

Regulatory issues for radiation sterilization centres

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Abstract. Presently radiation sterilization of medical products is regulated by ISO 11137:1995 and EN552. Both standards will be harmonized into a new ISO 11137:200X standard comprising of three parts. While sterilization centres operating today must comply with today's regulations they will have to comply with the new standard after it becomes effective. This paper describes the application of ISO 11137:200X and highlights the requirements for sterilization centres.

1. Introduction

Radiation sterilization of medical products is currently regulated by two standards, ISO 11137:1995[1] and EN552 [2]. These standards will be harmonized in the very near future into ISO 11137 part 1, part 2 and part 3 [3, 4, 5]. Currently all three parts of ISO 11137:200X are at the Final Draft International Standard stage (FDIS). Since the last experts meeting of ISO TC 198 WG2 in April 2005, no more technical changes are expected and all three parts are expected to be published together in 2006. In the European Union countries the new ISO standard becomes effective as soon as it is cited in the Official Journal of the European Communities and when it has been implemented in at least one member state.

The new ISO 11137:200X standard will establish the requirements for the development, validation and routine control of a sterilization process for medical products. It makes normative references to ISO 13485 (Medical devices – Quality management systems) [6], ISO 10012-1 (Quality assurance requirements for measuring equipment) [7], ISO 11737-1 and ISO 11737-2 (Sterilization of health care products – Microbiological methods) [8, 9], and thus all these are indispensable for the



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application of ISO 11137:200X. Hence application of ISO 11137:200X places requirements on the quality management (QM) system of the irradiation centre as well as on the actual sterilization process.

Validation, as it shall be understood in this paper, consists of defining requirements for producing a sterile product and testing if the requirements (such as specified dose) have been met. Validation is not only testing, but it is the definition of design and testing requirements including the performance of the tests. The requirement definition has to adhere to the applicable norms and standards. Global requirements together with a risk analysis lead to functional requirements and process requirements. For each requirement definition document a test protocol must exist to verify the adherence to the respective requirements. A master validation plan summarizes the relevant documents for a specific product. A good description on validation, even though it was meant to apply to software can be found in ref [10].

2. History of quality management systems

Medical product manufacturers and sterilization centres in Europe commonly used the harmonized quality system standards EN 46001 and EN 46002 as a basis for their quality systems in combination with the EN ISO 9001/2:1994 standard. In addition, some manufacturers included the requirements of ISO 13485 and ISO 13488 standards. All of the above mentioned standards were published in 1996 or before. (As these standards are not valid any more, they are not listed in the bibliography.)

As of December 2003, ISO 9001/2:1994 is obsolete. The new ISO 9001:2000 emphasizes the process model and focuses on continual improvement and customer satisfaction. However, this standard does not adequately address regulatory requirements and was deemed not suitable for the medical industry. Therefore a replacement for then current standards EN 46001/2 and ISO 13485 was necessary and a new version of ISO 13485 was published in July 2003. The standard is structured in a way similar to ISO 9001:2000. ISO 13485:2003 is a "stand-alone standard" and can be used without the standard ISO 9001:2000.

The primary objective of ISO 13485:2003 is to facilitate harmonized medical device regulatory requirements for QM systems. As a result, it includes some particular requirements for medical devices and excludes some of the requirements of ISO 9001 that are not appropriate as regulatory requirements. Because of these exclusions, organizations whose quality management systems conform to this international standard cannot claim conformity to ISO 9001 unless their quality management systems conform to all the requirements of ISO 9001.

If regulatory requirements permit exclusions of design and development controls, this can be used as a justification for their exclusion from the sterilization centre's QM system. These regulations can provide alternative arrangements that are to be addressed in the quality management system. It is the responsibility of the organization to ensure that claims of conformity with ISO 13485:2003 reflect exclusion of design and development controls.

3. Requirements for radiation sterilization

For the purpose of this paper, two primary responsible parties are distinguished in the radiation sterilization process. The *medical device manufacturer* bears the ultimate responsibility for sterility assurance and compliance of his production process (including the sterilization process) to an ISO 13485 compliant QM system. The *sterilization centre* provides an important step in the manufacturing of the medical product; hence it must have the irradiation process under control. This paper is concerned mainly with the requirements for a sterilization centre.

