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Packaging for terminally sterilized medical devices — Guidance on the application of ISO 11607-1 and ISO 11607-2

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National foreword

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The UK participation in its preparation was entrusted to Technical Committee CH/198, Sterilization of medical devices.

A list of organizations represented on this committee can be obtained on request to its secretary.

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**Packaging for terminally sterilized medical devices - Guidance
on the application of ISO 11607-1 and ISO 11607-2 (ISO
16775:2014)**

Emballages des dispositifs médicaux stérilisés au stade
terminal - Lignes directrices relatives à l'application de l'ISO
11607-1 et l'ISO 11607-2 (ISO 16775:2014)

Verpackungen für in der Endanwendung sterilisierte
Medizinprodukte - Leitfaden für die Anwendung von ISO
11607-1 und ISO 11607-2 (ISO 16775:2014)

This Technical Specification (CEN/TS) was approved by CEN on 18 February 2014 for provisional application.

The period of validity of this CEN/TS is limited initially to three years. After two years the members of CEN will be requested to submit their comments, particularly on the question whether the CEN/TS can be converted into a European Standard.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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Foreword

This document (CEN ISO/TS 16775:2014) has been prepared by Technical Committee ISO/TC 198 "Sterilization of health care products" in collaboration with Technical Committee CEN/TC 102 "Sterilizers for medical purposes" the secretariat of which is held by DIN.

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Endorsement notice

The text of ISO/TS 16775:2014 has been approved by CEN as CEN ISO/TS 16775:2014 without any modification.

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2. www.iso.org/directives

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 198, *Sterilization of health care products*.

Introduction

Sterile barrier systems need to ensure the sterility of their contents until opened for use and ensure aseptic presentation.

The sterile barrier system, depending on conditions of handling, distribution or storage, may provide adequate protection for the sterile medical device. In circumstances where the packaged and sterilized device undergoes repeated handling, additional protective packaging may need to be combined with the sterile barrier system to create a packaging system.

Each establishment should evaluate the performance of each sterile barrier system or packaging system before selection and implementation to ensure conditions for sterilization, storage, and handling can be met. Each establishment that manages sterile items should have a documented plan of education on how to store, handle and transport sterile items.

Regional differences in quality management systems and other requirements exist and these might involve different approaches to human resource management. In any case however a sound education process is a key element and facilities should ensure that its personnel are aware of the relevance and importance of their packaging and sterilization activities for the safety of the patient.

ISO 11607-1 specifies the requirements for materials, sterile barrier systems, and packaging systems, including the qualification of the packaging system design and evaluation of that design, ISO 11607-2 specifies the requirements for packaging process validation. Both of these documents provide standards to ensure medical device protection, the ability to sterilize, maintenance of sterile package integrity and aseptic presentation. The scope of each of these standards applies to health care facilities and wherever medical devices are packaged and sterilized. It is recognized that the circumstances of the application of these standards will be different when they are used in a health care facility from when they are used by a medical device manufacturer or reprocessor.

The conditions of use of this guidance may vary widely around the world. ISO 11607-1 and ISO 11607-2 and this guidance document provide a guideline for use, subject to interpretation by circumstance and regulatory environments. In some regions of the world health care facility compliance to the series ISO 11607 is a national or regional regulatory requirement, in some regions the series ISO 11607 is considered guidance for health care facilities. For instance, it is recognized that in certain regions or regulatory applications conformance to ISO 11607-1 may be demonstrated but not conformance to ISO 11607-2, which requires process validation by the user. In other regions, where compliance to both ISO 11607-1 and ISO 11607-2 is a national regulatory requirement, this document will also provide guidance on performing validation. [Clause 3](#) of this guidance document is applicable to health care facilities and [Clause 4](#) is applicable to industry. Further guidance is given in [Annexes A](#) to [S](#) that may be applicable to health care facilities and/or industry, as indicated.

In Europe ISO 11607-1 assists the conformity assessment procedure for manufacturers and is designed and used as a tool for demonstrating compliance with the relevant essential requirements of the Medical Device Directive. Compliance with the standard is always voluntary.

At the time of publication of this document, Amendments to ISO 11607-1 and ISO 11607-2 are in the ballot process. This guidance document already considers the revised versions with the understanding that specific references to numbering may have changed. Annex B of ISO 11607-1 on test methods has been extensively revised and should be considered when available.

Packaging for terminally sterilized medical devices — Guidance on the application of ISO 11607-1 and ISO 11607-2

1 Scope

This Technical Specification provides guidance for the application of the requirements contained in ISO 11607-1 and ISO 11607-2. It does not add to, or otherwise change, the requirements of ISO 11607-1 and/or ISO 11607-2. This is an informative document, not normative. It does not include requirements to be used as basis of regulatory inspection or certification assessment activities.

The guidance can be used to better understand the requirements of ISO 11607-1 and/or ISO 11607-2 and illustrates some of the variety of methods and approaches available for meeting the requirements of those International Standards. It is not required that this document be used to demonstrate compliance with them.

Guidelines are given for evaluation, selection and use of packaging materials, preformed sterile barrier systems, sterile barrier systems and packaging systems. Guidance on validation requirements for forming, sealing and assembly processes is also given.

This Technical Specification provides information for health care facilities (see [Clause 3](#)) and for the medical devices industry (see [Clause 4](#)).

It does not provide guidance for applications of packaging materials and systems after their opening. In the use of packaging for other purposes such as a “sterile field” or transport of contaminated items, other regulatory standards will apply.

2 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 11607-1 and ISO 11607-2 and the following apply.

2.1

packaging system

combination of the sterile barrier system and protective packaging

[SOURCE: ISO/TS 11139:2006, 2.28]

Note 1 to entry: The packaging system includes the sterile barrier system and the protective packaging. However, if the sterile barrier system protects the medical device, facilitates aseptic presentation, and is resilient enough not to require additional protective packaging, the sterile barrier system would also fulfil the requirements of a packaging system. Protective packaging is not always necessary however aseptic opening/presentation has to be ensured in all cases.

