STERILIZATION OF MEDICAL DEVICES:

VALIDATION OF RADIATION STERILIZATION

BGS
IDEEN PLUS ENERGIE

CONTENTS:

1. INTRODUCTION

The medical technology industry is regarded as fast-growing, future-oriented and innovative. According to the medical technology association BVMed, German manufacturers of medical equipment achieve approximately one third of their turnover with devices that are not older than three years.[1] Based on estimates of the Federal Ministry of Health, there are about 400,000 different medical devices in total.[2] Apart from devices for diagnostics, surgery and intensive medicine, examples also include implants, bandaging material, operating material and laboratory diagnostic products. For many of these devices, as well as for pharmaceutical primary packaging material and bioreactors, sterility is a mandatory prerequisite for placing such devices on the market. To this end, it is important to take into account the sterilization procedure already in the design phase of the device, since the choice of the method is, amongst other things, closely associated with a number of issues concerning materials and always presupposes a validation of the device.

1. cf. BVMed Branchenbericht Medizintechnologien 2020 (industry report medical technologies), May 2020
2. ibid

Based on the special technology as well as the expense for the operation of the corresponding facilities, sterilization processes are generally outsourced to specialized service providers. Overall, a trend towards radiation sterilization has become apparent in Germany in the past years due to the benefits of the process in relation to its convenience and cycle times. Sterilization is carried out particularly frequently using gamma rays and increasingly also beta rays. X-ray sterilization is in the early stages of development. The necessary steps for the validation of radiation sterilization are complex as with all methods of sterilization and require close cooperation between the manufacturer and the sterilization provider.

It should also be noted: Whenever changes are subsequently made to the device itself or its manufacturing process, these must be assessed by the manufacturer; under certain circumstances, a revalidation of the selected method will have to be carried out. Also for strategic decisions to reduce failure risks and supply gaps – for example, the double qualification of the device for a further facility or an additional sterilization provider – a validation of the method is imperative.

For the manufacturer, validation processes are often associated with numerous questions: How time-consuming is the process and which steps are generally necessary? Which resources are required? What has to be undertaken specifically if a product is to be validated for a second facility? And: What has to be observed when changing from another method of sterilization to radiation sterilization?

How is sterility for medical devices defined?
The DIN EN 556-1 standard defines a medical device to be sterile if the theoretical probability of finding a viable reproducible germ on the product is less than 1:1,000,000. It can therefore be noted: There is no such thing as absolute sterility!

2. STERILIZATION AS FINAL STEP IN PRODUCTION

Sterility is indispensable in medical diagnostics and for medical devices, such as implants or disposable products for the operating theatre (catheters, cannulas, stents, wound coverings). But even using the greatest hygienic care and controlled production processes in the clean room, it is not possible to produce a sterile product. In order to achieve a sterile state, devices have to undergo a subsequent sterilization process.

To transpose devices into a sterile state, different processes and technologies have established themselves. A validation process precedes each sterilization.
This is required when

- → a device is launched on the market,
- → a second facility or second supplier is qualified while maintaining the chosen method of sterilization, as well as
- → a change is made from an established method to another method of sterilization.

What do validation and verification mean?
Validation is a complex process in the course of which proof is furnished that the normative demands made on the manufacturing of a medical device are fulfilled. In turn, by means of verification, it is confirmed that the initially established demands from the validation continue to be fulfilled (see also DIN EN ISO 11139).

3. CHOICE OF STERILIZATION METHOD: WHICH DEVICES CAN BE STERILIZED USING RADIATION?

Different methods are available to sterilize devices. Among the most common is the sterilization with beta and gamma rays. In addition, sterilization can be carried out using chemical procedures, for example, by exposing the devices to ethylene oxide or heat. When a new device to be sterilized is being designed, it first has to be clarified whether the method of radiation sterilization can be applied. The same applies when changing from another established method of sterilization to radiation sterilization. When evaluating this, amongst other things, the materials used, the technical design, the functionality, packaging, and the packaging scheme of the device play an important role. The simpler the design of a device, the smoother the validation process will be.

