T E X W I P E

TechNote CRW-6

Texwipe Sterile Products:
Sterilized, Validated, Documented and Pyrogen Tested

Introduction

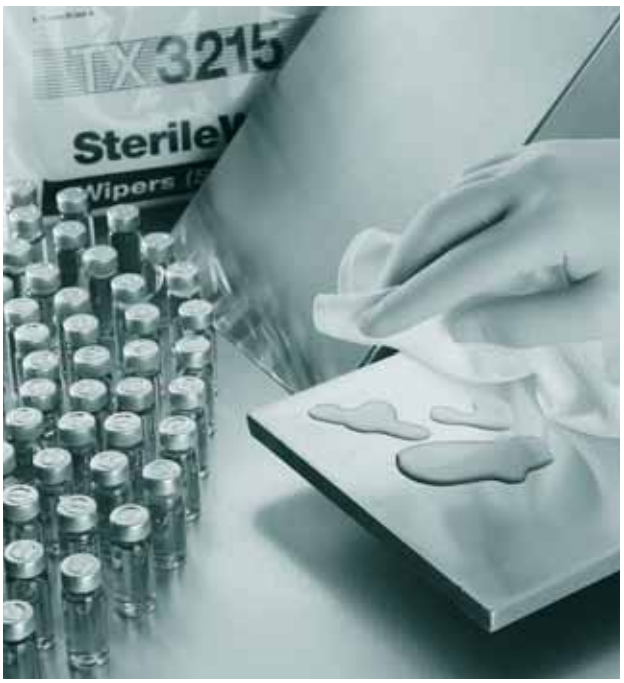
SterileWipes™ and Sterile Flexpacks were developed by Texwipe to clean sterile environments quickly and easily, without compromising the sterile nature of those environments. Although wipers are not medical devices, The Texwipe Company LLC has chosen to follow the guidelines of the Association for the Advancement of Medical Instrumentation (AAMI) concerning the validation of radiation sterilization and the requirements of the United States Pharmacopeia 23 (Supplement 1 <161> Transfusion and Infusion Assemblies and Similar Medical Devices) for endotoxin testing.

Sterilization, Validation, Documentation

Wipers are typically sterilized by gamma irradiation, electron beam, or steam autoclaving. Table 1 (see page 2) summarizes the features of gamma irradiation and electron beam sterilization.

Texwipe has chosen gamma irradiation over other sterilization techniques for the following reasons:

1. Gamma irradiation has more penetrating power than electron beam. Figure 1 (see page 2) illustrates this point.
2. Gamma irradiation is a relatively easy process to validate. This is especially important because Texwipe sterile products adhere to AAMI standards.
3. Gamma radiation leaves no residues from treatment.
4. Gamma radiation is compatible with many of the wiper materials and solutions used in Texwipe products.
5. Gamma irradiation has been shown to reduce endotoxin levels to a greater extent than electron beam irradiation. (Bacterial endotoxins, or pyrogens, are fever-causing materials from the outer cell membranes of Gram-negative bacteria. These will be discussed in more detail on page 2 of this TechNote.) Steam autoclaving does not reduce endotoxin levels.[1] Figure 2 (see page 2) depicts the reduction of endotoxin levels after gamma and electron-beam irradiation.[2]



[1]Reid. B. D., "Gamma Processing Technology: An Alternative Technology for Terminal Sterilization of Parenterals," PDA Journal of Pharmaceutical Science & Technology, Vol. 49, No. 2, 1995, pp. 83-89

[2]Guyomard, S., V. Goury, J. Laizier and J.C. Darbord, "Defining of the Pyrogenic Assurance Level (PAL) of Irradiated Medical Devices," International Journal of Pharmaceutics, Vol. 40, 1987, pp. 173-174

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Table 1

Comparison of Gamma and Electron-Beam Irradiation Techniques for Sterilization

Feature	Gamma (cobalt-60 source)	Electron-Beam
Penetration	Greater	Less (energy dependent)
Field Uniformity	More uniform (wide gamma ray field)	Less uniform (narrow electron beam)
Dose Uniformity	More uniform	Less uniform
Dose Rate	Slower	Faster
Experience	More	Less
Sterilization	Equal	Equal
Validation	Simpler	More complex
De-pyrogenation	Better	Worse

Figure 1 (below) compares the normalized dose versus depth for a product irradiated by electron beam at 10MeV energy with another irradiated by gamma rays from a cobalt-60 source. This graph illustrates the more limited penetration of the electron beam and is valid for most plastics and objects with the density of water. Electron beams penetrate only about 6 cm of water and about as deeply into 70% isopropyl alcohol/30% water solutions, since the densities are about the same. The dose from gamma irradiation is 60% of the surface dose at the depth where the electron beam dose is virtually zero.