2.2

protective packaging

configuration of materials designed to prevent damage to the sterile barrier system and its contents assembly until the point of use

[SOURCE: ISO/TS 11139:2006, 2.37]

Note 1 to entry: National or regional regulations may require that protective packaging is used to avoid the potential contamination of the surgical environment. These regulations may also require that the protective packaging is removed prior to introduction of the sterile barrier system into the surgical environment.

Note 2 to entry: Protective packaging protects the sterile barrier and the contents. Examples would include a dust cover, a box, transport tray.

2.3 sterile barrier system SBS

minimum package that prevents ingress of microorganisms and allows aseptic presentation of product at the point of use

[SOURCE: ISO/TS 11139:2006, 2.44]

2.4 preformed sterile barrier system

sterile barrier system that is supplied partially assembled for filling and final closure or sealing

EXAMPLE Pouches, bags, and open reusable container.

[SOURCE: ISO/TS 11139:2006, 2.31]

Note 1 to entry: Preformed sterile barrier systems exist in a wide range of forms. The examples listed above are not intended to be all inclusive.

3 Guidance for health care facilities

IMPORTANT — Written instructions for use should be obtained from the packaging material and/or medical device manufacturer concerning their recommendations for sterilization and the subsequent maintenance of sterility of a sterile barrier system.

3.1 Test methods

For guidance on the requirements for test methods contained in ISO 11607-1 and ISO 11607-2, see the health care annexes of this document.

3.2 Guidance for conformance to ISO 11607-1

3.2.1 General guidance for materials, preformed sterile barrier systems and sterile barrier systems

3.2.1.1 Preformed sterile barrier systems should be evaluated before purchase and use. Therefore, the supplier should consider providing a statement of compliance to the applicable sections of ISO 11607-1 for the materials and/or preformed sterile barrier systems to be purchased. Before introducing associated components (e. g. labels, tapes, tray liners) into production, users should confirm that they will be suitable for use in their specific applications and conditions of use.

3.2.1.2 The key concepts that apply to all packaging materials and components are as follows:

- a) they should be made of known and traceable materials with processes capable of meeting the requirements of ISO 11607-1 (see requirements in ISO 11607-1:2006, 5.1.3, 5.1.4 and 5.1.5);
- b) they should be non-toxic, for guidance see [A.3.3](#) (see requirement in ISO 11607-1:2006, 5.1.6);

NOTE 1 If the sterile barrier system or associated components contain natural rubber latex, the sterile barrier system should be labelled indicating natural rubber latex is present.

- c) there should be documented evidence that the ingress of microorganisms can be prevented when demonstrated under test conditions which consider sterilization process, handling, distribution, transport and storage (see requirement in ISO 11607-1:2006, 5.1.6 and 5.2);

- d) they should have a demonstrated ability to meet the required physical properties for materials and closures (such as weight or grade, seal width and seal strength), resist tearing or puncture, be capable of opening or peeling in a continuous and homogenous manner, without delamination tearing (see requirements in ISO 11607-1:2006, 5.1.7 and 5.1.9);
- e) they should be compatible with the intended sterilization process and parameters capable of producing a sterile medical device (see requirement in ISO 11607-1:2006, 5.3);
- f) they should be compatible with the labelling system; if present, have colour fast printing inks that do not degrade, fade or become illegible after exposure to the intended sterilization process (see requirement in ISO 11607-1:2006, 5.4);
- g) they should be protected from the effects of environmental conditions (e.g. relative humidity, direct sunlight or fluorescent light, temperature) during storage (see requirement in ISO 11607-1:2006, 5.5 and Clause 7);

NOTE 2 Suggested storage conditions and shelf life should be provided by the material or preformed sterile barrier system manufacturer. If anticipated or actual storage is outside these conditions the manufacturer should be consulted.

- h) they should allow aseptic presentation.

NOTE 3 Instructions for aseptic presentation should be provided by the manufacturer of the medical device and/or packaging system.

NOTE 4 The internet is a useful tool for finding information on materials, see [Annex N](#).

3.2.2 Design and development guidance for packaging systems (ISO 11607-1:2006, 6.1 and 6.2)

3.2.2.1 Selection criteria

When a health care facility determines which packaging system to use, the design and development guidance for those packaging systems should be considered (see requirements in ISO 11607-1:2006, 6.1 and 6.2). When a health care facility uses a contract packager or sterilizer additional considerations are necessary (see [Annex P](#)).

The materials and systems chosen should:

- a) be intended for use in medical packaging applications, as stated by the manufacturer;
- b) be supported by technical information from the manufacturer confirming that it meets the requirements of ISO 11607-1 that relate to materials;
- c) provide adequate protection for the medical device(s) during specified intended storage and transportation conditions to the point of use;
- d) allow for and be compatible with the intended sterilization process, and have the ability to withstand conditions of the chosen process;

NOTE Not all materials are appropriate for all sterilization processes. Information on compatibility with a given sterilization process is typically provided by the manufacturer of the medical device and/or packaging system. For further explanation of challenges of common sterilization processes see [Annex B](#).

- e) maintain sterile barrier integrity until its time of use;
- f) ensure aseptic presentation at the point of use;
- g) allow a method of closure that is tamper evident;
- h) allow for ease of identification of contents.

The user of the packaging materials should ensure that the sterile barrier system or packaging system complies with ISO 11607-1, that requirements concerning product compatibility are met and that processes for packaging, sterilization, storage and distribution are validated and controlled.

3.2.2.2 Selection considerations

The selection process at the health care facility should include an evaluation of the ability of both the sterile barrier system and protective packaging (if required) utilized to maintain the integrity of that sterile barrier system until its time of use and permit aseptic presentation at the point of use.