Beta and gamma rays enable the sterilization of plastic products and a diverse range of other materials in their sealed final packaging. Another advantage of radiation sterilization is that the products can be placed on the market directly after the treatment, which in turn means substantial time saved. The irradiation is residue-free and takes place without any mentionable increase in temperature. Since the entire device is irradiated, radiation sterilization is also recommendable in the case of complex geometries, whereby irradiation with electrons has some limitations depending on the structure and density of the device. Sterilization using rays is not suited for devices containing microelectronic components. In the case of polymers, it is necessary to check their resistance towards ionising rays which can result in discolouration or even a reduction of functionality. In this context, particular problems arise with PTFE and polyacetals such as POM (please see table 3).

4. TECHNICAL BASICS: PRINCIPLE OF IRRADIATION WITH BETA AND GAMMA RAYS

Irradiation causes damage of the DNA in the nucleus of microorganisms. In this way, they reliably lose their ability to reproduce or die; the devices become sterile. Undesirable crosslinking or degradative side reactions of macromolecules may occur, e.g. in polymer materials of the medical device or the packaging. Both technologies follow this principle, whereby there are differences between beta and gamma rays as listed in the following table.

Tabelle 1: Technological differences between electron radiation and gamma rays

Parameters	Electron radiation	Gamma rays
Dose rate	high	low
Depth of penetration	medium	very high
Irradiation time	a few seconds	several hours
Energy source	Electric current	Cobalt-60
Irradiation unit	Single cartons	Pallets
Description of procedure	Electrons are emitted in a hot cathode and then accelerated to a very high velocity in a high-vacuum by means of a strong electric field. Upon leaving the accelerator, the electron beam is deflected by a magnetic field onto the product in lines at a high frequency.	Gamma rays are created through the decay of a radioactive isotype, e.g. Cobalt-60. The rays have a high penetration depth and penetrate entire pallets or lots. Individual sources of Cobalt-60 are arranged and integrated into the source rack, by which means a unique radiation field is generated. The products to be sterilized are transported through this radiation field via a fixed pre-specified path. In the process, the necessary radiation dose is emitted into the product.

5. VALIDATION OF RADIATION STERILIZATION

The path to a sterile product requires validation and the radiation sterilization processes are regulated by the procedural standard DIN EN ISO 11137. The validation is divided into three stages:

- → the microbiological,
- → the dosimetric and
- → the application-related validation.

These stages are interdependent and require a close exchange of expertise between the manufacturer and service provider. The three stages of validation are described more closely in the further course of the paper.

5.1 MICROBIOLOGICAL VALIDATION

The microbiological validation is used to determine the radiation dose that transposes a non-sterile device into a sterile one. For this purpose, the initial microbiological condition is first determined on representative samples, this means the number and type of microorganisms.

In the course of the second part of the microbiological validation, further sample items are subsequently irradiated with the dose known as the verification dose. This serves to furnish proof that all pieces can be transposed to a sterile condition using this dose.

To this end, different methods can be chosen which are described in the second part of the DIN EN ISO 11137 standard.
A distinction is made amongst the following procedures of microbiological validation:

- → Method for Procedure 1:
- → Method for Procedure VD_{max}^{15} and VD_{max}^{25}
- → Method for Procedure 2

The method applied is dependent, for example, on

- → the bacterial count and the initial microbiological situation,
- → production conditions (degree of automation, production environment/clean room production/manual work),
- → materials selection (use of natural materials with a higher preliminary microbial load, such as cotton, or synthetic materials like plastics),
- → batch size and production quantities (constant production, units)
- → and also the costs.

IMPORTANT: The manufacturing of devices should take place under supervised and controlled conditions. The permissible fluctuation of the bioburden has to be defined.

Prior to revising the standard in 2006, Procedures 1 and 2 were the standard methods. The Procedures VD_{max}^{15} and VD_{max}^{25} have been added as new methods in the course of updating the standards. The latter are applied most frequently, since the first determination of a standard irradiation dose of 15 kGy (VD_{max}^{15}) or 25 kGy (VD_{max}^{25}) is possible at considerably reduced costs and testing efforts. Procedure 1 is the second most frequently used method. Instead, Procedure 2 is only seldom chosen due to the high effort and expense.

The following overview explains the essential differences between the three methods:

- → **Method for Procedure 1: Determination of dose using the bioburden**
  In Procedure 1, it is important to estimate how resistant the microbial population on the device is to irradiation. The tables set down in the DIN EN ISO 11137-2 standard specify this correlation. Corresponding to the average bioburden of a product, relevant dose rates are stated in these tables, which

* SAL means Sterility Assurance Level

guarantee a certain sterility assurance level (SAL*) in the case of standard resistance distribution in the microbial population.

