What's in Store for Aseptic Processing Technologies in 2022 and Beyond?

By 2028, the global market for injectable drugs is set to reach $69.13 billion, growing at a CAGR of 8.9%. There are many reasons for this boom in demand, from the drive to develop innovative treatments for rare diseases to heightened demand for faster vaccine rollouts.

However, as these drug products are injected directly into the body and therefore bypass the body's natural defences, parenterals such as injectables and topicals used in ophthalmics require aseptic processing to ensure total sterility.

Aseptic processing is a fast-growing market, expected to reach 12.5 billion USD by 2027. Recent spikes in growth for this market are driven by the latest innovations in vaccine development for the COVID-19 pandemic, as well as the rise of biopharma treatments to manage serious chronic conditions.

As a result of this growth, there have been a number of innovations and techniques adopted to enhance efficiencies across aseptic processes.

The Aseptic Processing Technology Landscape in 2022

The legal requirements for aseptic product manufacturing have undergone many changes in recent years. As a result, containment technology experts have had to explore further innovations to ensure these regulations are met, resulting in rising growth of the aseptic technology market.

Aseptic procedures must follow long-established strict guidelines to ensure the safety of all drug products. Most prominently, all cleanroom environments must adhere to Good Manufacturing Practice (GMP) guidelines for the manufacture of sterile products – meaning that all cleanroom spaces must be classified according to the required characteristics of the environment.

These environments must meet rigorous classifications to remain compliant with ISO14644, which stipulates that cleanroom spaces must be categorised as Grade A, B, C or D. As a result, pharmaceutical technologies have been developed alongside these regulations to ensure safe and compliant aseptic processing techniques are followed across cleanrooms.

Alongside these well-established guidelines however, manufacturers must also ensure that their aseptic processes are aligned with any new updates that come into force.

In 2018, amendments to Annex 1 of the GMP were drafted, and are set to come into effect imminently. These revisions offer significant changes to the aseptic requirements across cleanroom spaces.

These amendments place a stronger emphasis on pharmaceutical companies to minimise the number of manual interventions across aseptic cleanroom processes as much as possible, while still maintaining optimal sterility.

As a result, this has further motivated technology manufacturers to ramp up their development of innovative new technologies to not only help boost efficiencies and productivity, but to also help their customers remain compliant.

These technologies have been designed to minimise manual interventions by allowing manufacturers to sidestep lengthy cleaning and validation procedures, resulting in less production downtime.

In previous versions of Annex 1, all connections for aseptic processes were required to be performed under highly-classified Grade A environments.

However, some of the latest technological amendments take into account recent technological advancements being implemented across cleanrooms, making it possible in some cases to declassify cleanroom environments while still performing compliant aseptic manufacturing processes.

Limitations of Existing Aseptic Processing Technologies

Across sterile manufacturing environments, there are many potential sources of contamination that can pose serious risks when it comes to drug manufacturing.

From the microbes and potential pathogens carried by human operators to the particles of other APIs, there are many potential contaminants that must be contained. If any were to make their way into the drug manufacturing areas and processes, they can pose a serious risk to the health and safety of patients taking these drug products.

To maintain high levels of sterility across cleanrooms and production lines, drug manufacturers are required to implement highly specialised equipment and infrastructures, as well as following stringent operating processes.

Achieving sterility across critical cleanroom areas and operations (e.g. fill/finish processes) has traditionally been done through the use of equipment such as restricted access barrier systems (RABS).

Manufacturers using RABS must ensure they have the right airflow measures in place, provide a physical barrier for operator interventions across critical zones, and have automated processes and procedures in place to minimise manual interventions as much as possible.

Isolator systems are also used across pharmaceutical cleanrooms to separate operators from the drug product during manual handling. These isolators help prevent any ingress of contaminants, as enclosures are accessed by operators via attached gloves to perform manual interventions, while remaining totally separate from the drug product material.

Alongside these systems, drug manufacturers must implement and follow regulatory guidelines for their cleanroom processes, stringent cleaning techniques and rigorous air classification management procedures.

While both of these systems are proven to be highly effective, they can be hugely expensive to acquire and install into cleanroom spaces. They also call for strict cleaning regimes to be carried out between each use, which can lead to significant

production downtime and impact on overall productivity.