The choice of packaging components will be dependent on the risk associated with the medical device, its conditions of use, the storage and transport requirements and health care procedures practiced at the facility. These risks should be analysed by the health care facility and procedures put in place to mitigate/control those risks (see [Annex K](#)).

To choose the most appropriate material for the sterile barrier system and/or packaging system, the following should be considered:

- a) Duration and conditions of storage may affect the type of sterile barrier system or packaging system needed. Some items may be stored for some time before use and may require a more durable sterile barrier system and/or the addition of protective packaging. The more the sterile barrier system or packaging system is handled the greater the probability that cracks, lid deformation, gasket damage, tears, holes or material separation may occur.
- b) Size, weight and shape of the item to be sterilized should be considered. Some items will require more durable or more flexible sterile barrier systems than others.
- c) If multiple types of packaging components are to be used it is important to verify that components are compatible with each other as well as the product contained inside and the intended sterilization process.
- d) The means and conditions of transport should be considered. While in some cases routes are exclusively inside the facility, they can also be between different facilities. Exposure of the packaging systems to the uncontrolled environment may significantly increase the risk of loss of integrity of the package, compromise aseptic opening or contaminate the contents.

3.2.2.3 Assembly considerations

The following aspects should be considered:

- a) Medical devices should be oriented to facilitate aseptic presentation.
- b) Sharp items should be shielded so that the user is protected from injury and the sterile barrier system and medical device is protected from damage.
- c) Associated components can be used inside the sterile barrier system in order to ease or facilitate the organization, drying or aseptic presentation (e. g. inner wrap, instrument organizer tray, tray liners or a containment device around the medical device).
- d) The protection devices or associated components should:
 - 1) be non-toxic, be intended for use in medical packaging applications, as stated by the manufacturer;
 - 2) provide protection of the medical device(s) during storage and transportation to the point of use;
 - 3) allow for and be compatible with the intended sterilization process, and have the ability to withstand conditions of chosen process;

NOTE 1 Not all materials are appropriate for all sterilization processes. Information on compatibility with a given sterilization process is typically provided by the manufacturer. For further explanation of challenges of common sterilization processes see [Annex B](#).

- 4) not undergo chemical or physical change to such an extent that the performance or safety is impaired or the medical device that they contact is adversely affected;
 - 5) not compromise aseptic presentation;
 - 6) allow for easy identification of contents;
 - 7) be stored in a controlled environment to maintain cleanliness and fitness for use.
- e) The weight of the packaging system and its contents should not exceed national regulations for manual handling.

NOTE 2 Current national regulations range from about 5 kg to 11,4 kg.

3.2.2.4 Labelling considerations

Part of the selection process should include consideration of how labelling is to be accomplished. The facility's labelling procedure for the sterile barrier system or packaging system should include the following:

- a) When identification is performed in a health care facility:
 - for pouches and reels the label should be placed on the film if applied before sterilization or on either side if after, the label should not conceal the device;
 - for pouches and reels printing or writing should be placed outside the area enclosed by the outside dimensions of the seals;
 - care should be taken when applying labels to filled sterile barrier systems so as not to damage packaging materials or contents.
- b) Writing on wrapped packages should be on the closure tape, not directly on wrappers.
- c) Special labels intended for a specific sterilization process may be written on. If these labels are used they should not impede the sterilization process (i.e. should not block the breathable area of the package).
- d) Labelling should remain securely adhered to the sterile barrier system through the sterilization process and storage until the point of use.
- e) Labels or closure tapes used as labels, and their adhesive systems should be non-toxic.
- f) Only non-toxic ink that is suitable for use with the chosen sterilization process should be used.
- g) Ballpoint pens or any writing instrument with the potential for creating a hole or puncture in the sterile barrier system should not be used.

3.2.2.5 Regulatory considerations

Specific national or regional regulatory requirements may apply. These requirements should be considered during the selection process for a sterile barrier system and/or for a packaging system.

3.2.2.6 Common choices for sterile barrier systems

3.2.2.6.1 General

Sterile barrier systems can be manufactured using mainly, but not limited to, the following concepts:

- sealable pouches and reels; and/or
- sterilization wrap; and/or
- reusable container.

Aspects to be considered in using these systems follow.

3.2.2.6.2 Sealable pouches and reels (preformed sterile barrier systems)

Sealable pouches and reels are typically purchased in two forms:

- The continuous roll or reel type is sealed along both edges. The roll is unwound and cut to the desired length. The medical device is placed between the two layers and both ends are sealed.
- The pouch is pre-cut to a specific size and sealed on three sides. The medical device is placed inside the pouch and the fourth side is sealed.

The following aspects should be considered:

- a) The size of the pouch and the strength of the packaging materials should be based on the medical device which is going to be packaged. Items either too large for a package or with sharp edges will put extra pressure on the seals and the materials. This may cause rupture. There should be enough space to make seal closure possible. Too many small items in the sterile barrier system may cause the items to move around, rupture the seal, penetrate or abrade the package materials. Thin or fragile materials can be damaged during handling, transport, and distribution.
- b) If not specified otherwise by the manufacturer the preformed sterile barrier system should be filled up to a maximum of 75 % of the inner surface area of the porous side. Care should also be taken to ensure that the distance from the seals is increased for products of greater height.
- c) When two pouches are used, the inner pouch should be able to move within the outer pouch. This allows penetration of the sterilant and prevents the pouches from sticking together during the sterilization process. Folding of the inner pouch in order to fit into the outer pouch or folding of the outer pouches should be avoided in order to prevent stressing or damage to the sterile barrier system. For combining two pouches made from film and porous material it is important that film meets film and porous material meets porous material for identification of content and permeation of sterilant.
- d) All pouch seals, including closure seal, should be smooth, i.e. without folds, bubbles, or wrinkles.
- e) Self-seal pouches and those closed with tape may provide less security than heat sealed pouches. Sealing procedure should dictate that folds and closures should not be skewed, and care should be taken to ensure that both corners are well sealed, in order to ensure a complete closure across the entire end. Correct tape placement is critical to provide complete closure and thus sterile barrier system integrity. Special attention should be paid to proper method of closure to ensure package integrity.
- f) Sealing devices should be able to control and monitor critical process parameters (e.g. temperature, pressure, sealing time/speed) in accordance with their validation criteria (e.g. alarms, warning system or machine stop in the event of any critical process parameter deviation). Operators should not modify critical process parameters unless they have been suitably trained, fully comply with appropriate operating procedures and stay within the validation process. The sealer should be capable of attaining the sealing conditions suggested by the preformed sterile barrier system

manufacturer. Sealing devices manufactured and intended for preformed sterile barrier systems should be used.