In the case of Procedure 1, a SAL of 10^{-2} is chosen for the test with the verification dose. This means the validation can be recognised following irradiation of the devices with the relevant verification dose, if a maximum of two devices out of 100 show a positive result in the sterility test (i.e. are non-sterile).

In this case, the germs found on the device are equally or less resistant to the irradiation treatment. If validation is successful, the required dose for routine radiation that guarantees a SAL of 10^{-6} can likewise be taken from the tables. The exemplary sequence of steps using this method is briefly described later on in the white paper.

→ **Method for Procedure VD_{max}^{25}: Confirmation of a selected sterilization dose**

Similar to Procedure 1, it is also important in the VD_{max}^{25} procedure to estimate whether the microbial population on the device is equally or less resistant to irradiation compared to the test. The tables of the DIN EN ISO 11137-2 standard are also used here for evaluating the dose. In the case of the VD_{max}^{25} method, a SAL of 10^{-1} is selected for the test with the verification dose. This means the validation can be declared successful, if following irradiation of the devices with the relevant verification dose, a maximum of one device out of ten shows a positive result in the sterility test (i.e. is non-sterile).

In this case, the germs found on the device are equally or less resistant to the irradiation treatment. If validation is successful, a sterilization dose of 25 kGy is sufficient to guarantee a SAL of 10^{-6}. This method makes it possible to realise validation at considerably less cost since only ten devices have to be tested for sterility in the dose experiment rather than 100 individual irradiated product units. A further difference of the method VD_{max}^{25} to method 1 is a limit of the average bioburden of 1,000 colony-forming units (CFU) per product unit.

The exemplary sequence of steps performed in this method will also be briefly described later on in the white paper The steps of Procedure VD_{max}^{15} are comparable to those of Procedure VD_{max}^{25}. The main difference here is a limit of the average bioburden of 1.5 colony-forming units (CFU) per product unit.

→ **Method for Procedure 2: Determination of dose through extrapolation**
Procedure 2 is seldom used due to its high complexity and the associated cost and effort of the validation. In this procedure, information about the resistance of the germs is gathered such as the germs that are actually on the products. In the process, 280 product units are irradiated with gradually increased doses. Following successful irradiation, these 280 product units undergo a sterility test on an individual basis. For each dose level, the number of positive tests are subsequently determined. In the case of an increasing dose, the number of detected positive sterility tests decreases accordingly. This result reflects the resistance of the product-specific germs to irradiation. In the further course, a dose range is determined based on which a further 100 samples will be irradiated. This is the actual dose verification test. Following irradiation, these 100 samples also undergo a sterility test. The validation can be recognised following irradiation of the products with the relevant verification dose, if a maximum of two devices show a positive result in the sterility test (i.e. are non-sterile). This is equivalent to a SAL of 10^{-2}. The sterilization dose is then determined by means of an equation.

Compared to the method in Procedures 1 and VD_{max}^{25}, the bioburden is not determined outside of routine monitoring.

Table 2: Procedure overview of selected microbiological validations

Procedure	Sample number for determining bioburden	Sample number for irradiation with VD/ sterility test*	Limits/values [CFU]
Procedure 1	3 x 10 pieces 10 per batch 3 batches	Table 5, 6 **100 pieces** from one batch **SAL 10^{-2}**	0.1–1,000,000
VD_{max}^{15}	3 x 10 pieces 10 per batch 3 batches	Table 10 **10 pieces** from one batch **SAL 10^{-1}**	max. 1.5
VD_{max}^{25}	3 x 10 pieces 10 per batch 3 batches	Table 9 **10 pieces** from one batch **SAL 10^{-1}**	max. 1,000
Procedure	**Sample number for irradiation with staggered doses**	**Sample number for irradiation with VD/ sterility test**	**Limits/values [CFU]**
Procedure 2A Procedure 2B	3 x 180 pieces 180 per batch 3 batches	**100 pieces** from one batch **SAL 10^{-2}**	1–1,000,000 0.1–1.5

* cf. DIN EN 11137-2

EXEMPLARY PROCEDURE FOR MICROBIOLOGICAL VALIDATION BASED ON PROCEDURE 1:

In order to determine the bioburden using this method, ten samples each from three different production batches are examined.

