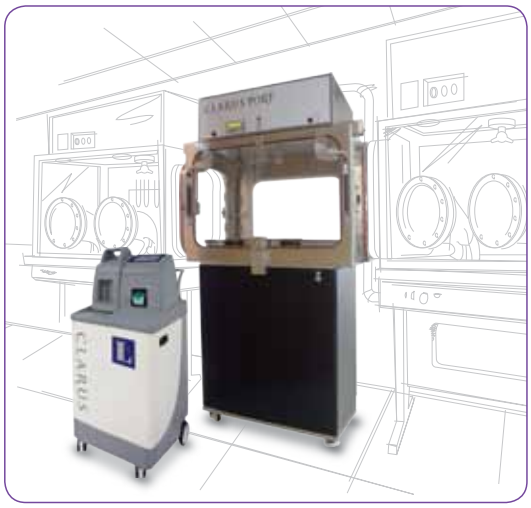

Applications and integration of hydrogen peroxide vapour for biotech/bioprocess clients

Richard Lucas, Ph.D., Bioquell UK Ltd.

The increase in size and scale of bio-processing is presenting a new challenge. Traditional methods of sterilisation, to maintain clean facilities, are becoming difficult to deploy in a controlled and regulatory compliant way.

This white paper discusses the role and requirements of a modern bio-decontamination solution. It explores the key areas that need to be considered when seeking a solution and provides an illustration of the application of hydrogen peroxide vapour bio-decontamination technology within the biological production industry.

bioquell

Hydrogen peroxide vapour as a modern bio-decontamination solution

The challenge

The utilisation of mammalian or bacterial cell lines in the production of modern drug or cellular therapies represents a considerable challenge to the maintenance of clean facilities. The very conditions required for the growth, culture and maintenance of these cellular factories present an ideal environment for the accidental culture of extraneous, undesired biological contaminants such as viruses and microbes as well as material such as spores, fungi and mycoplasma.

The increase in size and scale of bioprocessing also presents a challenge. Traditional methods of sterilisation such as steam and manual cleaning become increasingly difficult to deploy in large complex production areas in a controlled and regulatory compliant manner.

Historical perspective

Historically, production of classic small molecule drug products has predominantly been performed chemically, in an environment hostile to the presence and culture of most biological contaminants. Additionally these products are commonly amenable to terminal gamma or steam sterilisation ensuring the integrity of the product at the point of final packing or filling. Modern biopharmaceuticals present a multiple challenge when considering the need to present a safe and defined final product at the point of patient contact.

Nature of biological contamination

Biological products are manufactured in complex production lines commonly involving seeding trains, bioreactors and numerous clearing and filtration steps in order to produce the desired final product. A number of these production steps present opportunities for contamination to be introduced or even cultured alongside the desired cell line.

The contamination may be critical to process integrity or may merely reduce cell titre in seeding. However, modern in-line process monitoring and recording has raised the challenge of maintaining critical parameters across a production line to ensure batch to batch consistency in order to meet increasing levels of regulatory compliance.

Broad spectrum efficacy

Although a particular contaminant may be the specific cause for concern, a bio-decontamination method should ideally display broad spectrum efficacy against any potential contaminant thus minimising the need for additional cleaning procedures. The commonly employed *Geobacillus stearothermophilus* biological indicators are representative of the most difficult classification of organisms to kill; they are bacterial endospores and thus act as a strong surrogate for evidence of deactivation of other biological entities.

Process control and monitoring

Deployment of a bio-decontamination technique in these heavily regulated environments increasingly requires the use of controlled and monitored processes that by definition can be validated to ensure efficacy. This is in strong contradiction to the formaldehyde fumigation method of room and facility decontamination. This inherently uncontrolled and unmonitored process presents challenges in generating data on actual contact times of the biocide with the environment as well as presenting a considerable risk to the health of staff, formaldehyde being recently classified by WHO as a human carcinogen.