- g) Closing accessories that compress the package or medical device should not be used (e.g. ropes, string, elastic bands, paperclips, staples or similar items).
- h) The pouch should be loaded so that the enclosed medical device will be presented aseptically. For instance, the grip of the medical device should be placed toward the opening end. It should be noted that the seal areas are considered non-sterile when opened.^[108]
- i) The pouch should be opened according to the manufacturer instructions, if there is a specific orientation needed to prevent fibres delamination when opening that orientation should be followed. The formed package should show by design which direction the packaging has to be opened (e.g. arrow sign, shape of seal).
- j) Reels (rolls) are used for the packaging of medical devices of diverse dimensions that do not easily fit standard preformed pouch sizes. Due to the fact that the packaging is sealed on two sides the pointed seal (chevron) is missing. In the absence of the chevron, the peel direction for reels should be provided by the manufacturer. Additionally, it is advisable to have more space above the seal that is intended to be opened according to the manufacturer's information.

NOTE In most areas of the world, certain sterile barrier systems, which are not peelable and require cutting to gain access to the product inside, are used in lieu of peelable preformed sterile barrier systems. For example, some of the sterile barrier systems formed using either sterilization bags, header bags, or pouches produced using reel material constructed from one layer of porous material and one layer of plastics film, sealed together along the parallel sides. In these applications, there is a greater risk of the product coming into contact with the non-sterile outer surface of the sterile barrier system and extra care should be taken to ensure aseptic presentation. This is achieved by cutting the top off and then inverting to allow the medical device to drop out onto a suitable surface without touching the outsides.

3.2.2.6.3 Sterilization wrap

Sterilization wrap comes in many sizes and grades to accommodate a wide range of applications. It is also available in single use or reusable fabric forms. Careful consideration should be given to the item to be wrapped and the technique to be used. Sterilization wrap can be used for wrapping of individual medical devices or medical devices in instrument cases, cassettes or instrument organizing trays.

The following aspects should be considered:

- a) The grade of the sterilization wrap should be chosen according to the size, shape and weight of the medical devices to be wrapped or based on guidelines within the health care facility and wrap manufacturer's recommendations for use.
- b) The size of the sterilization wrap should be selected to achieve adequate coverage of the item being packaged. It is essential to wrap the item securely to prevent gaps, billowing and air pockets from forming. The item should not be wrapped too tightly as this could create holes or tears in the wrap. It is also necessary that the sterilization wrap be large enough to accommodate movement of the wrap during the sterilization cycle without ripping or tearing. When choosing sheets of sterilization wrap the wrapper should be large enough to cover the medical device, but it should not be so big that it has to be wrapped several times around the medical device, as this may impede sterilant penetration.
- c) Proper wrapping technique is essential to provide a tortuous pathway to impede microbial migration into the sterile barrier system. A wrapping technique can be used if the manufacturer has demonstrated the efficacy of this technique and recommends it for this application (see [3.2.2.1](#)). The wrapping method chosen should allow aseptic presentation of the medical device. The health care facility should verify or validate the application in its own facilities per national or regional regulations. National standards or professional guidelines for wrapping techniques may be available. Examples are given in [Annex C](#).

- d) The sterilization wrapping technique should be designed in a manner that the opened wrapper should drape away from the sterile field.
- e) The assembly surface area for wrapping should be flat, smooth, of adequate size, well lit and clean.
- f) The wrapped package should be designed in a manner so that all edges are secured and do not interfere with aseptic presentation into the sterile field.
- g) Closure systems should provide evidence of tampering.
- h) Indicator tape is the most common closure for wrapped packages and there are different kinds of tape based on the method of sterilization. There are different tapes designed for use on woven or nonwoven wrappers. Closures that compress the package or medical device should not be used (e.g. ropes, strings, elastic bands, paperclips, staples or similar items).
- i) When reusable fabrics are used as sterilization wrap there are additional requirements to ensure the suitability of the wrap prior to each use (see requirements in ISO 11607-1:2006, 5.1.11 and 5.1.12).

3.2.2.6.4 Reusable containers

A rigid reusable container is designed to hold medical devices and accessories and is sterilized without exterior wrapping. This container typically consists of a bottom or base with carrying handles and a lid that is secured to the base by a latching mechanism. It may contain a basket or tray to hold medical devices. The container incorporates a means for air evacuation and sterilant penetration. In regional or other standards it may be referred to as a “rigid container” or a “reusable container”.

Instrument cases, cassettes or organizing trays are containment devices but not sterile barrier systems. They should be contained in a sterile barrier system.