The requirements for development, validation and routine control of a radiation sterilization process for medical products are laid out in ISO 11137:200X. Interestingly, "This standard does not require that a complete QM system complying with ISO 13485 be implemented, nor does it require that those QM system elements that are specified be subject to third party assessment". In plain words this means

that ISO 11137:200X only requires specific elements of ISO 13485 to be complied with and it does not require that a notified body certify (accredit) the QM system of a sterilization centre before a sterilization process can be implemented¹. The QM systems of the medical device manufacturers, however, will have to comply fully with ISO 13485:2003. Hence, medical device manufacturers will audit the QM system of the sterilization centre and may (and typically will) require an accreditation by a notified body for the sterilization centre's QM system in order to do business with this sterilization centre.

3.1. Application of ISO 13485

The required QM system elements are concerned with documentation, management responsibility, product realization, measurement, analysis and improvement. Procedures that are related to these elements are required to comply with “applicable clauses” of ISO 13485.

3.1.1. Documentation

ISO 11137:200X states that procedures for development, validation, routine control and product release from sterilization shall be specified. This should be considered as a minimum requirement for the sterilization centre. All documents shall be controlled. This means that they are reviewed and approved for their adequacy of use. Changes and updates shall be evaluated, recorded and approved. The current revision status or version of a document must be evident. The documents must be legible and identifiable. External documents must be identified and their distribution controlled. Unintentional use of obsolete documents must be prevented. If obsolete documents are retained they must be identified as such.

Records shall remain legible, readily identifiable and retrievable. Retention of records is a shared responsibility between the medical device manufacturer and the sterilization centre. The retention time shall be equal to the life time of the medical product or as agreed upon between the medical device manufacturer and the sterilization centre. Typically this means retention times between 2–7 years. Section 0 will explain in more detail the issues of electronic record retention.

3.1.2. Management responsibilities

The management of the sterilization centre must be committed to quality. It shall establish quality management objectives and procedures, and ensure that objectives are achieved. Resources shall be provided; responsibilities and authorities shall be defined, documented and communicated within the organization. Typically this means that a quality assurance manager is assigned who is responsible for implementation of and adherence to the procedures. Competence and awareness can only be a result of training. All personnel shall be trained regularly (i.e. after changes and annually) on quality procedures. The work environment influences product safety. Hence it is advisable to establish and implement procedures regarding cleanliness and clothing of workers, address workers safety and define quarantine rules for product and sick personnel.

3.1.3. Product realization

Procedures for purchasing and incoming inspections for purchased materials shall be implemented. The sterilization centre must take reasonable steps to verify that customers' products conform to specification. This is typically done by comparing paperwork and label, visual damage inspection, as well as performing weight and dimension measurements on sample cartons. Once products have been received they shall readily be identified and traceable in the sterilization centre. Physical segregation of sterile and non-sterile product is common practice. Segregation by electronic record keeping and electronic traceability may be possible, however it is easier implemented in automated warehouse storage systems than in facilities that manually handle product storage.

¹ There may be additional national or regional requirements.

3.1.4. Measurement, analysis and improvement

Recognizing and controlling nonconforming product is a key requirement in the irradiation process. Nonconformities must be followed by corrective actions. Several options exist for corrective actions: a) eliminate the nonconformity; b) authorize the use, release or acceptance of the products under concessions; c) or ensure that the product is not used as originally intended (discard or destroy the product).

In order to fulfil these requirements the sterilization centre must implement ISO 13485 compliant procedures to identify and deal with all nonconformities. All equipment, measurement systems and instrumentation (especially dosimetry systems) must be calibrated. Procedures in accordance with ISO 10012 [7] shall be specified to establish calibration and traceability to national or international standards. All equipment shall be re-calibrated at specified intervals. Uncertainty of measurement plays a significant role in detecting nonconformities. Section 0 addresses dosimetry systems and uncertainty estimation of measurements. In the scope of this paper we shall not divulge too much effort on explaining measurement uncertainty. Sterilization centres are encouraged to hire or outsource the respective knowledge.

3.2. Application of ISO 11137:200X

The responsibilities to achieve a sterile product are shared between medical device manufacturer (for example, the one who issues the CE-conformity certificate for the product destined for the European market) and the sterilization centre. The division of responsibilities must be agreed upon between these two parties. The medical device manufacturers' responsibilities include:

- establishing a sterilization dose
- developing product families
- establishing the maximum acceptable dose
- controlling the manufacturing process, including meeting the specifications for the product sent to the sterilization centre (such as product density, orientation, dimensions, packaging, etc)
- revision of specifications for the sterilization centre that affect the dose distribution or validity of the sterilization process used; e.g. product packaging, materials, dose requirements, etc.
- change control of the product, including a review of variables affecting radiation sterilization
- product release

Performance qualification of the sterilization centre is a shared responsibility. While the medical device manufacturer needs to qualify the product as a whole, the sterilization centre must qualify the correct dose delivery according to specification.

