

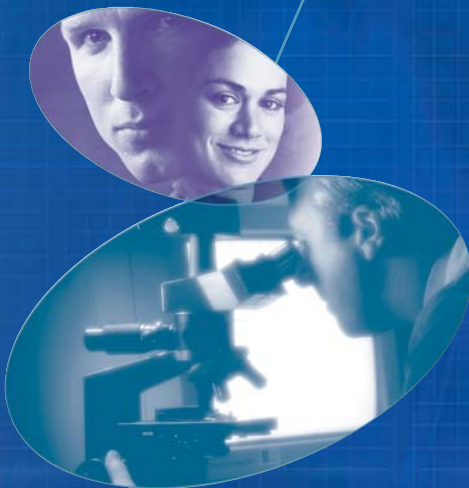


LABORATORY ACCELERATOR BEAMS ETO GAMMA

MICROBIOLOGICAL ASPECTS FOR

- CONSERVATION
- DECONTAMINATION
- STERILIZATION

OF PRODUCTS BY MEANS
OF GAMMA RADIATION



CUSTOMER FOCUSED · QUALITY ASSURED

EFFECTS OF IONISING RADIATION ON MICROORGANISMS

During manufacturing, micro-biological contamination can affect your products. The sources of contamination are the employees, work surfaces, machine installations, raw materials, components and air.

Whether the bacteria adhere to your product, remain viable or even multiply, depends on their characteristics and environmental demands as well as on the surface and the type of material in the product.

Many products must be disinfected before use. Depending on their sort and application, the goal will be preservation, decontamination or sterilization.

Sterile is defined as: 'Free of viable microorganisms'. For healthcare products this concept is expressed as the theoretical probability of the survival of microorganisms.

Gamma radiation is a frequently used sterilization method. Gamma radiation has a direct or indirect effect on vital molecules and structures in the nucleus of the microorganism.

Applying a sufficiently high dose, the damage will be so substantial that the organisms are rendered no longer viable. The radiation resistance of specific microorganisms is referenced as the D_{10} value.

This is the irradiation dose that is necessary to reduce population of bacteria by 90%. Gram-negative bacteria are usually substantially more sensitive to radiation than fungi and yeasts (D_{10} value <1.2 kGy). Certain spore forming bacteria are also resistant to radiation (D_{10} value up to 3 kGy).

The environmental conditions under which the irradiation takes place, can exert influence on the eliminating effect:

- In a humid environment including oxygen, most of the bacteria will be eliminated more efficiently than in a dry environment without oxygen
- Bacteria and yeasts can be up to two or three times more sensitive in an oxygen rich environment compared to an environment with little oxygen





STERILITY AND SAL

The ability to inactivate the microbial contamination of a product does not solely depend on the absorbed dose of radiation, but also on the quantity and the resistance of the bacteria present. The differences in resistance of the microorganisms arise because of the differences in composition and structure of the cells.

Below are some D_{10} values of typical contaminants.

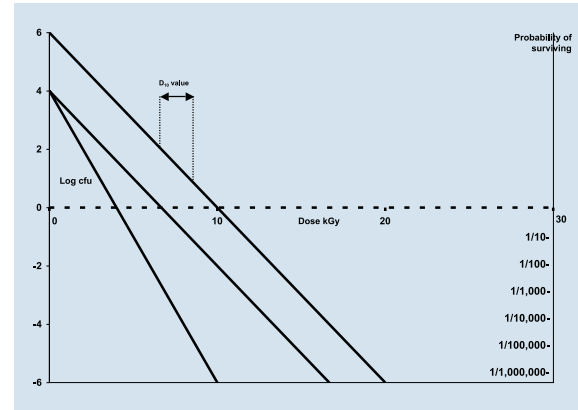
Microorganism	D_{10} value in kGy
Clostridium perfringens	1.2 - 2.0
Clostridium botulinum	1.2 - 3.3
Bacillus subtilis	0.6
Bacillus pumilus	3.0
Lactobacillus brevis	1.2
Micrococcus radiodurans	2.2
Streptococcus faecium	2.8
Staphylococcus aureus	0.2
Aspergillus niger	0.5
Penicillium notatum	0.2
Torulopsis candida	0.4
Pseudomonas spp.	0.03 - 0.1
Salmonella typhimurium	0.2
Escherichia coli	0.1

For CE-marked medical devices, that are sterilized in the final packaging, the harmonized Standard EN 556 (Sterilization of Medical Devices – Requirements for Medical Devices to be designated sterile) requires the attainment of a SAL (Sterility Assurance Level) of at least 10^{-6} for a product to be labelled sterile. This means that the theoretical probability of survival must be smaller than or equal to 1 to a million.