When using rigid containers the following should be considered (see requirements in ISO 11607-1:2006, 5.1.10):

- a) Only filters which are proven to be compatible with the specific container, particular sterilization process and capable of maintaining sterility should be used. Filter manufacturer should give documented evidence that demonstrates these capabilities.
- b) Containers should be inspected and prepared in accordance with the manufacturer's instructions.
- c) Tamper evident devices appropriate for the sterilization process should be secured in accordance with the container manufacturer's instructions and indicate that the sterile barrier system has not been opened intentionally or accidentally and therefore the contents exposed to potential contamination before intended use.
- d) Each container should have a visible identification label and/or information card unless the container is designed for emergency-use sterilization and used for that purpose. ID label and card should be appropriate for the sterilization process.
- e) The sealing surfaces of the base and lid should be inspected for damage at each time of use to ensure the proper closure of the container.
- f) The instrument organizing tray dimensions should be suitable for use with the specific container and sterilization method.
- g) Procedures should be in place for the cleaning, disinfecting and maintenance processes for containers after each use. These processes should be validated. Containers should not be used beyond the manufacturer's stated usable life (see requirements in ISO 11607-1:2006, 5.1.12). Procedures should be in place to ensure that the manufacturer's stated usable life is not exceeded (see requirements in ISO 11607-1:2006, 5.1.12).
- h) As with all sterile barrier systems, to ensure aseptic presentation the outside of the container and the joint between top and bottom should not come in contact with sterilized contents.

3.2.2.7 Protective packaging

Protective packaging may be used to protect or prolong the shelf life of properly packaged and sterilized items that could be subjected to environmental challenges or multiple handling. Transportation or movement of the sterile barrier system in particular may require protective packaging to be applied to ensure that transportation and handling does not affect the sterile barrier system. Sterilized packages should be handled as little as possible. Loss of sterile barrier system integrity is regarded as event related rather than time related, this is why it is so crucial to guard against damage to the sterile barrier system.

When protective packaging is used, the sterile barrier system should be clearly identifiable. Protective packaging is designed to provide additional protection against damage and outside elements. If any protective packaging is to be applied after steam sterilization, it should be applied once the items are thoroughly cool and dry.

National or regional regulations may require that protective packaging is used to avoid the potential contamination of the surgical environment. These regulations may also require that the protective packaging is removed prior to introduction of the sterile barrier system into the surgical environment.

3.2.3 Packaging system performance testing (ISO 11607-1:2006, 5.3, 5.4, 5.5, 6.3)

Before any packaging system is used in a facility for the first time, its performance should be tested. Performance testing should allow verification on how well the sterile barrier system or packaging system holds up to the rigors of anticipated conditions of handling, distribution and transportation, before and after sterilization. The sterile barrier system needs to maintain its integrity without any holes, tears or seal/closure rupture that may be caused by the imposed stresses.

Performance testing should:

- a) be evaluated through all the intended processes of sterilization, handling, distribution and storage, up to the point of use;
- b) be evaluated for expected worst-case scenarios. In determining these, a number of factors should be considered. These include but are not limited to:
 - 1) Assembly of sterile barrier systems which contain the medical device configuration which presents the greatest challenge to the sterile barrier system (e.g. biggest, heaviest, most dense, sharpest items see ISO 11607-1:2006, 6.3.4).
 - 2) Samples for verification testing should be prepared to allow monitoring of the efficacy of the sterilization process depending on national or regional requirements for the monitoring of sterilization efficacy. Examples include but are not limited to biological, chemical indicators or process challenge device (PCD) by measuring and recording of physical parameters using thermocouples or data loggers. Determination of suitability may be carried out concurrently with validation of the sterilization process(es) to be used. Medical devices should be packaged and sterilized in accordance with the instructions of the manufacturer of the medical device and preformed sterile barrier system.
 - 3) Sterilization of the sterile barrier system in the intended sterilization process, considering mixed loads or fully loaded sterilizer chambers.
 - 4) Distribution / handling / storage / opening of the sterile barrier system.

Consideration should be given to the environment and other conditions in which the sterile barrier system or packaging system will be stored. Product pressed tightly into bins and storage locations increases the chance of shear action between two sets of packaged medical devices and can be detrimental causing pinholes and tears.

It is particularly important to consider all conditions of storage and distribution, as many sterilization sites are not adjacent to the point of use.

After performance testing, health care facilities should visually inspect the sample sterile barrier systems for package integrity (no holes or tears) and seal integrity, then verify that sterilization parameters have been achieved.

If more thorough testing is desired, alternative test methods may be found in ISO 11607-1:2006, Annex B.

If a sterile barrier system is designed to be reusable and a degradation of performance characteristics is predicted by the manufacturer (see ISO 11607-1:2006, 5.1.11 and 5.1.12) the monitoring or inspection system used should clearly identify when the end of the useful life has been reached as defined by the manufacturer.

3.2.4 Sterile barrier system stability evaluation (shelf life) (ISO 11607-1:2006, 6.4)

Evaluation on the ability of the sterile barrier system materials or preformed sterile barrier systems to maintain their performance characteristics and seal integrity over time is normally performed by the manufacturer of the preformed sterile barrier system (see also requirements in ISO 11607-1:2006, 6.4.7).

However, even though the materials have been shown to be an acceptable microbial barrier, the health care facility should demonstrate that the assembled sterile barrier system or packaging system can maintain integrity under the anticipated environmental conditions until the time of use.

Loss of sterile barrier system integrity is regarded as event related rather than time related and is dependent on the performance of the sterile barrier system or packaging system, as well as the possible interaction between the medical device and the selected sterile barrier system, the storage conditions, the conditions during transport and the amount of handling. Appropriate storage environment includes a wide variety of considerations, i.e. preventing any damage, maintaining temperature and humidity stability, limit exposure to dust and sunlight, keep protective packaging in place, minimizing handling, physical separation of clean and contaminated items etc.

Maximizing maintenance of package integrity by limiting the risk of damage to the sterile barrier system can be greatly influenced by adequate inventory control and management systems.

NOTE National or regional guidance may give further information on storage requirements, such as distance from floor and ceiling, stock rotation, cleaning of storage area, more specific limits on temperature and humidity, type of shelving non-porous, enclosed and dedicated room, ventilation air exchanges and air quality, air borne particles.

3.2.5 Documentation

The health care facility should follow a plan or criteria for evaluating the choice of sterile barrier systems. Results of testing should be compared to the acceptance criteria. The results of the evaluation should be documented.