The sterilization centre has responsibilities that are explained in the following subsections.

3.2.1. Processing categories

A processing category is defined as a group of different products that can be sterilized together. Processing categories shall be established for routine processing based on assessment of product related variables that affect dose to product and processing specification. Processing categories are unique to radiation processing. Periodic reviews of processing categories shall be made at least annually.

For large gamma and X ray irradiators, typically the OQ dose mapping data (3.2.3) can be used as a basis for assessment of processing categories. Two main criteria are similar dose requirements and

similar densities. The same processing category then allows sterilizing product at the same timer settings (or conveyor speed) without violating the specified dose limits for the product within the processing category.

For electron beam sterilization, dose map specific to individual product is performed during PQ (3.2.4). Grouping of product in processing categories is only appropriate if the product, its packaging and the loading pattern of the product into the irradiation containers results in the ability to process the products with the same machine parameters without exceeding the specified dose limits.

3.2.2. Installation Qualification (IQ)

Processing equipment and its methods and modes of operation must be described. When changes to equipment are made, the changes need to be recorded and remain part of the equipment description. All software used to control and/or monitor the process must be validated according to its intended use. For each type of irradiator ISO 11137:200X provides a minimum list of items that shall be specified.

All operating procedures for individual equipment must be documented. The equipment and its software are tested against their design specification. Test methods and results must be recorded. Modifications or repair of equipment may invalidate previous tests. Each time a modification is performed the effect on the whole system must be evaluated and tested.

3.2.3. Operational Qualification (OQ)

Operational qualification verifies the dose delivery process when all the equipment and software of individual equipment function together. It is mandatory that all instrumentation and test equipment used for monitoring and controlling have been calibrated prior to OQ. All features of the irradiator shall be used and tested.

During OQ, homogeneous product (sometimes called phantom product) is irradiated and the dose distribution measured. The sterilization centre tests the ability and reproducibility to deliver dose to homogeneous product for each processing path. Acceptance criteria include the ability to deliver dose in the specified range for the sterilization process for each path through the irradiator. The dose mapping data is analyzed and used to determine the relationship between machine parameters (timer settings, beam current, conveyor speed, etc) and dose. Process interruptions and partially filled containers are evaluated for their effect on the dose distribution in containers. Conclusions are drawn to describe the irradiation process and the effects single or multiple process interruptions have on the conformity of product.

While dose mapping of homogeneous phantom product is an integral part of OQ, dose mapping of actual product is an integral part of PQ. This paragraph applies to both, OQ and PQ. ASTM E2303-03 [11] attempts to generalize dose mapping requirements. It introduces concepts that apply to all radiation processing applications. Since the actual dose distribution varies significantly depending on the technology employed this ASTM standard cannot give a detailed dosimeter placement procedure. It places emphasis on good statistical practices for dose mapping procedures. While this standard is not a requirement for radiation sterilization it does (as well as other ASTM standards) give useful guidance to fulfil the requirements of ISO 11137.

3.2.4. Performance Qualification (PQ)

PQ is defined as “process of obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product meeting its specification”. At the sterilization centre, this is primarily achieved through “dose mapping ... using product loaded in irradiation containers in accordance with a specified loading pattern”. Data from dose mapping then establishes the required process parameters for sterilization. It must be stressed that dose mapping of product, especially for

electron beam irradiation, is not a trivial task. Experienced experts are required to perform such dose mappings correctly. Failure to identify minimum and maximum dose zones in a specific product, and to reproducibly deliver minimum or maximum dose to the respective zone, can be a safety risk for the end user of the medical product. A process, where this basic requirement to dose mapping cannot be fulfilled is out-of-control and hence not acceptable. Routine dose monitoring positions shall be defined by the sterilization centre in order to allow regular checks of the correct application of dose. During PQ, the relation between dose at these monitoring positions and the maximum and minimum dose shall be established. These monitoring positions may be on or off the product container. The manner of loading the product shall be specified and then always used for sterilization. Processing categories can be used to reduce the amount of dose mapping required. A representative number of product containers shall be used for dose mapping for each path through the irradiator. A key objective is to determine variability of dose distribution between irradiation containers.