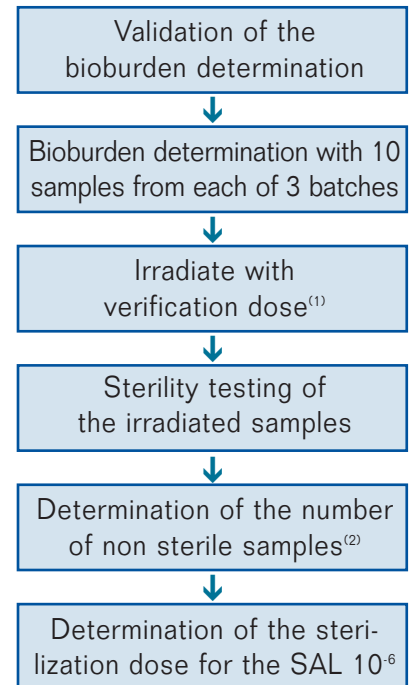
The term Sterility Assurance Level (SAL) stands for probability of a single viable microorganism occurring on an item after sterilization.

In order to secure a safe sterilization process, it is necessary to have information regarding the bioburden of the product, the number and their radiation resistance.

High bioburden consisting of resistant microorganisms increases the demand for an efficient sterilization process. That is why it is important to maintain low and consistent numbers of bioburden during manufacture.



Validation procedure: Method 1 and VD_{max} method



⁽¹⁾ Method 1: 100 samples
 VD_{max} method: 10 samples

⁽²⁾ Method 1: maximum 2 samples may be positive (not sterile)
 VD_{max} method: maximum 1 sample may be positive (after successful confirmatory test)

MICROBIOLOGICAL VALIDATION

The international Standard ISO 11137-2:2006 describes various methods to validate the minimum sterilization dose.

These methods include:

- **Method 1 "Using bioburden information"**

Information must be obtained regarding the number of the microorganisms on or in a product (Bioburden determination). This is then compared to a standard distribution of resistances (SDR) to determine the minimum sterilization dose.

- **Method 2 "Using fractional dose irradiation"**

Information must be obtained regarding the resistance to radiation of the microorganisms as they occur on the product. This data is then used to calculate the minimum sterilization dose.

- **VD_{max} method "Substantiation of 15 and 25 kGy"**

This method involves the selection of the minimum sterilization dose (either 15 or 25 kGy) then laboratory testing to demonstrate that a SAL 10⁻⁶ has been achieved with the selected minimum sterilization dose. The following limits on allowable numbers of bioburden apply 15 kGy < 1.5 cfu (Colony Forming Units) per product unit 25 kGy < 1,000 cfu per product unit.



Validation procedure: Method 2

Irradiation of 20 samples from each of three batches at 9 incremental doses



Individual sterility testing of each sample



Record number of sterility failures at each dose level



Determine the verification dose and the batch to which it is applied



Irradiate with verification dose



Individual sterility testing of each of the 100 samples



Record the number of failures



Calculate the minimum sterilization dose



Product units are required 840 in total, of which 640 are tested



OUR SERVICES



Determination of the contamination level

- Determination of the number of microorganisms
- Determination of the total number of microorganisms on food, raw materials and cosmetic products including aerobic and anaerobic bacteria, spores and fungi
- Bioburden determination on healthcare products and packaging materials including aerobic and anaerobic bacteria, spores and fungi
- Bacterial characterization and identification

Microbiological validation of sterilization process

- Microbiological validation of irradiated sterilization
- ISO 11137-2:2006, method 1 and 2
- ISO 11137-2:2006 method VD_{max} (15 and 25 kGy)
- Revalidations (Periodic Dose Audits)
- Bioburden Monitoring

LAL/Pyrogen tests

- LAL/Pyrogen determination on endotoxins: gel clot and turbometric method

Accelerated ageing tests

- Artificial ageing tests, standard temperature of 55 °C held for up to 5 years

Other services

- Consultancy services
- Drafting validation plans
- Microbiological monitoring of production areas

- **GAMMA**
- **ETO**
- ▲ **ACCELERATOR BEAMS**
- ◆ **LABORATORY**



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