Validation documents and gathered data should be maintained in accordance with the facility's policy. In ISO 11607-1:2006, 7.1 requires that documented information shall include the type, size or grade and batch number identification of the materials tested, the sterilization processes, any known expiry dates or suggested storage conditions, any known restrictions on handling or use, and for reusable materials, the frequency allowed and nature of maintenance.

3.3 Guidance on conformance to ISO 11607-2, *Validation requirements for forming, sealing and assembly processes*

3.3.1 General

ISO 11607-2 addresses the validation requirements for all packaging processes. This includes the assembly or filling and the following processes:

- sealing process: pouch, reel, or bag forming and sealing;

- wrapping process: sterilization wrap folding and closing of sterilization wraps;
- container process: closing of reusable containers.

Validation of processes may rely on data from previous installation qualification (IQ) and operational qualification (OQ). That data can be used for determination of the tolerances for critical parameters.

The packaging process activities should be executed in the frame of a formal quality management system. While there are regional differences between health care quality systems, key elements include, (but are not limited to) an efficient system of document control, a formal education process, process control/monitoring, and a corrective/preventive action system to maintain (and continuously improve) the effectiveness of the packaging processes.

The definitions for IQ, OQ and Performance Qualification (PQ) in ISO 11607-2 all refer to equipment used in the sealing or closing process. However all forming, sealing and assembly processes require manual operations. Consequently the functions performed by persons should be included as part of the validation.

Typically an IQ is only performed when there is equipment to be installed. Alternatively, for a process that involves only people and their execution of tasks, the development of the Standard Operating Procedures (SOP) and the training on them may be considered by some facilities to be an IQ. The training of the specific operators employed for the OQ and PQ should be documented in those reports.

3.3.2 Method of validation

3.3.2.1 General

Fundamentally, a documented method of validation or a standard procedure for validation should exist.

This documented method or procedure consists of:

- a) drafting of a validation plan (see [3.3.2.2](#));
- b) implementation of validation (see [3.3.2.3](#)) consisting of:
 - 1) IQ (see ISO 11607-2:2006, 5.2);
 - 2) OQ (see ISO 11607-2:2006, 5.3);
 - 3) PQ (see ISO 11607-2:2006, 5.4);
- c) procedure for addressing failure and corrective action to be taken;
- d) validation approval (see [3.3.2.4](#));
- e) process control and routine monitoring (see [3.3.2.5](#));
- f) process/packaging changes and revalidation (see [3.3.2.6](#)).

3.3.2.2 Drafting of validation plan

At a minimum, the validation plan should include the following information:

- a) responsibilities (i.e. facility, location, name of person responsible for validation and operator);
- b) description of the sealing and closure procedures/SOP's (e.g. heat sealing of pouches, wrapping and closing of sterile barrier system, loading and closure of container);
- c) description of the sterile barrier systems used and if relevant, of optional protective packaging (e.g. manufacturer's description);

- d) description of sterile barrier system contents utilized. Sterile barrier systems should be assembled as for normal use, see [3.2.2.3](#), [3.2.2.4](#), [3.2.2.6](#) and [3.2.2.7](#);
- e) description of the sterilization process (e.g. moist heat sterilization at 134 °C and 121 °C, Ethylene oxide (EO), Gas plasma, low temperature steam formaldehyde (LTSF)), including the process parameters and loading configuration used;
- f) description of transport, distribution and storage of the respective sterile barrier systems;
- g) qualification steps (IQ, OQ and PQ), (see ISO 11607-2:2006, 5.2, 5.3 and 5.4) for further explanations for each process see [3.3.2.7](#), [3.3.2.8](#), [3.3.2.9](#);
- h) sample size taking into consideration that the number of units to be tested should be based upon a statistically valid rationale (see [Annex L](#));

NOTE It is important to understand that the sample size greatly influences the confidence level and the reliability. Tools for determining sample size can easily be found by searching the internet using the keywords "sample, size, calculator".

- i) acceptance criteria taking into consideration that the user should determine which attributes(s) will be evaluated, the method of evaluation and the results that will be considered acceptable;
- j) validation approval.

The validation plan checklist in [D.2](#) to [D.4](#) can be used. A separate validation plan should be used for each different combination of sterilization procedure and sterile barrier system and/or packaging system (manufacturer, type, etc.), the [Table D.1](#) shown in [Annex D](#) can be used for organizational purposes.

3.3.2.3 Implementation of validation

After drafting the validation plan, the validation activities will commence according to the validation plan. For guidance specific to each of the three processes described in [3.3.1](#) above please refer to the following sections: sealing process ([3.3.2.7](#)), wrapping process ([3.3.2.8](#)), and container process ([3.3.2.9](#)).

3.3.2.4 Validation approval

The documented and evaluated validation report should allow traceability and should be approved by the responsible person as defined in the approved validation plan (see [D.2](#) to [D.4](#)).

Deviations should be resolved and approved prior to approval of the validation report. The impact of the deviation on the validation study should be assessed to establish if the study should be repeated.

The IQ report should be approved prior to the execution of the OQ. Also, the OQ report should be approved prior to the execution of the PQ.

After each step, failures or deviations should be investigated to determine the root cause and implement corrective action before starting the next validation step. The need for completely or partially repeating the previous validation step should be evaluated. Corrective or preventive actions should be managed using a formal system and the effectiveness of the actions should be evaluated and documented.

3.3.2.5 Process control and routine monitoring

Procedures should be established to ensure that the packaging process is under control and within the established parameters during routine operation.

Critical process parameters should be routinely monitored and documented.

3.3.2.6 Process/packaging changes and revalidation

3.3.2.6.1 Processes should be revalidated if changes are made to the equipment, product, packaging materials or packaging process, which could potentially compromise the original validation and affect the sterility, safety or efficacy of sterile medical devices however, a documented rationale should be developed to support this conclusion.