3.2.5. Irradiation for setting dose limits

The sterilization centre should help the medical device manufacturer with test irradiations for dose settings, materials compatibility studies and bioburden studies. These tests typically require very precise dose delivery and very little dose variation over the product. In many cases this excludes irradiation in the normal production containers. Samples like this typically require their own procedure for loading pattern definition and dose analysis.

3.2.6. Specific responsibilities of the sterilization centre

The sterilization centre does not certify sterility; instead it certifies delivery of dose according to specification. It is only able to do this if

- monitoring and controlling of the process parameters function according to specification, and all equipment and instrumentation are calibrated,
- changes to processing equipment are executed in compliance with implemented procedures and with ISO 11137:200X, e.g. requalified for the intended use after the change,
- the evaluation of dose mapping data and processing categories are performed by appropriately trained and knowledgeable personnel,
- all personnel in the sterilization centre are competent and aware of QM procedures and do not try to bypass them for any reason,
- all procedures, methods, measurements and results are recorded and retained.

It is important for the sterilization centre to insist that the medical device manufacturer coordinate any changes to the product specifications with the sterilization centre. In the absence of such coordination, all effort on the part of the sterilization centre to achieve the correct dose will be useless. Especially for electron beam sterilization, a change in packaging will invalidate the dose map results of the product.

4. Issues of ISO 11137 revision and harmonization

4.1. General

The general title of ISO 11137:200X is ‘*Sterilization of health care products – Radiation –*’, and under this there are three parts as follows:

Part 1: Requirements for the development, validation and routine control of a sterilization process for medical products,

Part 2: Establishing the sterilization dose,

Part 3: Guidance on dosimetric aspects.

4.2. Part 1: Requirements & guidance

In Europe, EN552 regulates radiation sterilization processes that use electron beam with electron energies up to 10 MeV and gamma irradiators. It does not apply to X ray irradiators or to electron beam sterilization using electron energies above 10 MeV.

ISO 11137:1995 regulates radiation sterilization processes that use electron beam and X rays, regardless of the incident electron energy, and gamma rays from ^{60}Co or ^{137}Cs sources. Hence all electron beam sterilization processes using energies above 10 MeV must conform to ISO 11137.

The harmonized standard will regulate sterilization processes that use electron beam and X rays with no energy limit, and gamma radiation from ^{60}Co or ^{137}Cs sources. As a compromise, ISO 11137:200X places requirements on testing for activation for sterilization with electron beam when the incident electron energy is above 10 MeV, and for sterilization with X rays when the incident electron energy exceeds 5 MeV. Activation of the product shall be evaluated and results shall be documented. An example for such documentation can be found in [12].

The transfer of sterilization dose of 'dry' product between similar irradiators requires no testing. Otherwise, the dose rate effects and temperatures are a concern and require some testing. This requirement places responsibility on the medical device manufacturers, but the sterilization centre should be aware of this when trying to acquire customers who previously sterilized at a different facility.

Processing categories have been introduced in the harmonised standard; hence grouping of products for routine processing is addressed in the standard.

Product release based solely on monitoring and controlling of the process parameters is not addressed in the standard; however, the sterilization centre is required to certify the radiation dose received. It remains the responsibility of the sterilization centre to define the frequency at which dosimeters are used in routine processing. For example, electron beam sterilization centres may be able to justify a period of several hours between routine dosimeter checks, provided that the process is tightly controlled.

4.3. Part 2: Establishing the sterilization dose

Method 1 and method 2 remain essentially unchanged allowing setting a sterilization dose below 25 kGy. Dose substantiation methods VD_{max} for 15 kGy and 25 kGy have been introduced in the standard. Dose substantiation for 25 kGy has been available through ISO 13409 and AAMI TIR 27, and is known as $\text{VD}_{\text{max}} 25$. $\text{VD}_{\text{max}} 15$ essentially estimates an average batch bioburden and can provide sterilization dose substantiation for low bioburden products (less than 10 cfu)

Other issues such as dose audit, test time requirements and product families have also been addressed in Part 2, however they typically do not influence the processes at the sterilization centre.

4.4. Part 3: Guidance on dosimetric aspects

This part gives guidance on dosimetric aspects as they apply to requirements elaborated in Part 1. In developing this part, care has been taken not to duplicate applicable ASTM or ISO/ASTM standards; instead, relevant standards are cross referenced. Sterilization centres are encouraged to use both, Part 3 and relevant ASTM or ISO/ASTM standards [13] in order to setup, calibrate and operate their dosimetry systems.

