requirements for sanitization of clean rooms, and validation considerations for switching sanitizers Definitions .

Disinfectant -Substance that destroys most forms of microorganisms on inanimate objects but not necessarily spores.

Fogging -Use of a chemical, typically a sterilant, in a gaseous or vaporous state to destroy microorganisms in a facility. Also known as fumigation.

Sanitizer -Substance that significantly reduces the bacterial population on inanimate objects.

Sterilant -Substance that destroys or eliminates all forms of life on inanimate objects including vegetative bacteria, viruses, bacterial spores, fungi, and fungal spores.

Regulatory Expectations for Sanitization:
There are regulatory expectations for the periodic sanitization of clean rooms to ensure conformance to expected environmental bioburden levels though none of these explicitly require the use of fogging (2), (3), (4). For biological facilities where viral contamination is a concern, there may be regulatory reasons to sanitize via fogging with some frequency as both Annex 2 of the European Commission and the World Health Organization's GMPs for biological products mention the terms "shall" and "should" with regards to fumigation (4), (5). Many non-biologics facilities successfully meet the general regulatory expectations for sanitization through the use of only liquid sanitizers, disinfectants, and sterilants. However, fogging can be very effective and may offer advantages over the use of liquid sanitizers in certain situations (e.g. very high ceilings, inaccessible surfaces that require sanitization, etc).

Selection Criteria:
The selection of a sanitizer is complex due to the number of criteria that must be considered.

- Environment, health and safety considerations of the sanitizer, including but not limited to air emissions restrictions, toxicity of the sanitizer, and potential fire implications.
- Products need to be evaluated to ensure they will not be affected.
- The number and type of micro-organisms to be controlled must be evaluated and understood.
- The sanitizer must be able to reach all of the areas that require sanitization for the required time under the required conditions.
- The chemical must be compatible with the types of materials found in the facility.
- There must be adequate ventilation to clear any vapours generated by the chemical following use.
- The product must be able to withstand exposure to the level of residual sanitizer that may remain in the facility.
- The life-cycle cost of the use of the sanitizer should be evaluated including initial capital investment in equipment, consumables, validation, and labour.

– Corrodes heavy metals
- Oxidizing agent that may have fire safety implications

Vapor-Phase Hydrogen Peroxide
Advantages
– No residuals (byproducts are H2O&O2)
– Relatively rapid aeration following use
– Fair material compatibility
– Widespread use in pharmaceutical industry

Disadvantages
– Requires specialized equipment that may be costly to purchase and validate
– Requires control over temperature and humidity
– Corrodes heavy metals
– Does not penetrate like a gas
- Absorption/de-absorption issues
- Oxidizing agent that may have fire safety implications

Validation Requirements
Whether a liquid, gas, or vapor is chosen, a new sanitizer must be qualified according to Aseptic Area Environmental Control. The qualification should include an assessment of the number and types of microorganisms to be controlled. This could be determined either through historical review of environmental monitoring data or a special study. Once the types of microorganisms typically found in the facility are known, laboratory studies should be conducted to determine the environmental isolate that is the least susceptible to the chosen sanitizer.

For a liquid application, these studies typically involve inoculating a suspension of each test isolate into the use dilution of the sanitizer at expiration. After a set time period, the solutions are either neutralized or filtered to stop microbiocidal properties of the sanitizer and the number of survivors determined. It is critical to validate the neutralization or membrane filtration step to ensure organisms surviving at the endpoint will be recovered.

The isolate with the highest survival rate is assumed the least susceptible to the chosen sanitizer. Official methods for qualifying chemicals as sanitizers, disinfectants, or sterilants are available from the AOAC or European standards committee.

Although the user need not repeat these tests, they may be useful guides in designing laboratory studies.

For a fogging agent, lab studies are performed in a glove box or other suitable environment that allows exposure of inoculated carriers to the chemical for a set time period followed by prompt aeration, removal, or segregation to halt microbiocidal activity. The isolate showing the highest number of survivors following exposure to the chemical at the actual use concentration and environmental conditions is considered the least susceptible to the fumigant.

The organisms selected for screening should include representatives identified during