NOTE The following is a list of changes that could affect the status of a validated process and necessitate the need for revalidation:

- sterile barrier system material changes;
- new equipment;
- transfer of processes and/or equipment from one facility or location to another;
- sterilization process changes;
- review of end user complaints or non-conforming product, negative trends in quality or process control indicators;
- change in sterile barrier system contents that are outside the parameters of the worst-case originally evaluated;
- change of transport route or means (e.g. from within the building only to transport between buildings which may involve significantly changed challenges to the package).

3.3.2.6.2 The need for revalidation should be evaluated and documented. If the change does not require that all aspects of the original validation be repeated, this revalidation does not have to be as extensive as the initial validation, however a documented rationale should be developed to support.

3.3.2.6.3 A documented rationale should be written for the acceptance of changes that are judged to not need revalidation activities (e.g. change of material or material supplier if the supplier provides evidence that the materials are essentially equivalent).

3.3.2.6.4 Periodic revalidation activities, verifications or reviews should be considered since multiple minor changes could cumulatively affect the validation status of the process.

Revalidations can also be used to show that the operation staff still has the required knowledge and competence to carry out the processes in an efficient way and they can also be used to retrain personnel and to realign practices.

3.3.2.7 Validation of the sealing process (pouch, reel or bag forming and sealing) of preformed sterile barrier systems

NOTE Information on the validation of the sealing process of the preformed seals should be available from the preformed sterile barrier system manufacturer; this process validation pertains to the closure seal(s) made at the health care facility's site.

3.3.2.7.1 Installation Qualification

This means that the sealing device should be appropriate and correctly installed. The sealing equipment should come pre-calibrated from the factory with a calibration certificate and the facility should have an ongoing calibration program in place to ensure the correct sealing parameters at the sealing interface. In addition the user should be trained on how to correctly operate the sealing device.

The following IQ aspects should be considered: environmental conditions such as cleanliness, temperature, humidity; documented/operated training; operating manual or procedure.

The following questions should be addressed:

- a) Are the critical process parameters defined (e.g. the critical process parameters are at least temperature, contact pressure and sealing/dwell time)?

NOTE 1 If using rotary sealing equipment the dwell time is typically expressed as a sealing speed (i.e. metres per minute). If using a bar sealer, the dwell time is the amount of time the heated bars are in contact with the packaging materials.

- b) Is the sealing temperature based on the preformed sterile barrier system manufacturer's recommendations?
- c) Is the sealing device equipped with systems to control and monitor the critical process parameters?
- d) Is the sealing device equipped with an alarm, warning system or machine stop in the event that the critical process parameters exceed the limits?
- e) Are the specifications for seals to be created known and understood (i.e. specific seal width if regulated by national standards)?
- f) Are documented plans for preventative maintenance and cleaning available to the users?
- g) Have all users been trained how to operate the sealing device and has this been documented?

For the implementation of the IQ the use of a checklist is recommended.

NOTE 2 The IQ checklist in [E.1](#) can be used for documentation purposes.

3.3.2.7.2 Operational Qualification

The sealing temperature range to be used in a health care facility should be determined by that facility using information provided by the preformed sterile barrier system manufacturer and the sealing equipment manufacturer.

The preformed sterile barrier system manufacturer typically provides upper and lower temperature limits, at a defined pressure and dwell time.

The sealing equipment manufacturer typically provides information on how the sealing device monitors critical parameters.

Contact pressure and seal/dwell time are generally present to a certain range by the sealing equipment manufacturer and it is important to ensure that the equipment is capable of obtaining the limits recommended by the preformed sterile barrier system manufacturer. In conditions of use different sterile barrier systems may require different sealing temperatures.

Using the information provided the user should seal sterile barrier systems at the upper and lower limits and evaluate the quality of the seals produced. The sealing equipment should be checked before use that it has been calibrated.

Operators should be trained and assessed for competency in heat sealing process.

Packages should be assembled in accordance with a documented procedure. In assembling these packages the worst-case configuration should be included (see [Annex H](#)).

Samples should be sealed and evaluated at each upper and lower variable parameter limit. For a limit to be considered successfully established, all samples should pass the acceptance criteria. The acceptance criteria for sealed sterile barrier systems should include:

- a) intact seal for a specified seal width;
- b) no channels or open seals;
- c) no punctures or tears;

- d) no wrinkles or creases that traverse the seal width;
- e) after the intended sterilization process, no material delamination or fibre tear upon peel opening that would interfere with the aseptic presentation.

When destructive tests are used for the evaluation of seals multiple sets of packaged products per sealing parameter have to be prepared.

In order to achieve the above acceptance criteria after sterilization a minimum seal strength may be necessary (e.g. EN 868-5 indicates a minimum reference value of 1,5 N per 15 mm for moist heat sterilization processes and 1,2 N per 15 mm for other sterilization processes). If the measurement of seal strength is not performed during OQ, there may be a higher risk of not meeting the acceptance criteria during PQ, which would require performing the OQ again.

These quality properties should be checked with an appropriate system (e.g. commercially available dye penetration test kits or other seal integrity indicator, see Annex A.7.3). The results should be documented.

NOTE 1 Seal integrity indicator should consist of the same material as the porous material of the pouch or reel (e.g. EN 868-3). If the quality properties are achieved at both the upper and lower limits, the set point is typically the average of these two values (e.g. lower limit = 170° C and upper limit = 190° C; sealing temperature = 180° C).

NOTE 2 The OQ checklist in F.1 can be used to define the sealing temperature.

3.3.2.7.3 Performance Qualification

The PQ demonstrates that the process, including both the equipment and the operator, will consistently produce acceptable sterile barrier systems under specified operating conditions.