5. Process control

Process control primarily needs to be understood literally: the process must be under control, otherwise it cannot be validated. The critical element of the radiation sterilization process (at a sterilization centre) is the dose that is delivered to the product. Process parameters should be established and applied. Methods need to be in place to assure that the delivered dose is reliable, accurate and reproducible. Guidance on establishing process parameters is given in AAMI TIR 29 [14]. Methods for process control differ between electron beam and gamma irradiation centres. When this paper was written, no X ray irradiation centres were in commercial operation to sterilize medical products.

5.1. Computer and software requirements

Process control does not automatically mean computer controlled. However in today's computer age most methods to control the process include computers and software. Software used in medical device manufacturing needs to be validated; several validation methods exist but shall not be explained in the scope of this paper. Typically software design is outsourced to a software design firm and not performed in the sterilization centre. However the sterilization centre needs to understand if their software design firm performs their software development and validation according to acceptable standards and methods, therefore a brief introduction shall be given here.

Especially for sterilized product to be sold on the US market, the US Food and Drug Administration (USFDA) places requirements on software validation. The requirements are stated in Title 21 Code of Federal Register (CFR) Part 820. In a guidance document [10] the FDA explains methods which, if applied, would lead to conforming software products. Essentially the software must be validated for its intended use (This brings up a lot of issues about the use of standard office software in a validated sterilization process – typically the design of standard office software does not have to comply to stringent software validation requirements). It should be noted that any changes of software must also be validated. An often found practice, to just change a few parameters or source code lines to 'make the system work' or perform better, is not allowed!

While the previous paragraph mainly deals with the requirements for the software developer, the sterilization centre must focus on two important things that are intrinsically connected to software validation:

- electronic record keeping, and
- electronic signatures.

Thus, each record and changes to it must be traceable to the person who generated and approved the record or its change. The change itself must be identified. A password alone is typically not approved as a source of identification for the purpose of record keeping. Title 21 CFR part 11 states the requirements for electronic records and electronic signatures for the product destined for the US market. FDA auditors will emphasize the compliance to 21 CFR part 11 during audits of the sterilization centre. Serious or frequent non-compliances to 21 CFR part 11 may lead to serious consequences for the sale of medical products on the US market.

It should be noted that electronic record keeping and electronic signatures are not a subject of interest to the USA only. Similar regulations may exist in many other countries, especially in the European Union countries.

5.2. Electron beam irradiators

For electron beam sterilization, the reliability of the process and its consistency is assured by controlling and monitoring the beam characteristics, conveyor speed and other process parameters. Once these parameters are established, products that are processed using the specified parameters will receive the specified dose as long as product characteristics including packaging and orientation in the package remain unchanged. Changeover from one product to another can be done quickly as there is very little effect on adjacent products.

Dose mapping with homogeneous phantom product is used to determine the ability and reproducibility of dose delivery to product. Since large dose gradients are expected in electron beam processing the choice of dosimeters and their locations will play an important role. Some dosimeters influence the radiation field significantly, so that further measurements in the shadow of a dosimeter may lead to false results.

5.3. Gamma irradiations

Multi-pass gamma irradiators process different products at the same time on a continuing basis. Dose delivery is influenced by shadowing of product with other product, partially loaded containers and other parameters. In scheduling the operation of a multi-pass gamma irradiator, one has to take into account products of different densities. In batch irradiators, only small quantities of product are irradiated at the same time. This makes it easier to achieve the same irradiation conditions as in the previous sterilization batch.

Large multi-pass irradiators generate most of the important dose map data during OQ using homogeneous phantom product. In this way, limiting operating conditions are established for sterilizing product of different densities, of different sterilization doses, or partially loaded containers.

5.4. X ray irradiators

Most concepts for X ray irradiators borrow design elements from both, electron beam accelerators and gamma irradiators. As in an electron beam irradiation, the area where the product receives the largest dose in a X ray irradiator is small compared to that in a gamma irradiator. As in a gamma irradiator, all products need to be treated with X rays from two sides at least. This requirement comes from the physical properties (namely absorption) of photons, the general category for gamma rays and X rays. While gamma facilities perform this double sided irradiation typically by having product pass on either side of the gamma source, the product needs to be turned around in X ray irradiators to change the side facing the beam. As in double sided processing in electron beam irradiators, this requires an extra pass of the product in front of the X ray target.

As long as X ray systems do not use multi-lanes for their product pass in front of the source, there is very little effect of adjacent product on dose distribution. Some concepts however do rely on multi-lane processing in order to improve the energy utilization of the X ray field and to improve maximum to minimum dose ratio. An X ray irradiator can be more like an electron beam irradiator or like a gamma irradiator, depending on the choice of lanes, the method of scheduling of product with different densities, and the sterilization dose.