Following the evaluation of these 30 individual tests, an overall average burden of all batches is determined. According to table 5 of DIN EN ISO 11137-2, a verification dose for a SAL 10^{-2} can consequently be determined. In the following verification dose experiment, 100 individual devices are irradiated with the established verification dose in defined, very narrow limits. In doing so, the actual dose is not allowed to deviate from the verification dose by more than 10 percent. Afterwards, the 100 irradiated samples undergo a sterility test. The validation can then be recognised, if no more than a maximum of two test results show positive in the sterility test of the examined samples (non-sterility). The sterilization dose which has to be routinely achieved at a minimum can be derived from table 5 from DIN EN ISO 11137-2. Here the sterilization dose is chosen which is necessary to achieve the stipulated SAL.

EXEMPLARY PROCEDURE FOR MICROBIOLOGICAL VALIDATION BASED ON PROCEDURE VD_{MAX}^{25}:

In order to determine the bioburden using this method, ten samples each from three different production batches are examined.

Following the evaluation of these 30 individual tests, an overall average bioburden is determined. According to table 9 of DIN EN ISO 11137-2, a verification dose for a SAL 10^{-1} can consequently be determined. In the following verification dose experiment, ten more non-sterile product units will be irradiated with the verification dose determined. In doing so, the actual dose is not allowed to deviate from the verification dose by more than 10 percent. Afterwards, the ten irradiated samples undergo a sterility test. The validation can then be recognised, if no more than a maximum of one test result shows positive in the sterility test of the examined samples (non-sterility).

The method for Procedure 2 deviates from these steps described above. For more details, please see table 2.

5.2 DOSIMETRIC VALIDATION

The goal of the dosimetric validation is to describe the dose distribution in relation to a defined product arrangement in the packaging during irradiation. As results of this test, the positions of the minimal and maximal dose and the adjustment factors for the routine irradiation process are determined, while taking customer requirements into account.

The following preliminary considerations are applied for the dosimetric validation and have to be defined:

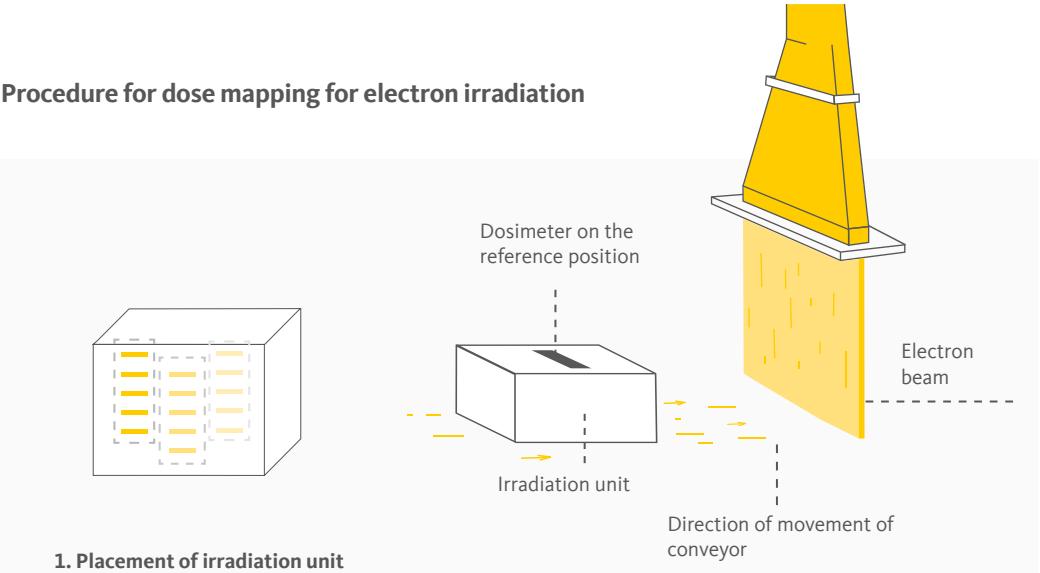
- → Number of dose mappings to be carried out
- → Product (single article/processing class)
- → Alignment of devices in the radiation field
- → Evaluation of partial loads
- → Packaging
- → Arrangement of the product in the packaging

Results arising from determining the dose distribution are:

- → Positions of maximum doses
- → Positions of minimal doses
- → Release limits for routine dose measuement to calculate the minimal and maximum dose
- → In the case of multiple measurements, the statistical evaluation of individual results

Procedure for dose mapping for electron irradiation

When irradiating the device with accelerated electrons, dose mapping is carried out on individual transport cartons as these represent the final irradiation unit.



