Nitrogen Dioxide Sterilization Expands the Designer's Toolbox

Sterilization is a necessary process for virtually every type of medical device. Therefore, it is critical for designers to be mindful of how materials will interact with a given process, at what stage the sterilization will be best implemented, and other variables. With that in mind, this article highlights a sterilization process that offers more flexibility than many of the options designers may be familiar with.

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Medical devices are increasingly complex with intricate geometries, long lumens, and drug-delivery capabilities. This complexity has created challenges with compatibility between materials processed and many traditional sterilization methods. Room-temperature, nitrogen dioxide (NO_2) sterilization technology is a tool for medical device manufacturers that is helping solve these challenges. Employing NO_2 gas as a sterilant offers unique benefits over traditional sterilization techniques. The greatest benefits for manufacturers can be realized when sterilization methods are considered early in the product design process.

The Noxilizer RTS 360 Industrial NO_2 Sterilizer provides a flexible sterilization option for engineers designing complex devices and drug-device combination products.

Evaluating Sterilization Methods

Evaluating sterilization options early in the product design process and collaborating with technical experts will ensure product goals are achieved.

At the beginning of the design phase, a sterilization technique needs to be selected. The method of sterilization will impact material selection, device design, and packaging. Also, the relevant standards need to be considered.

When using a gas sterilization process (e.g., EO or NO_2), the gas path to all surfaces of the device needs to be a part of the design. NO_2 does not penetrate materials to the same degree as EO; therefore, aeration is faster. While EO can penetrate through many polymers, this comes with the cost of lengthy aeration of the products after sterilization is complete.

Radiation sterilization methods avoid the gas-penetration issue, but material might discolor or become brittle due to the radiation. Commonly used medical device materials, such as Teflon, polypropylene, and acetyl compounds, are not tolerant of radiation sterilization. However, gamma radiation is a very fast process and product can be released without waiting up to seven days for biological indicator incubation.

Most sterilization methods are performed as part of contract sterilization. Contract sterilization is a necessity for all but the largest medical device companies. Facility modifications required for EO and radiation sterilization systems can be prohibitively expensive. An effective alternative is the use of NO_2, which can be installed in-house, without facility modifications.

NO_2 Sterilization

NO_2 technology is recognized as a flexible sterilization option to safely and efficiently sterilize complex devices, materials, and drug-device combination products. Noxilizer's (www.noxilizer.com) advanced room-temperature surface sterilization process uses NO_2, in combination with humidity, to inactivate resistant microorganisms and deliver sterile product. The NO_2 process has a shorter cycle – typically less than three hours. The process operates at room temperature, with minimal vacuum, making it ideally suited for heat, radiation, and moisture-sensitive products. Additionally, there are no harmful sterilant residuals, and no lengthy post-sterilization aeration needed.

NO_2 is a well-researched gas with a favorable safety profile – non-carcinogenic and non-flammable. An NO_2 system can be safely and easily

installed in-house, in-line with assembly, enabling sterilization as a part of the production line. This makes bringing sterilization in-house easy and safe, and results in faster turnaround times, increased productivity, and reduced costs.

One important difference between terminal sterilization with NO_2 compared to EO or radiation processes is that the NO_2 process is completed after the product is sealed in the sterile barrier packaging and before loading in secondary packages (e.g., boxes). The NO_2 process is not compatible with cellulosic materials such as paper. However, sterilizing products prior to placing in large cardboard cartons increases the density of the load, in terms of devices per volume, increasing the efficiency of the process.

Device Design – Physical design, size, shape, surface texture, and geometric complexity can place constraints on sterilization options. As a non-condensing gas, NO_2 can be an excellent choice for room-temperature sterilization of challenging devices, such as lumens, needles, and similar geometries. Understanding the gas path is important as the sterilant gas needs to have access to all surfaces of the device. NO_2 sterilization process parameters can be adjusted to assist in driving the sterilant into the medical device load.

Material Selection – Noxilizer has tested a broad range of medical device materials (see sidebar), with many showing no degradation and no increase in cytotoxic response. Furthermore, NO_2 is less oxidative than other sterilants. As with all methods, NO_2 has a few material compatibility issues, however these may generally be overcome through the selection of alternative materials during the product development process.

Packaging – NO_2 sterilization is compatible with commonly used sterile barrier packaging including Tyvek pouches, Tyvek/Mylar pouches, and thermoform trays with Tyvek lids. Rapid sterilization processes are more sensitive to adhesive coatings on Tyvek. These coatings need to be evaluated during the development of the sterilization cycle. Also, labels can hinder the gas from passing through Tyvek layers. Where possible, labels should be added after sterilization.

Conclusion

The growing complexity of medical and drug delivery devices presents challenges in the selection of an appropriate sterilization process. Manufacturers with complex or sensitive products now have another tool in the sterilization toolbox. NO_2 delivers safe, room-temperature sterilization with a broad range of material compatibility and low levels of residuals using a rapid, efficient process. Considering NO_2 among sterilization alternatives early in product design will provide greatest benefits to designers and manufacturers.

NO_2 Compatible Materials*

Stainless Steel
Polyethylene
Cyclic Polyolefins (e.g., COC and COP)
Silicone
Aluminum
Polypropylene
Polycarbonate
Pharmaceutical Rubber Compounds
Gold (Plating)
Polyester (e.g., PET/PETG)
Polyetherimide (Ultem)
Two Part Epoxies (non-urethane)
Fluoropolymers
Polysulfones
PEEK / PAEK
Conformal Coatings (e.g., Parylene)
Viton (Gaskets)
PVC
Polystyrene

*This list is not exhaustive.