SPOTLIGHT feature

Drug Discovery & Pharmaceuticals

How Regulatory Compliance is Driving the Rise of Automated Aseptic Processing Lines in Liquid Filling

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In contemporary biopharmaceutical manufacturing, the role of sterile fill/ finish remains at the very forefront of the user process consideration.

Being held to the highest of regulatory standards and compliance ensures that when administering sterile injectables to patients, the efficacy of those is not compromised. An example of this being, drug products manufactured in a way that enabled the presence of micro-organisms and other contaminants to reside within the final container. This could have severe and/or even fatal consequences.

To guarantee the above is avoided, it is now essential that any injectable product is manufactured under stringent environmental controls. Taking the full line in to consideration, this would include:

- Rotary vial washers which need to be thoroughly cleansed to ensure the 3-log reduction of endotoxin following a LAL test
- Depyrogenation tunnels to de-pyrogenate containers prior to being aseptically filled
- Aseptic liquid filling, stoppering, and capping machines inspections - these may include IPC/individual check weighing stations, too
- External vial washer controls to minimise the risk of contamination on the outside of the vial. This is becoming a more popular technique employed, minimising the risk of vial/batch contamination and rejection.

Governing bodies such as the Food and Drug Administration (FDA), have become the gatekeepers of good manufacturing practice, setting standards the industry must maintain, and disciplining companies who fall below. Following the development and growth of these governing agencies, a noticeable shift in the manufacturing approach has become apparent. The days of aseptic processing being predominantly manually driven, which in turn lowered efficiency, accuracy, stringency, and results in many cases, have thankfully been superseded.

The marked rise of strict validation underpinning the industry, appears to be driving the market in this direction, with companies and customers alike now tending to favour increasingly technologically driven environments with full electronic audit trails and data.

No longer is it acceptable to demonstrate a wide variation in either batch to batch or intra-batch results. Products must be shown to be processed in a replicable/reproducible way, yielding results within the specified tolerance of the product itself.

Anything less can now lead to a rejection of the batch, at a large potential cost to the manufacturer. It is this income damaging risk that has played a significant role in sharpening the attention and focus of manufacturers.

This validation has prompted the design and development of instruments capable of not only reaching speeds that manual processing would be unable to achieve, but also a level of documentation that again, a manual procedure would have difficulty in reaching parity with.

Continuous aseptic processing, such as liquid filling therefore demonstrates significant advantages, which is why automated methods are now the chosen mode of practice *(Figure 1)*.

Figure 1. Automated liquid filling offers significant advantages.

Figure 2. Technologically driven environments with full electronic audit trails and data are increasingly favoured.

When considering aseptic automated liquid filling, contemporary units are now expected to offer the best practice capabilities, so the process is not only completed as it should be, but that sufficient documentation and data on the process itself, along with the equipment used, is also present *(Figure 2)*. A benefit, should external auditors need to see such details during audit situations.

Any audits demand a strict adherence to cGMP guidelines for the following areas; these will include (though not exclusively):

- Cleaning validation (CIP/SIP)
- Software compliance to GAMP 5 or CFR 21 Part 11
- Batch reports that should provide the opportunity to garner any salient information pertaining to the cycle in question
- Machine validation, to make sure the equipment was qualified both pre-delivery, and post-delivery, satisfying all set performance and build criteria
- Availability of all relevant machine documentation such as full user manuals, material certificates, declaration of conformity, electrical and mechanical schematics to name the most often requested items
- Flexibility and parts availability thus allowing a system set up to process one set of vials, to be changed to a set up for a different vial size, or changed from a vial to syringe set up, for instance; flexibility is the key with these instruments
- Check weighing - 100% check weights, or a suitably compliant alternative weighing process if required
- RABS/ Isolator integration into both to meet the customer requirements

In an industry where liquid filling continues to be an essential step, it remains imperative things are done to meet the highest compliance standards expected.

While emphasis will be on the company and operator of the system to use the instrument in the correct way, it is also true that there is a great expectation now placed on the equipment manufacturer too. This expectation is that the goods were produced to all current standards, accompanied by a transparent documentation package corroborating the manufacture itself. For instance, the 316L stainless steel parts are actually 316L and not 304.

If you are looking into either replacing part of your aseptic processing line such as aseptic liquid fillers, rotary vial washers or need a full aseptic assembly, speak to a specialist at Biopharma Group who will be able to assess your requirements and provide a solution best suited to your processing needs; get in touch today: http://bit.ly/BPSContact or visit https://biopharma.co.uk/bps/home/