Figure 2 (below) quantifies the reduction of endotoxin levels. At the typical irradiation dose of 25 kGy, the levels of e. coli endotoxin, as measured by Guyomard et al,[2] were reduced by almost 80% when irradiated by gamma rays, and only 10% when irradiated by electron beam.

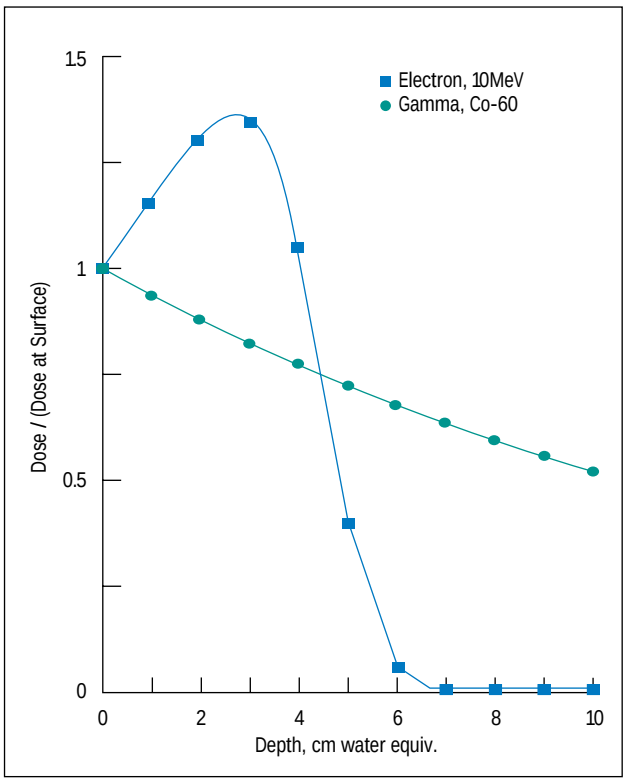

Figure 1
Dose vs. Depth Comparison of E-Beam and Gamma Sterilization

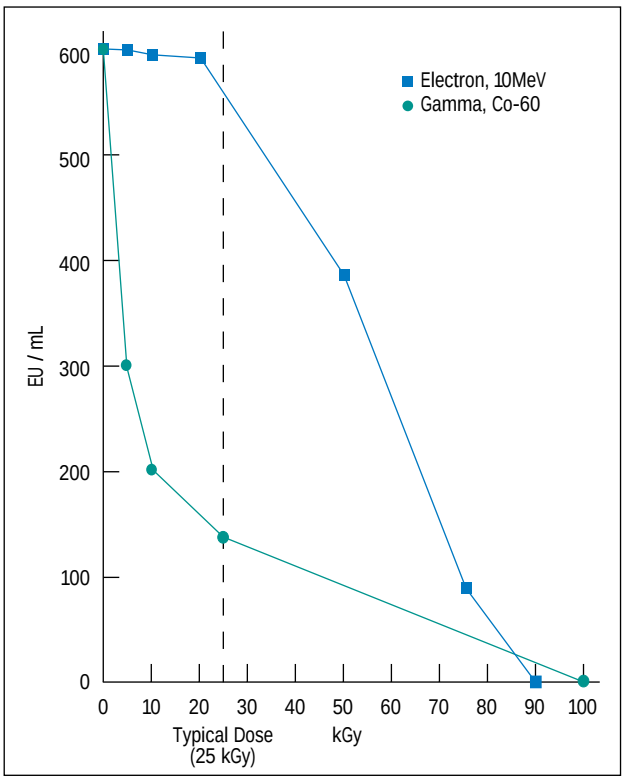

Figure 2
Effects of Gamma Rays and Accelerated Electrons on Endotoxins (E. coli dried on polystyrene)