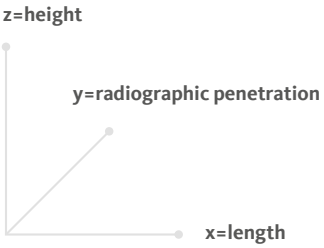
1. Placement of irradiation unit with dosimeters (yellow) in selected areas over the entire height of the carton

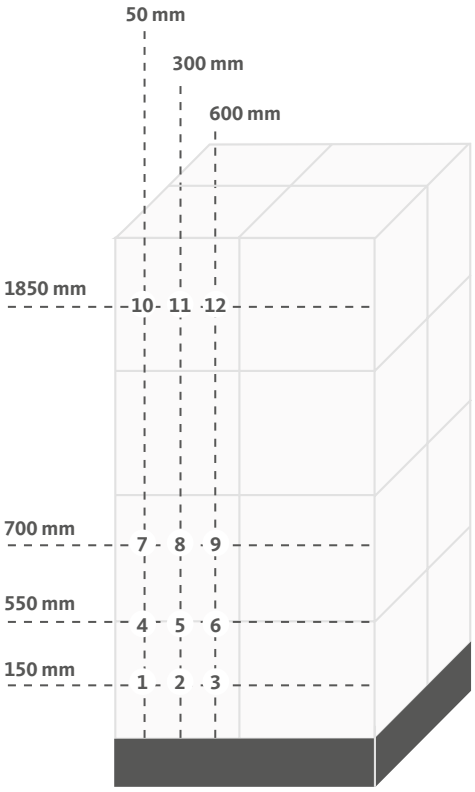
2. Irradiation unit + reference dosimeter are irradiated

Dosimetric validation using gamma rays

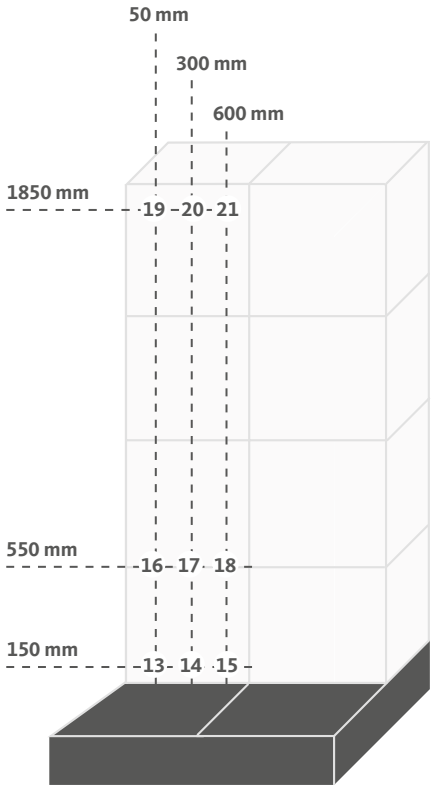
In the gamma facility, entire pallets are irradiated. For this reason, the dosimetric validation is carried out on the pallets. The dosimeter distribution is illustrated here as an example.

This ensues from the qualification of the facility and, if required, will be determined in consultation with the customer, depending on the product.





Level 1: front side of pallet



Level 2: geometric centre plane of pallet

5.3 APPLICATION-RELATED VALIDATION

In the case of application-related validations, the properties of the medical device and its primary packaging are evaluated following the manufacturing process. Since not only the microorganisms are destroyed through radiation with beta and gamma rays, but the properties and functions of materials, packaging and devices may also change; these changes have to be examined. Changes in the device often correlate with the radiation dose. To be able to evaluate dose-induced changes, selected samples are irradiated with the maximum dose in very narrow limits and analysed subsequently. Depending on the device, different downstream tests are required.

In particular, polymer materials may change through irradiation. This is set against a background of chemical reactions triggered by radiation energy, such as crosslinking, chain scissions or degradative reactions in connection with atmospheric oxygen. The following table provides a first overview whether material is generally suited for radiation sterilization. In this context, only mechanical key figures were taken into account (e.g. heat deflection temperature, wear and friction, elastomeric properties, etc.). As a rule, metals, metal alloys and ceramics react normally towards irradiation.

