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driven, which in turn lowered efficiency, accuracy, stringency, and results in many cases, have thankfully been superseded.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/

Partnership Formed to Expand Options for Accessing Drug Metabolites

Hypha Discovery Ltd, the leading specialist CRO for drug metabolite provision, and Cypex Ltd, experts in the provision of recombinant xenobiotic metabolising enzymes, have formed a partnership wherein Hypha can scale-up and purify metabolites made by Cypex enzymes.

The partnership utilises the expert services Hypha Discovery already provides to pharmaceutical and agrochemical clients using its One Stop Metabolite Shop. The one-stop shop comprises a combination of both biological and chemical techniques so clients can quickly establish a method to identify and scale up production of any type of metabolite to support R&D needs. Expanding this toolbox to include additional xenobiotic-metabolising enzymes developed by Cypex, provides Hypha with even more options for synthesising and purifying metabolite standards for clients.

Cypex's portfolio of recombinant enzymes is underpinned by patented technology which enables the expression of human and other mammalian drug-metabolising enzymes in bacteria. Access to Cypex's enzymes augments the suite of PolyCYPs enzymes developed by Hypha scientists for accessing CYP derived metabolites. The partnership enables access to metabolites derived from CYP, FMO, AOX, UGT, SULT, CES, MOA enzymes from a variety of clinically relevant species, as well as humans.

Liam Evans, CEO of Hypha Discovery, commented: "We are delighted to further develop our relationship with Cypex, which strengthens Hypha's position as the go-to company for metabolites. We value this opportunity to collaborate with the team at Cypex and are excited by the synergies that this partnership brings."

Michael Voice, Director of Cypex, added: "There is an obvious synergy between Cypex's enzyme products and Hypha's expertise in metabolite production, purification and identification. Our customers will not only have access to a wider range of services, they are also assured of the excellent level of personal service that both Cypex and Hypha pride themselves upon. I am delighted to be working with the team at Hypha to better serve our customers."

More information online: ilmt.co/PL/zyoQ

For More Info, email: 51343pr@reply-direct.com

New C18 Cannabinoid HPLC Columns

The analysis of cannabinoid samples, to perform complete profiling of the various cannabis and hemp strains and more accurate potency testing, is becoming more essential. There are at least 100 identified cannabinoids that have been isolated from cannabis sativa. These minor cannabinoids can possibly interfere with the chromatography of the five most common cannabinoids: tetrahydrocannabinol (THC), delta-9-tetrahydrocannabinolic acid A (THCA), cannabidiol (CBD), cannabidiolic acid (CBDA), and cannabinol (CBN). **ES Industries Inc** have developed a new C18 column - Epic C18 Cannabinoid to fully resolve the 11 major and most frequently observed minor cannabinoids using commercial standards. The baseline separation achieved with the Epic C18 Cannabinoid column ensures positive identification and accurate quantitation for the cannabinoids of interest. Epic C18 Cannabinoid is based on the robust Epic bonding chemistry developed by ES Industries. The superior performance of Epic C18 Cannabinoid is a product of high density bonding which has been achieved through refinements in the processes and catalyst development. High bonding density is one of the most important factors in producing a robust stationary phase and robust HPLC column. The eleven component cannabinoid analysis is achieved with Epic C18 Cannabinoid using a simple isocratic mobile phase which is more easily transferable between instruments/laboratories, compared to more complex methods that incorporate atypical mobile phase gradients or additives.

More information online: ilmt.co/PL/zyje

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Affordable GC for Brewing QC Announced

Ellutia Chromatography solutions can now offer a range of Beer and Brewing testing packages. The lower entry price makes GC Analysis affordable for more laboratories without sacrificing analytical performance. Based around the compact and versatile 200 series Gas Chromatograph Ellutia can offer systems for applications such as alcohol profiling, Diacetyl and other VDK's, DMS in Malt, Nitrosamines in Beer and Malt. Systems can be configured for manual injection or a range of autosampler options can be added.

The 200 Series Gas Chromatograph from Ellutia is a compact high-performance GC at an affordable price making gas chromatography accessible to every lab. Originally Designed for use in education, the 200 Series GC is simple to operate with rugged construction making it the ideal first GC for Scientists looking to start Gas Chromatography. The Analytical performance however matches much larger costlier instruments from other manufacturers meaning it is just at home in a commercial lab as it is in the classroom.

More information online: ilmt.co/PL/V16m

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Screening for Nitrosamines in Pharmaceutical Products

Nitrosamine are carcinogenic compounds so need to be monitored to ensure unsafe levels are not found in consumer products. Due to unsafe levels being found in a number of pharmaceutical products the EMA (European Medicines Agency) is requiring pharmaceutical companies to complete and submit a risk assessment by 26th March. This means many pharmaceutical manufacturers will potentially need to screen their products for nitrosamine content.

The Ellutia 800 Series TEA is perfectly suited to nitrosamine detection thanks to is selectivity and sensitivity for Nitroso compounds. For testing of pharmaceutical drugs, The 800 Series TEA can be interfaced to a chemical stripping system that allows for rapid testing of ATNC (Apparent Total N-nitrosamine content). This quickly gives an accurate result for the total nitrosamine content of a sample showing both volatile and non-volatile components.

Any positive sample can then be further analysed by an 800 Series TEA interfaced to a GC where volatile nitrosamines such as NDMA (N-Nitrosodimethylamine) can be separated and quantified.

More information online: ilmt.co/PL/PDk0

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