WHITE PAPER

Annex 1: How automated room bio-decontamination with hydrogen peroxide vapour helps ensure compliance

Annex 1, a GMP document published by the European Commission, EMA, and PIC/S, holds paramount importance for pharmaceutical companies involved in sterile product manufacturing. Compliance with Annex 1 regulates the safety, efficacy, and quality of sterile pharmaceutical products. As of the 25th of August 2023, all clauses of EU Volume 4 Annex 1 (with the exception of 8.123) should have been applied within Europe with the rest of the world expected to follow suit. The working assumption is that some clause compliance will have been achieved through the extension of existing processes. Automated disinfection processes, and the regulatory environment in which they operate, have advanced significantly since the previous revision of Annex 1 and in particular three clauses could benefit from technology adoption.

Clause 4.33 states "The disinfection of cleanrooms is particularly important." The disinfection method of any cleanroom must be understood and documented so that risks of organism resistance can be mitigated, primarily through rotation of disinfection agents and periodic use of a sporicide. Annex 1 discusses the use of vapour disinfection and specifically mentions vapour-phase hydrogen peroxide as an option, but also highlights the need for this method to be understood and validated. The adoption of advanced automated processes also supports the drive of Annex 1 for continual improvement

Clause 4.14 reinforces 4.33 emphasizing the decontamination of critical facilities, including cleanrooms and HVAC (Heating, Ventilation and Air conditioning) systems. Although the need to decontaminate an appropriately designed HVAC system is likely to be rare, provision for this eventuality must be considered. Most systems, whether designed with decontamination in mind or not, are able to be disinfected using an automated vapour bio-decontamination method. However, it should be noted that slight variations from the original technical drawings are typical. Detailed, and current, decontamination protocols will have to be compiled in close collaboration with the facilities management team and the service provider. Primarily this protocol will concentrate on safety, but effectiveness and the process limitations must also be understood and included in any implemented procedure to ensure compliance with clause 4.36 and the need to understand the process.

Clause 9.13 falls under the environment and process monitoring section and looks at corrective and preventative plans in case of limit excursion. In addition to containment actions (i.e., affected batch quarantine/recall) and root cause analysis, action plans are needed to prevent further deterioration of the environment. While finding the root cause will be the key to understanding the issue, containment and remediation of the environment should represent a standard part of the process which can be preplanned. This will ensure the safety and efficiency of any process implemented as the event can be considered and planned when pressure and stress are lower.

Vapour-phase hydrogen peroxide can represent a good solution to meeting the three clauses above as well as increasing efficiencies and reducing risks inherent in other methods of disinfection. However, as Annex 1 states, the key to the successful implementation of this process is understanding the agent and the dispersal system employed. This ties in with regulatory approvals such as the European Biocidal Products Regulation (BPR) which approves biocidal products in 2 parts, their active ingredients, and the method of application. In fact, the BPR goes further to include the type of environment in which the product can be used.

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There are typically 2 paths to implement any automated bio-decontamination technology to a facility: equipment ownership and outsourced service. Both have their advantages and disadvantages, but when it comes to understanding and implementing a vapour-phase hydrogen peroxide system an outsourced service would enable a turnkey solution to be put in place quickly and easily. This is especially true for infrequent use or large-scale applications as a service provider will be able to apply current expertise and the latest technology without the need for capital outlay.

Another offering available on the market is that which provides a dedicated response package, tailored to meet the exact requirements. This can include everything from a site survey and initial safety documentation to full site plans and protocols; it can even extend to service equipment being placed at a particular site to ensure availability and mitigate risk of transport disruption / delays. These documents can then form part of a Contamination Control Strategy and ultimately be approved through the Quality Management System, meaning that a documented and approved response for a limit excursion is in place. This service can then equally be used for fulfilling the requirement for using rotational sporicide and HVAC disinfection.

Ecolab's Bioquell Rapid Bio Decontamination Service (RBDS) offers an outsourced solution to room level disinfection with every bio-decontamination cycle verified using Biological Indicators. Using BPR approved hydrogen peroxide vapour technology (Bioquell HPV-AQ: Approval Number EU-0027469-0000), service packages can be tailored to your requirements from a single bio-decontamination for commissioning and decommissioning through to a comprehensive package to cover a guaranteed 24-hour response for emergencies and regular bio-decontamination capabilities.

With a team of dedicated experts who cover a number of different markets, consultancy on facility remediation is also within the scope of the service enabling the definition of an efficient and efficacious service package.

Summary

Annex 1 can be a prompt to re-evaluate the existing solutions in place to ensure GMP compliance. It is also a good juncture to ensure that those solutions are compliant with the latest regulations and offer the best fit for the rapidly changing GMP environment. Using outsourced service providers enables the adoption of technology into a facility with minimal lost time to operations whilst ensuring that the technology is applied in a way that reduces risk, increases efficiency, and fits with your current, and future, ways of working.

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