Material transfer

Maintenance of clean room condition is inherently dependent on appropriate operator protection and a sizable effort is employed in ensuring the workforce minimises contaminants brought into monitored environments. Of equal concern is the movement of materials into and out of clean rooms both in terms of prevention of outside contaminants entering a cleanroom through, for example, maintenance equipment, monitoring equipment and support equipment. In many instances this equipment is not amenable to steam sterilisation, for example in an autoclave.

The application of hydrogen peroxide vapour to biological production

Proactive vs. emergency decontamination of a facility

There are a number of both in-house and external benefits to carrying out a proactive decontamination, namely the preparation of plans for facility decontamination are already in place so any emergency work required following outbreak of contamination can be deployed more rapidly.

The ability to synchronise any scheduled maintenance downtime with a decontamination cycle also ensures minimisation of the risk of contamination of an area by any maintenance work while also ensuring bio-burden levels are proactively kept to an absolute minimum.

From a regulatory standpoint, having a bio-decontamination plan in place prior to any outbreak reassures the regulator that the plan of action was put together in a defined and logical manner and prior validation of the efficacy of a cycle assists in demonstrating efficacy of decontamination.

Room / facility decontamination

Over 20 years Bioquell has amassed industry leading expertise in the bio-decontamination of a wide range of facilities, including hospitals, biomedical facilities, pharmaceutical production areas and bioprocess production facilities.

This expertise coupled with the infinite scalability of Bioquell's Room Bio-decontamination Service (RBDS) allows even the largest production areas to be decontaminated as one cycle in a controlled manner ensuring rapid 6-log sporicidal kill of any contaminated zones.

Material transfer solutions

As transfer in and out of production areas comes under regulatory supervision and classical spray and wipe manual methods face the challenge of validation, Bioquell provides equipment for the rapid entry and exit of equipment and materials into and out of areas through whole solution material transfer products.

Load presentation is critical to successful validation of these processes and represents a significant part of the validation procedure for material transfer solutions; validation of 'worst case' loads ensures confidence in this critical process.

Validation

The regulatory aspects of qualification (validation) generally relate to being able to prove in a definitive way, typically by documented evidence, that the equipment complies with the specifications; that the critical parameters of the processes are under control; that the process parameters are repeatable and that there is adequate margin of safety in the process to take account of minor variations in the process performance or environmental conditions.

Nothing can be assumed. Any read-across between results must be backed up by rationale and of course all relevant data is recorded, signed and available in a suitable format. There are also requirements for training, standard operating procedures and methods of monitoring and taking corrective action as necessary.

Conclusion

Hydrogen peroxide vapour represents a rapid, integratable technique for the residue-free bio-decontamination of both routine and challenging areas within a Biotech production facility, whilst allowing maintenance of clean room integrity, protection of workforce and protection of product through integrated material transfer solutions.

For more details on hydrogen peroxide vapour systems, call +44(0)1264 835 835 or email info@bioquell.com.

bioquell

Disclaimer: Bioquell UK Ltd or its affiliates, distributors, agents or licensees (together 'Bioquell') recommends that customers ensure that the requisite level of bio-decontamination is achieved using standard biological indicators such as 6-log *Geobacillus stearothermophilus* spores; and the Bioquell technologies, subject to appropriate cycle development, are designed to be able to provide such levels of bio-deactivation.

For further information on Bioquell's technology including an up-to-date listing of the scientific papers supporting the effectiveness of Bioquell technology in the life sciences setting, or to arrange an initial consultation:

E: info@bioquell.com
W: www.bioquell.com

Bioquell UK
T: +44 (0)1264 835 835

Bioquell Ireland
T: +353 (0)61 603 622

Bioquell France
T: +33 (0)1 43 78 15 94

Bioquell USA
T: +1 (215) 682 0225

Bioquell Asia Pacific
T: +65 6592 5145

Bioquell China
T: +86 755 8631 0348

075/11