Validation Process Overview

Since Texwipe sterile products are sterilized according to AAMI guidelines for the validation of radiation sterilization, a strict processing regimen is followed. Wipers are tested for bioburden and the data are corrected for recovery. A sub-dose validation is performed to ensure that there are no unusually radiation-resistant bacterial strains present. Once the sub-process dose validation is achieved, the products are gamma irradiated at the dose determined by the bioburden and confirmed by the sub-process dose validation. All irradiated product is supplied with a Certificate of Processing. The flow chart (Figure 3 at right) describes these steps in more detail.

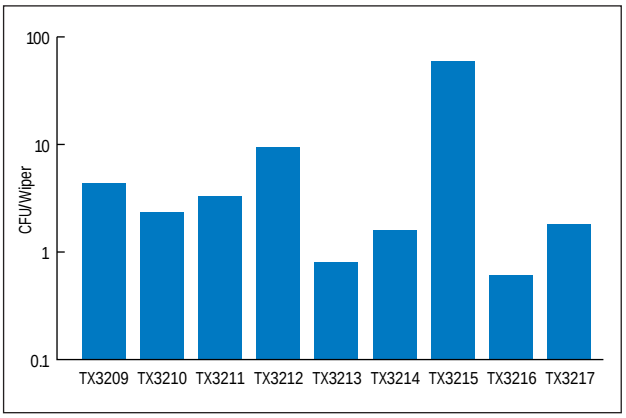

Figure 4
Corrected Bioburden Data
for Texwipe Wipers Prior to Sterilization

Table 2

Sub-Process Dose Validation Non-Sterility Test Results

(Number non-sterile from 100 samples at SAL = 10^{-2} dose)

Product	Number Non-Sterile	Number Allowed by AAMI Guidelines
TX3209	0	2
TX3210	0	2
TX3211	0	2
TX3212	0	2
TX3213	0	2
TX3214	0	2
TX3215	0	2
TX3216	0	2
TX3217	1	2

Figure 3

Sterility Validation Process

Bioburden Determination

Ten wipers from each of three different lots are tested to quantify the number of aerobic colony-forming units (cfu) per wiper. Figure 4 (this page, left column) shows the results of this testing.

Recovery Determination

Repeated extractions of each of three different wipers are performed to find the fraction of the total colony-forming units that is found from the first extraction, just as done to obtain bioburden. The bioburden data are corrected for this extraction efficiency.

Dose

A radiation dose (gamma radiation from cobalt-60) is chosen that is predicted to allow less than one in a million probability of any surviving colony-forming units on the item (Sterility Assurance Level = 1 ppm).

Sub-Process Dose Validation

This validation is done by irradiating with an appropriately lower dose, such that there is a 1/100 probability that any organisms can survive on an item, then testing 100 wipers so irradiated for sterility. AAMI indicates that if two or fewer of the 100 are non-sterile, the dose is validated. Routinely, all 100 are sterile. Table 2 (this page, left column) shows the results of this testing.

Irradiation

The product is treated and the dose monitored with dosimeters. A Certificate of Processing is returned with the irradiated lots, showing the minimum and maximum dose levels. If the minimum level exceeds that specified (calculated from the bioburden), the lots are released for sale.

Certificates of Processing and Compliance

The Certificate of Processing (also termed Certificate of Irradiation) accompanies the irradiated product. This must show that the dose levels were above the minimum determined by the bioburden assessment and validated by the sub-process dose sterility determinations, which are done by outside laboratories in accordance with ANSI/AAMI ST32-1991.

Vendor Audits

Vendor audits are done periodically by checking the bioburdens of the wipers, the records of irradiation, and the sterility of the wipers after sub-process dose irradiation.

Pyrogen Testing

Bacterial endotoxins, or pyrogens, are fever-causing materials from the outer cell membranes of Gram-negative bacteria. Most bacteria in clean water are Gram-negative. When the bacteria die, endotoxin is released into the water. An example of Gram-negative bacteria that we are all familiar with is *e.coli,* often found in contaminated water. Minute levels of these bacterial toxins are associated with certain bacterial diseases and the production of fever, shock, and death in humans and animals.