For isolators, operators are often faced with difficulties when transferring materials into and out of their chambers. When this happens, it may be necessary for operators to implement a docking isolator to aid the transfer process.

As well as incurring an additional step in the process, the sterilisation of the interior of the isolator may be carried out before any drug product materials can be transferred through. This, however, may not always be necessary as isolators can be decontaminated via automated processes.

When it comes to RABS equipment, there are further complexities that manufacturers must adhere to that cannot be achieved via automated processes. As all components that come into contact with the drug product material be steamed-in-place (SIP) prior to use, they must be cleaned and re-validated as soon as the door to the RABS is opened.

Manufacturers using RABS equipment must also ensure that their cleanrooms and gowning procedures are ISO 7 compliant, as their ability to open in the event that operator intervention is needed means they do not offer complete isolation from drug product materials.

The Latest Innovations in Aseptic Processing Technologies

Aseptic processing tech is evolving to keep up with Annex 1 and other changes in the aseptic landscape, helping to not only ensure compliance but also enhancing efficiencies while further minimising the potential for contamination.

One example of these advancements is the single use variant of the Split Butterfly Valve (SBV) – traditionally stainless steel devices consisting of two components – containing an 'active' and a 'passive' part which form a single 'butterfly' disk.

SBVs can help to reduce the need for pharma manufacturers to carry out additional processes within RABS equipment, such as manual cleaning and validation. This is because SBVs allow for decontamination within a closed environment, as they create an opening between the discs when the valve is sealed which enables a decontaminating gas to be flushed through. As a result, only the SBV component requires cleaning and validation, as opposed to the entire RAB system.

Now available as disposable components, SBVs connect to the container, process vessel, isolator or to a machine within a RABS aseptic filling line to allow drug product material to flow while preventing contact with the outside environment.

Single use aseptic components have become more prevalent across sterile processing environments, offering the same level of contained sterility before their disposal after use.

Single use charge bags are also increasingly used for the storage and transportation of drug product materials. These feature a valve which connects to the passive half of an SBV which transfers drug product material into the contained bag, preventing exposure to the outside environment.

These charge bags are designed for disposal after use, and much like the SBVs, they promise the uncompromised sterility and integrity of the drug product material.

Single use technologies such as these offer manufacturers greatly enhanced efficiencies and ease of use across their processes. Gamma sterilised before use, these components are pre-sterilised to ensure no contamination can occur before use.

Additionally, they can help companies remain compliant with Annex 1 by reducing the need for manual intervention required for cleaning and validation after each use. Provided that all other Annex 1 requirements are followed, drug manufacturers using single use components such as the SBV may be able to declassify their cleanroom environment while still performing compliant aseptic transfers.

Looking Ahead

In an industry as complex and dynamic as the pharmaceutical industry, advancements in aseptic processing technologies are ever-changing.

Pharmaceutical companies must continually strive to explore the latest technologies that not only help them stay competitive, enhance efficiencies and streamline processes, but they must also search for equipment that helps them stay compliant with the latest regulatory updates.

Technologies such as RABs and Isolators have been used across cleanrooms for decades, and they are expected to remain in place for years to come. However, these technologies have significant limitations, which is where newer innovations such as single use technologies come into play.

SUTs are increasingly popular across manufacturing spaces for the efficiency and productivity benefits they provide, and the latest updates to Annex 1 which recognise their benefits indicates that we'll see them become a staple of standard cleanroom technologies.

As we look ahead to the future of aseptic processing technologies, we can also expect to see greater digitalisation across production lines. Smart factory technologies are increasingly being implemented, helping to automate manual procedures.

These are devices and components that can be implemented within existing manufacturing lines to help automate and monitor production lines. They can help alert operators to any potential breaches in containment or flag any maintenance needs before they become an issue, further optimising aseptic processes.

As these technologies can automate key processes, they help to reduce the amount of manual operator interventions required to a minimum, helping pharma companies ensure further compliance with Annex 1 sterility requirements.

Overall, it's likely that the cleanrooms of the future will look drastically different from those that existed just a few years ago, helping to enhance the safety of drug products and boost compliance with existing and future regulations.

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