Table 3: Material resistance of polymers towards radiation

Group	Plastic	Resistance	Comments
Thermoplastics	Aromatic polyamidimides	***	High resistance, resistant through molecular ring structure
	Polysulfone (PSU)	***	colour, very resistant
	Polyimide (PI)	***	Very resistant through molecular ring structure
	Polystyrene (PS)	**	Very resistant; discolouration possible in transparent types; impact-proof types less resistant
	Acrylonitrile/ butadiene/styrene (ABS)	**	Breaks down at approx. 100 kGy and beyond; avoid high doses in impact-resistant settings
	Polycarbonate (PC)	**	special types with reduced yellowing obtainable; discolouration may disappear after heat treatment
	Aromatic polyesters (PET/PETG/PBT)	**	Extremely stable, retains its very good transparency; be sure to pre-dry prior to processing
	Styrene acrylonitrile copolymers (SAN)	**	Yellow colouring possible
	Polyvinyl fluoride (PVDF)	**	———
	Ethylene-Tetrafluor-Ethylene (ETFE)	**	———
	Polyethylene (LDPE/HDPE/LL-DPE/MDPE)	**	Crosslinked to higher strengths, at the same time reduction of elongation at break; LDPE most resistant
	Polymethyl meth-acrylate (PMMA)	*	Discolouration at about 20-40 kGy
	Cycloolefin copoly-mer (COC/COP)	*	behält seine gute Transparenz und Schlagzähigkeit
	Cellulose acetate butyrate (CAB)	*	Retains its good transparency and impact strength
	Polyamide (PA) Aliphatic and amorphous types	*	Discolouration possible; avoid thin films and fibres; PA 11 and PA 12 best suited
	Polyvinylchloride (PVC)	*	Standard types not suitable, release of corroding gases; special types with higher radiation resistance obtainable, discolouration possible
	Fluorinated Ethylene/ Propylene (FEP)	*	———

With regard to reduction of mechanical properties
* * * Excellent suitability
* * Well-suited
* Suitable with limitations
o Not recommendable

Group	Plastic	Resistance	Comments
Thermoplastics	Polypropylene (PP) copolymer	*	More stable than PP homopolymers; specially stabilised qualities are recommended
	Polypropylene (PP-H) homopolymer	*	Reduction of mechanical properties with increasing radiation doses in storage; only use stabilised types
	Polyacetal (POM)	o	Not recommended, extremely brittle
	Polytetrafluoreth-ylene (PTFE)	o	Breaks down rapidly, creates corroding gases, not suited
Thermosetting plastics	Phenol/formal dehyde (PF moulding material) Urea-formaldehyde (UF moulding material) Melamine-formalde-hyde (MF moulding material) Unsaturated polyes-ter resins (UP resins)	***	All thermosetting plastics are very resistant; in some of them, gaseous products may be separated
Elastomers	Nitrile rubber	**	———
	Ethylene propyl-ene diene rubber (EPDM) Polyurethane rubber Ethylene vinyl acetate (EVA) Thermoplastic poly-urethanes (TPU)	**	Products may experience additional crosslinking
	Natural rubber	*	Changes in properties very dependent on wall thickness
	Silicones	*	Increase in shore hardness possible
	Fluoroelastomers	*	———
	Butyl- bzw. Butyl and halobutyl rubbers Halogenated butyl rubbers	*	Breaks down, sterilization only possible in very narrow dose windows

With regard to reduction of mechanical properties
* * * Excellent suitability
* * Well-suited
* Suitable with limitations
o Not recommendable

Besides the mechanical key figures described in the table, the biological properties also play an essential role (inter alia biocompatibility and cytotoxicity). The DIN EN ISO 10993 standard "Biological testing of medical devices" describes possible tests depending on the product and case of application. In addition, it has to be ensured that both the product as well as the primary packaging maintain the defined properties beyond the declared expiry date. To this end, laboratory tests are carried out to examine the integrity of the sealing seams and germ tightness of the packaging system. All the tests involved in this process are described via the packaging validation. Increasingly, the transport route of the medical devices is also being taken into account: A corresponding transport validation is being tested, for example, to study the influence logistic processes have on the product quality.