Removing pyrogens from contaminated samples is extremely difficult. Sterilization techniques kill living organisms, and since pyrogens come from dead cells, standard sterilization techniques, with few exceptions, are not effective in reducing pyrogen levels. Prevention of bacterial contamination is the best course of action to ensure high-quality products. Therefore, it is essential to ensure that the materials used during the production of the parenteral drug or medical device do not contribute to the pyrogen levels.

The allowable limits of endotoxins in human and animal parenteral drugs, biological products and medical devices are established by the FDA. Texwipe SterileWipes and Sterile Flexpacks conform to the requirements of the United States Pharmacopeia 23 (Supplement 1 <161> Transfusion and Infusion Assemblies and Similar Medical Devices). This limit, applied to devices in contact, either directly or indirectly, with the cardiovascular system or lymphatic system, has been set at less than 20 endotoxin units/device (<20 EU/device).

Test Method

The widely used assay method for bacterial endotoxins is based on the blood cell extract, or amebocyte, from the horseshoe crab (*Limulus polyphemus*). Much like a human donates blood, the horseshoe crab "donates" some of its blood, which is broken down into its components, plasma and amebocytes. The LAL (*Limulus amebocyte lysate*) is produced by lysis (rupture) of these amebocytes, and the LAL reagent is a mixture of proteins and salts whose origin is the amebocyte. The LAL test is an effective measure of endotoxin levels as it is extremely sensitive. The typical gel clot test is capable of detecting endotoxin levels as low as 0.03EU/mL (about 0.003ng/mL or 0.003 parts per billion).

As outlined in USP 23, the test method includes the following steps:

1. Between three and ten wipers are extracted with LAL Quality Water (USP Water for Injection).

2. A standardized LAL reagent is mixed with the test samples and heated.

3. A firm gel is formed if the concentration of endotoxin exceeds the reagent labeled sensitivity.

continued on page 5

Table 3

Endotoxin Test Results for Wipers

Product Name	Substrate	Endotoxin Level
SterileWipe™ HS (TX3209)	Polypropylene-cellulose-polypropylene composite	<20 EU*/wiper
SterileWipe™ HS II (TX3210)	Polyester-cellulose blend	<20 EU/wiper
SterileWipe™ LP (TX3211)	Polyester	<20 EU/wiper
SterileWipe™ LP 10 (TX3212)	Sealed-edge polyester	<20 EU/wiper
Sterile PolySat™ (TX3213)	Polypropylene pre-wetted with 70% IPA/30% DIW**	<20 EU/wiper
Sterile TechniSat™ (TX3214)	Polyester-cellulose blend pre-wetted with 70% IPA/30% DIW	<20 EU/wiper
SterileWipe™ AS 10 (TX3215)	Sealed-edge polyester	<20 EU/wiper
Sterile PolySat (TX3216)	Polypropylene pre-wetted with 70% IPA/30% DIW	<20 EU/wiper
Sterile TechniSat (TX3217)	Polyester-cellulose blend pre-wetted with 70% IPA/30% DIW	<20 EU/wiper

*EU = endotoxin unit

**IPA = isopropyl alcohol; DIW = deionized water

Further, a validation assay is performed in the following manner:

1. The reagent is tested against an endotoxin standard, with serial dilutions.

2. The extracts are tested to assure they do not inhibit or enhance the formation of the gel when endotoxins are present.

3. This validation assay is performed in quadruplicate.

Test Results

Although wipers are not considered medical devices and are not required to conform to USP 23 standards, the test results in Table 3 (see page 4) indicate that Texwipe Sterile products do meet a standard of <20 Endotoxin Units/wiper.

Conclusion

Texwipe SterileWipes and Flexpacks are irradiated to a probability of Non-Sterility (also called Sterility Assurance Level) of 10^{-6} in accordance with AAMI standards and are tested for pyrogen levels per USP 23. This ensures the highest quality of wiper products available for cleaning and disinfection of equipment and environmental surfaces under sterile conditions. These products are ideal for cleaning pharmaceutical aseptic filling areas, sterile suites, prep rooms, microbiological laboratories, and biotech manufacturing facilities.

For additional information, please contact Texwipe Customer Support at one of the numbers listed below.

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