Piramal
Pharma Solutions

# THINKING INSIDE THE BOX - ISOLATOR TECHNOLOGY FOR ASEPTIC MANUFACTURING OF PARENTERALS

# INTRODUCTION

The manufacture of parenteral pharmaceuticals is a high stakes endeavor because any product imperfections, whether chemical or biologic in nature, are equally as bioavailable as the active ingredients. Patient safety and product quality are always a concern in pharemaceutical manufacturing, however, the risks are amplified for parenteral products that in many cases are directly injected into the bloodstream. This means the impact of product quality risks are higher than for any other pharmaceutical presentation. The use of isolator technology is a state-of-the-art engineering solution to mitigate manufacturing risks, improve the safety of injectable drug products, and provide a measure of safety to those who are manufacturing the products.

A significant risk during the manufacturing parententals is exposure of the product to the surrounding environment. The environment can expose the product to chemical contamination, degradation catalysts, and biological contaminants. A failure to control any one of these could result in a poorer quality finished product or the loss of a product batch; either would have impact on patient safety and considerable financial implications. The use of isolators allows for a highly-controlled, relatively small environment used to conduct manufacturing activities. Isolators are fully enclosed, sealed, and pressure controlled units that can be used to generate an aseptic, hepa filtered environment for the manufacture of injectable drug products.

In addition to the risk of environmental contaminants, many active pharmaceutical ingredients have very low Thresholds of Toxicological Concern (TTC) or Occupational Exposure Limit (OEL). It is vital that manufacturing operators working with these ingredients are protected from exposure. To mitigate the risk of exposure when manufacturing sterile injectables, isolator technology is ideally suited.

Isolators are not the same as clean rooms and do not have many of the concerns associated with traditional clean room manufacturing environments. Air flow, particulate monitoring, and aseptic technique are all treated differently inside an isolator environment. Human contact represents the greatest risk to the sterility assurance in any aseptic manufacturing environment; the use of isolators provides a physical barrier to eliminate the possibility of human contact. The removal of human contact nearly precludes the most common source of contamination for the product and the use of isolators ensure the product is maintained in a highly controlled environment until the primary container system is sealed.

The use of aseptic techniques inside an isolator environment provides increased control of the aseptic manufacturing process. Isolators are classified as an ISO Class 5 (Grade A/ Class 100) environment and are operated with a HEPA filtered environment. The internal atmosphere and surfaces are rendered free of

biological contaminants with qualified decontamination cycles using vaporized hydrogen peroxide (VHP). VHP is the gold standard in biodecontamination because it is effective on a broad range of microorgansims including bacteria, viruses, fungi, and spores.

Manufacturing staff utilize glove ports consisting of isobutulyene sleeves and gloves to execute manufacturing operations. The gloves and sleeves are secured to the isolator walls to create an air tight seal, which are pressure checked as part of the decontamination cycles. The aseptic environment inside the isolators can be adjusted to address any product-specific quality concerns to ensure that the product is not exposed to a potential degradation pathway.

An isolator-based facility is ideal for parenteral manufacturing because of the high degree of sterility assurance and containment afforded. Once manufacturing materials and components are rendered sterile, they do not leave the isolators until the primary container is sealed. Facilities which utilize isolator technology have the added ability to handle highly potent drugs such as cytotoxins, steroids, hormones, acutely toxic, and small dose pharmaceuticals. The Piramal Pharma Solutions facility in Lexington, KY has been manufacturing parenteral products using isolator-based filling lines for nearly 10 years without a sterility test failure.

Isolators are a highly specialized and effective technology designed for the manufacture of sterile injectable products. They allow for the greatest sterility assurance, product quality, and protection for the manufacturing staff. Isolators mitigate the most significant risk of manufacturing parenterals, human intervention. When selecting a future manufacturer of your parenteral products, why would you accept anything less than the best assurance of aseptic control? Ensure that your manufacturer utilizes isolator technology because safety and quality are of the utmost concern.

Piramal Pharma Solutions is a contract development and manufacturing organization (CDMO), offering end-to-end development and manufacturing solutions across the drug life cycle. We serve our clients through a globally integrated network of facilities in North America, Europe and Asia. This enables us to offer a comprehensive range of services including Drug Discovery Solutions, Process & Pharmaceutical Development services, Clinical Trial Supplies and Commercial supply of APIs and Finished dosage forms. We also offer specialized services like development and manufacture of Highly Potent APIs, Antibody Drug Conjugation and are well versed in technologies such as Bio-catalysis, Route Scouting etc. Our capability as an integrated service provider & experience with various technologies enables us to serve Innovator and Generic companies worldwide.

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