5.4 REVALIDATION

Those wishing to place sterile devices on the market must furnish proof about the effectiveness of the selected sterilization method at regular intervals. For this purpose, microbiological examinations are necessary at defined recurring time intervals. In addition to these examinations within the scope of the microbiological revalidation, all changes made to a medical device in the course of its lifetime are subject to an evaluation. In this context, it is particularly important whether the changes affect the quality of the devices. If this is the case, suitable corrective action has to be taken. For the manufacturing step of sterilization, it is recommended, together with the provider of the sterilization services, to assess how the changes affect the sterilization process in order to make necessary adjustments if required. Ideally, these changes should be announced sufficiently in advance, as it might be necessary to repeat part of the process validation or even the entire validation under certain circumstances.

6. DOUBLE QUALIFICATIONS: HOW CAN YOU CARRY OUT A FURTHER QUALIFICATION?

It is extremely important today for manufacturers to look into the existing production and supply chains and prevent failure risks in the best way possible. For this reason, a strategic decision may result in qualifying a sterile medical device already on the market for another sterilization method, for a second facility or another supplier. This leads to essential changes in the manufacturing process and has to be validated. The following table gives an overview of the necessary validation steps that arise when changing the sterilization method to radiation sterilization, or from gamma to beta rays or vice versa, or a change to another facility.

Table 4: Change in sterilization method, service provider or the plant, and the validation steps at a glance

Change in sterilization method	Validation steps		
	Microbiological validation* (MPQ)	**Dosimetric validation (PPQ)**	**Application-related validation (APQ)**
Responsibility	Plant operator + manufacturer	Plant operator	Manufacturer
Other sterilization method (e.g. EtO sterilization with damp heat) to radiation sterilization	Other method: Drawing up sterilization cycles with the associated sterilization tests pursuant to standard Rays: Carrying out of verification dose experiment pursuant to DIN EN ISO 11137-2	Other method: Drawing up of sterilization cycle (goal: determining the procedure parameters, e.g. temperature, humidity, time, pressure, degassing time Rays: Carrying out of triple dose mapping incl. statistical evaluation pursuant to DIN EN ISO 11137-3	Examination of product properties taking altered sterilization parameters into account incl. suitable primary packaging
Gamma to beta rays	Carrying out of verification dose experiment pursuant to DIN EN ISO 11137-2	Carrying out of triple dose mapping incl. statistical assessment pursuant to DIN EN ISO 11137-3	Examination of product properties taking altered sterilization parameters into account (beta rays are usually more material-friendly than gamma rays)
No change in method, but shift to another plant or operator	validation retains its validity since the manufacturing conditions remain unchanged	Ethylene oxide: Drawing up of sterilization cycle (goal: determining the procedure parameters, e.g. temperature, moistness, time, pressure, degassing time) Rays: Carrying out of triple dose mapping incl. statistical evaluation pursuant to DIN EN ISO 11137-3	No expenses, existing validation retains its validity since the manufacturing conditions remain unchanged