5.5. Dosimetry and measurement uncertainty

All sterilization standards consider ‘dose’ as a key parameter in order to determine if a product is sterile. However, measurement of dose is not a trivial task, and thus internationally recognised procedures should be followed [13]. A commercial dosimetry system consists of dosimeters, readout equipment and procedure for its use. Dosimeters may be films, small plastic blocks, fluids or pellets where there is a known and reproducible response to radiation dose. The dosimetry system must be calibrated and the calibration must be traceable to a national standard. ISO/ASTM standard 51261 gives guidelines for calibration procedures [15].

Although all experimental measurements are subject to error, we can still trust our measurements in terms of their precision and accuracy, if the dosimetry system is used properly. Precision indicates the reproducibility of a measurement. That is, the closeness in agreement among the values when the same quantity is measured several times under the conditions of repeatability. If the series of measurements is reproducible, then good precision is obtained as each measurement deviates only by a small amount from the average of the series. On the other hand, if there is a wide deviation among the series of measurements the precision is poor. A measurement is said to be accurate if it is close to the known ‘accepted’ or ‘most probable’ value. In our case the accuracy of a dose measurement depends on the

quality of the calibration curve with respect to the national or international standard it is based upon. The point the author would like to make on the sterilization centre is that both, precision and accuracy need to be adequate for the application.

The uncertainty of dose measurements at a sterilization centre must be determined. Typically, it is reported around 5-6%, taking into account precision and accuracy. Due consideration should be given to this dosimetry uncertainty while setting the process parameters for the sterilization process, in order to avoid underdosing or overdosing the product. Proper statistical procedures for this are described in Ref [16].

Many dosimetry systems require environmental parameters to be tightly controlled. The incoming inspection of dosimeters typically is a statistical process and does not verify each dosimeter. Hence individual dosimeter may be faulty or be exposed to conditions not suitable for its use. These individual dosimeters may then cause a dose measurement that deviates from the specification. Such an outlier in the dosimetry measurement can then question the sterility of a batch of product. Faced with an out-of-specification dose value, the sterilization centre has the responsibility to carefully examine it to determine if it is really an outlier that can be neglected or it indicates an out-of-control process. The sterilization facility shall use all sensible tools and data available to justify their reasoning. One such tool is monitoring of irradiator parameters and careful inspection of these values. Machine parameters of an accelerator can be controlled and monitored to a precision of better than 1%. Standard electrical instruments allow calibration of machine parameters to an accuracy of also better than 1%. Environmental factors typically do not influence the measurement of machine parameters and each individual measurement device is calibrated. Hence the dose delivery process is under better control than dose measurement process suggests in case of the above mentioned outlier. Monitoring the machine parameters is therefore an important step for quality control. It is also a requirement under ISO 11137:200X. Treatment of outliers is not a trivial task. Other factors can influence dose – such as product jams and product packaging issues – which may not affect the machine parameters. When an outlier is encountered, only experienced and trained personnel shall make a determination if the applied dose is still within the specified range for the respective product.

6. Conclusions

A sterilization centre must understand its processes and describe them in a quality manual. At present, the processes and procedures need to comply with ISO 11137:1995 or EN 552. In the future, they will need to comply with ISO 11137:200X, which may require changes to the processes, nomenclature and procedures employed. Training may then be required to update all workers. According to ISO 11137:200X, only certain elements of the QM system of the sterilization centre must comply with ISO 13485; however, clients and national or local regulations may force the centre to comply with it completely.

The most important requirement for the sterilization centre is to have its process under control. This means that process parameters must be carefully established, monitored and controlled. Deviations must lead to cause-and-effects analyses, and nonconformities must lead to corrective actions. All this is only possible if the measurements are performed with the best precision and accuracy attainable. For this reason all measurement systems and instrumentation must be calibrated with traceability to national or international standards.

The sterilization centre has to fulfil its responsibilities towards applying a validated irradiation process to the product to be sterilized. The facility and product must be characterized. IQ and OQ define and validate how the facility's irradiation process will be applied. During PQ the product specific procedures are specified and validated. Provided that all requirements are met, the sterilization centre can certify the correct application of the irradiation process, typically including the applied minimum and maximum dose which have been calculated based on product specification, dose mapping in relation to process parameters, and dose measurements at routine monitoring positions.

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