TECHNICAL TIP

GAMMA STERILIZATION VALIDATIONS $VD_{MAX}25$ AND METHOD 1:FREQUENTLY ASKED QUESTIONS

The Association for the Advancement of Medical Instrumentation (AAMI) generates numerous standards used by professionals in the medical device industry. Occasionally, the AAMI Standards board provides additional guidance to specific standards in the form of a Technical Information Report (TIR). These TIR's reflect common industry practices that evolve from an accumulated process knowledge base.

When gamma irradiation is selected for product sterilization, the dose at which the product is irradiated must be established and validated in accordance with appropriate AAMI standards. ANSI/ AAMI/ISO 11137: 2006 Sterilization of health care products- Radiation and ISO TS 13004. Sterilization of Healthcare Products Radiation - substantiation of a selected sterilization dose method VDmax SD Sterilization of health care products-Radiation -Substantiation of a selected sterilization dose- Method VDmax25 kGy as a sterilization dose-Method VDmax, provide are established methods for completing a validation process.

FAQs:

Which validation is right for me?

The $VD_{max}25$ option (formerly TIR27, now in 11137: 2006) is convenient when a company wants several product lines sterilized at the same minimum dose, when product is expensive to make, or for companies with markets where a 25 kGy dose is the accepted standard. Furthermore, the validation is less expensive because fewer tests are necessary. Bioburden counts must be 1000 CFU or less.

Method 1 (from 11137-2) determines the lowest sterilization dose necessary for the determined bioburden population. This Method should be used when the lowest possible sterilization dose is desired due to cost considerations, use of gamma sensitive materials, or when the bioburden count is above 1000 CFU.

If one of these validations establishes my minimum dose, how do I establish a maximum dose?

Performed early in product qualification, materials can be screened for compatibility with irradiation. Pre- and postirradiation properties related to functionality and appearance must be evaluated to determine maximum dose. Irradiating your product at a dose approximately 2.0 times that of the minimum (or greater), then testing the product's form, fit, and function, is an excellent way to establish maximum dose. Setting the maximum dose as high as possible allows the greatest flexibility in processing schedules when product is ready for routine sterilization. Accelerated aging and package testing are additional tests to be considered for product irradiated at the maximum dose.

Why is the verification dose experiment performed at a lower SAL than the sterilization dose?

In order to test a dose for SAL 10-6, one million products would need to be irradiated and sterility tested. SAL 10-2 (Method 1) or SAL 10-1 (VD_{max}) is used because only 100 or 10 products, respectively, must be used for the experiment.

What if my product sample is dosed at less than 90% of the target verification (sub-lethal) dose?

If the sterility test exhibits a failing number of positive tests, the verification dose experiment can be performed again and samples re-tested.

What if my product sample is dosed greater than the target verification (sub-lethal) dose plus 10%?

This is considered an overdose. During a verification (sublethal) dose experiment, it is not permissible to irradiate over 10% above the target. Do not sterility test the samples. Send new samples for irradiation prior to sterility testing.

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Do I need a Biological Indicator?

Bacillus pumilus, a spore-forming microorganism, served for many years as a biological indicator to test for sterility. Its use today has been discontinued. BIs also do not accurately represent natural form of bioburden on a product (spore strip vs. actually in or on product as a result of manufacture). Detailed methodology has been developed and publicized in ISO 11137-2 to determine minimum radiation dose to achieve a sterile product.

What are the basic steps?

For both types of validations, the first step is identical: Have bioburden testing performed on 10 products from three different batches, for a total of 30 products.

METHOD	ANSI/AAMI/ISO 11137 METHOD 1	ANSI/AAMI/ISO $VD_{max}25$
Find Sub-Lethal (Verification) Dose	Use Table 5 to find sub-lethal dose (SAL 10^{-2})	Use Table 9 to find sub-lethal dose (SAL 10^{-1})
Sub-Lethal (Verification) Dose Irradiation	Irradiation 100 product units at sub-lethal dose (+/- 10%)	Irradiation 10 product units at sub-lethal dose (+/- 10%)
Test of Sterility	Sterility test irradiated products	Sterility test irradiated products
Passing Criteria	Two or fewer positives out of 100	One or zero positives out of 10
Identify Minimum Sterilization Dose	Find appropriate minimum sterilization dose for desired SAL (10-6/10-3) in Table 5	Validate for minimum sterilization dose of 25 kGy
Routine Irradiations	Begin routine irradiations at sterilization dose	Begin routine irradiations at 25 kGy

Are there other options for dose setting besides VDmax25 and Method 1?

Yes. Contained in 11137-2 and ISO TS 13004 are additional methods including Method 2 (incremental dosing) and VD_{max} for selected doses of 15-35 kGy (in 2.5 kGy increments). Each method has specific limitations and requirements that must be fully investigated before selection.

Definitions:

Bioburden:

Population of viable microorganisms on a product. In the context of irradiation sterilization, bioburden is determined immediately prior to sterilization. The unit of measurement is CFU: Colony Forming Unit.

Test of Sterility:

Technical operation performed as part of development, validation or re-qualification to determine the presence or absence or viable microorganisms on product or portions thereof.

Sterility Assurance Level (SAL):

Probability of a viable microorganism being present on a product unit after sterilization. Normally expressed as 10-n, the SAL at a particular sterilization dose estimates the likelihood of one positive sterility test out of a total of 10n sterility tests.

Recovery Efficiency:

Measure of the ability of a specified technique to remove microorganisms from product.

Bacteriostasis/Fungistasis Testing (B&F):

Test performed with selected microorganisms to demonstrate the presence of substances that inhibit the multiplication of these microorganisms. This must be retested if any changes

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are made to the product. It is recommended that even without changes that the test be repeated every 1-3 years to account for any changes in raw materials or suppliers. The number of samples required for this testing should be confirmed with the laboratory performing the testing (usually 3-6).

REFERENCES

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2. ANSI/AAMI/ISO 11137-2:2006. Sterilization of health care products-Radiation-Part 2: Establishing the sterilization dose

3. ANSI/AAMI/ISO 11137-3:2006. Sterilization of health care products-Radiation-Part 3: Guidance on dosimetric aspects

4. AAMI TIR 33:2005. ISO TS 13004. Sterilization of Healthcare Products Radiation - substantiation of a selected sterilization dose method VDmax SD

5. AAMI/ANSI/ISO 11737-1: 2006. Sterilization of Medical devices-Microbiological methods-Part 1: Estimation of the population of microorganisms on product

6. AAMI/ANSI/ISO 11737-2:1998. Sterilization of Medical Devices-Microbiological Methods-Part 2: Tests of Sterility Performed in the Validation of a Sterilization Process

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