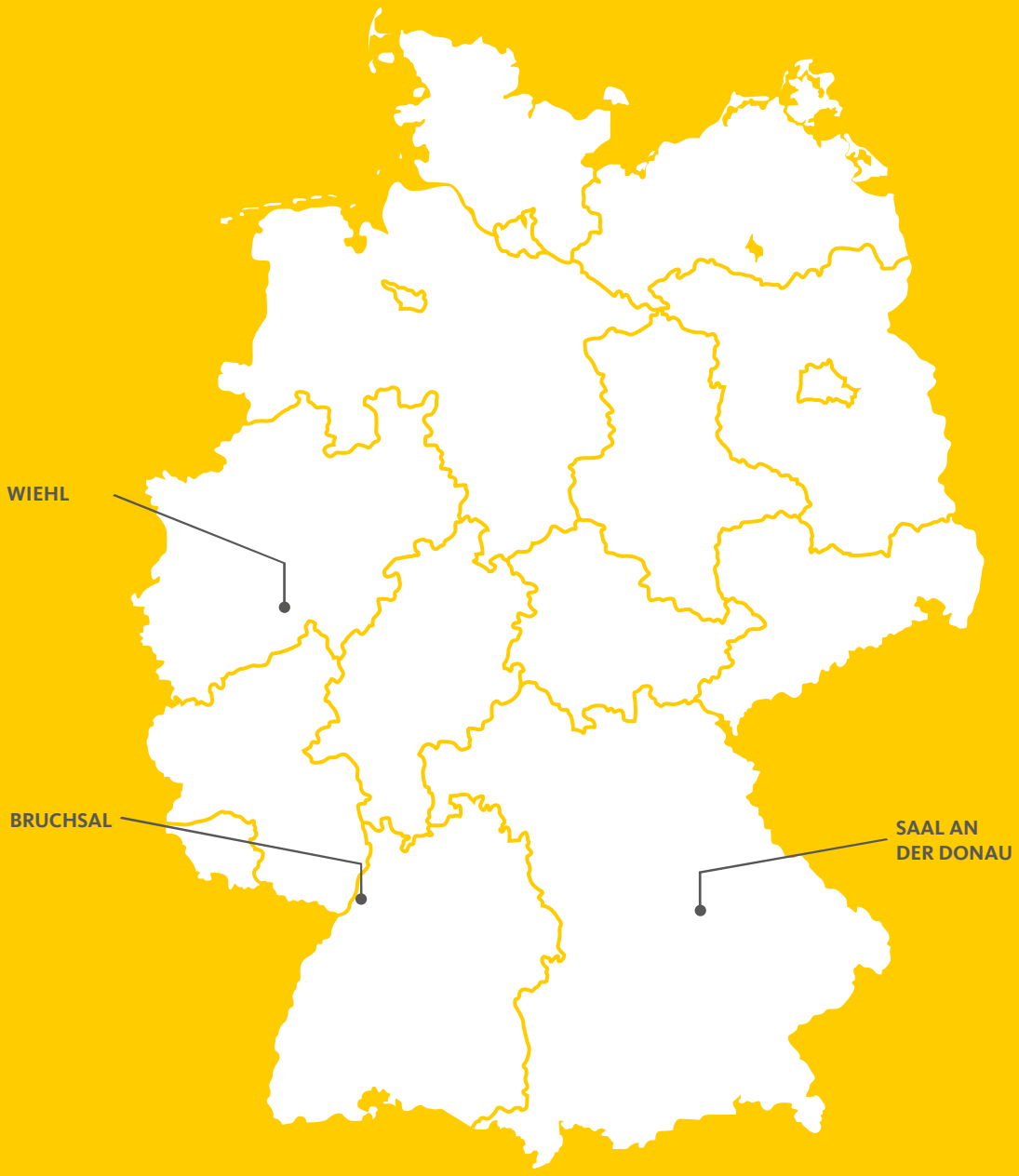
* Determination and confirmation of Sterility Assurance Level (SAL)

If the manufacturer plans to maintain the chosen method of sterilization and qualify his device for a second plant or supplier, the microbiological and application-related validation will retain their validity. In this case, it is important to validate the new plant and register the service provider – a process which, by comparison, requires the least effort and expense. The most expensive case, i.e. changing from one established sterilization procedure to another, requires registering the new service provider and the new plant as well as undertaking a microbiological and application-related validation.

From a strategic point of view, the qualification of medical devices for more than one plant or more than one service provider is a topic which each manufacturer should look at critically, and because of the long lead times, one cannot start early enough - the benefits arising from this outweigh the expenses of the validation process. Table 4 also shows that a procedure validation to qualify a device in another plant is possible with manageable investments.

SUMMARY

In view of the numerous normative standards that apply for placing sterile medical devices on the market, validation processes in medicine technology are more complex than in other industries. Undoubtedly, the process is elaborate and the normative and legal developments will not make it easier in the future. In order to ensure successful validation internally, it is essential to plan the validation itself, the personnel and financial resources related to it, and the time schedule. This applies for the validation of new devices as well as for changes in devices already on the market. When deciding on the corresponding sterilization service provider, the long-term commitment plays a decisive role. It is thus important to define the requirements of the manufacturer and plan the available sterilization and plant capacities for the long term accordingly. Thorough preparation and close contact and early involvement of the sterilization service provider enable validations to be reliably implemented. The experts at BGS are happy to exchange with you and provide their advice.



YOUR CONTACT TO US:

BGS BETA-GAMMA-SERVICE GMBH & CO. KG www.bgs.eu info@bgs.eu

FRITZ-KOTZ-STRASSE 12
51674 WIEHL

T +49 (0) 2261 7899-0
F +49 (0) 2261 7899-44

JOHN-DEERE-STRASSE 3
76646 BRUCHSAL

T +49 (0) 7251 786-0
F +49 (0) 7251 786-33

INDUSTRIESTRASSE 9
93342 SAAL A. D. DONAU

T +49 (0) 9441 1777-0
F +49 (0) 9441 1777-44

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