate that no cross-contamination occurs in order to maintain the highest quality and safety of all drug products.

The European Medicines Agency (EMA) has published guidelines for setting health-based exposure limits for use in risk identification in the manufacture of drug products in multi-product facilities.

The FDA also offers guidance on how to identify and understand risks for cross-contamination and implementation of appropriate control strategies.

Handling Oncology Drugs

Baxter BioPharma Solutions' Halle, Germany fill/finish facility has a long-standing history of manufacturing oncology drugs in a multi-product facility for early phase drug formulation through commercial scale-up, product launch and lifecycle management. Biologics, ADCs, small molecules and nanoparticle-based formulations such as emulsions, liposomes and suspensions are a few of the types of products manufactured. The Halle facility is focused on handling both cytotoxic and non-cytotoxic APIs. To help ensure the high quality and safety of all products at the facility, Baxter has established a comprehensive risk matrix that considers both the pharmacological and toxicological data, as well as the cleanability of any product that might be manufactured at the site.

Furthermore, all oncology products are manufactured in dedicated areas of the facility. State-of-the-art isolators and restricted barrier access systems (RABS) are equipped with separate HVAC and air exhaust systems. The highest filter classes are applied in the cleanrooms, and additional HEPA filters are used for the air exhaust. Clinical and commercial filling lines are equipped with automated loading/unloading, capping and inspection infrastructure. Baxter BioPharma Solutions has elected to use product-dedicated filling equipment within its Halle multi-product plant. Isolators are installed at every point where there is a risk of exposure or breakage – weighing, compounding, filling and freeze-drier unloading areas – to prevent contamination between rooms and through operator interaction. Once vials are filled and closed, they are also subjected to a final decontamination rinse to minimize the risk of contamination on the outside of the product packaging. These built-in operations are just some of the many ways Baxter BioPharma Solutions is committed to advancing quality manufacturing in a multi-product facility. P

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