The following should be considered:

- a) Evaluation of the sterile barrier system should be performed after the sterile barrier system has been sealed and sterilized.
- b) The batch documentation for batches used during the validation studies should form part of the validation records. The batch identification should include, but is not limited to:
 - 1) operator;
 - 2) time and date;
 - 3) sterilization process, parameters and cycle number ;
 - 4) sterile barrier system materials used;
 - 5) contents of sterile barrier system;
 - 6) heat sealing equipment used.
- c) The calibration of the test equipment and sealing equipment should be checked using the procedure recommended by the manufacturer. This should be carried out before sealing takes place.
- d) Samples should be sealed and evaluated. All samples should pass the acceptance criteria. For guidance on sample size see 3.3.2.2 h).

In order to achieve the acceptance criteria after sterilization a minimum seal strength may be necessary, (e.g. EN 868-5 indicates a minimum reference value of 1,5 N per 15 mm for steam sterilization processes and 1,2 N per 15 mm for other sterilization processes).

When destructive tests are used for the evaluation of seals multiple sets of packaged product per sealing parameter have to be prepared.

- e) Three batches or sets of sealed sterile barrier systems should be made; these batches should encompass the potential significant sources of variation such as operator, time of day, material (size

source, lot), sterile barrier system contents. Package contents that present the greatest challenge (worst-case) should be included.

- f) Test samples of the sterile barrier system should be sterilized using the sterilization process(es) previously identified as being appropriate to demonstrate suitability of the sterile barrier system. Three batches of test samples should be exposed to the same sterilization process in three separate cycles to demonstrate reproducibility.
- g) The sterile barrier systems should be evaluated after exposure to the sterilization process and after the expected worst-case handling, distribution, and storage conditions until the point of use, using acceptance criteria from OQ. Results should be documented. See also [3.2.3](#) and ISO 11607-1:2006, 6.3.

NOTE The checklist for the PQ in [G.1](#) can be used for documentation purposes.

3.3.2.7.4 Self-sealing or taped pouches

While the use of self-sealing or taped pouches is discouraged when heat sealing equipment and pouches are available, the assembly and closure of these should be validated if they are used (see requirements in ISO 11607-2:2006, 5.1.1). All appropriate elements and steps of validation detailed in ISO 11607-2:2006, Clause 5 should be addressed.

3.3.2.8 Validation of the wrapping process (folding and closing of sterilization wraps)

3.3.2.8.1 Installation Qualification

Although a wrapping process is typically a manual process, the following IQ aspects should be considered: environmental conditions such as cleanliness, temperature, humidity; documented/operated training; operating manual or procedure.

3.3.2.8.2 Operational Qualification

There should be a documented procedure for assembly of packages. This method should consider [3.2.2.3](#) and [3.2.2.6.3](#). Guidance on the assembly and closure of wrapped packages can be obtained from the wrap manufacturer.

Operators should be trained and assessed for competency. The folding methods should constitute a tortuous pathway to impede passage of microorganisms (see [Annex C](#)).

Packages should be assembled in accordance with a documented procedure. In assembling these packages the worst-case configuration should be included, see [Annex H](#). Samples should be closed/sealed and evaluated. All samples should pass the acceptance criteria. For guidance on sample size see [3.3.2.2 h\)](#) and [Annex L](#).

Depending upon the test methods used for the evaluation of the closure(s) multiple sets per batch should be prepared.

Sterile barrier systems are evaluated for sterile barrier system integrity and proper closure. Acceptance criteria should include, but are not limited to:

- a) closure continuity and integrity;
- b) absence of channels, openings or gaps;
- c) absence of punctures or tears;
- d) absence of material delamination or separation upon opening;
- e) unwrapping or opening should demonstrate that the sterile barrier system is capable of enabling aseptic presentation of the contents.

- f) sterilization parameters are achieved
- g) drying parameters are achieved.

In addition to the evaluation of the closed sterile barrier systems the package should be opened and assessed for conformance to the documented assembly procedure.

NOTE The OQ checklist in [F.2](#) can be used.

3.3.2.8.3 Performance Qualification

The PQ demonstrates that the wrapping process will consistently produce acceptable sterile barrier systems under specified operating conditions:

- a) Evaluation of the sterile barrier system should be performed after the sterile barrier system has been closed and sterilized.
- b) The batch documentation for batches used during the validation studies should form part of the validation records. The batch identification should include, but is not limited to:
 - 1) operator;
 - 2) time and date;
 - 3) sterilization process, parameters and cycle number;
 - 4) sterile barrier system materials used;
 - 5) closure tape used;
 - 6) contents of sterile barrier system;
- c) Three batches of test samples should be exposed to the same sterilization process in three separate cycles to demonstrate reproducibility.
- d) Three batches or sets of closed sterile barrier systems should be assembled in accordance with the facility's documented procedures. These three batches should encompass the potential significant sources of variation such as operator, time of day, material (size, source, lot), sterile barrier system contents. The contents that present the greatest challenge (worst-case) should be included. If a reusable sterile barrier system is exposed to multiple and/or different sterilization processes to achieve terminal sterilization the validation should cover all processes in the order performed. The reuse of sterile barrier systems intended for single use is bad practice and should not be permitted.
- e) Samples should be sealed/closed and evaluated. All samples should pass the acceptance criteria. For guidance on sample size see [3.3.2.2 h\)](#).
- f) Depending upon the test methods used for the evaluation of the closure(s) multiple sets per batch should be prepared.
- g) The sterile barrier systems should be evaluated after exposure to the sterilization process and after the expected worst-case handling, distribution, and storage conditions until the point of use, using acceptance criteria from OQ. Results should be documented.

NOTE The checklist for the wrapping process PQ in [G.2](#) can be used for documentation purposes.

3.3.2.9 Validation of the container process (filling and closing of re-usable containers)

ISO 11607-2 and this guidance address filling and closing of re-usable containers; however, they do not address cleaning or decontamination of these containers prior to their reuse. In real hospital application, reusable containers should however be subjected to a validated cleaning/decontamination process prior to filling and closing.

When performing process validations using reusable containers, it is important to make sure that all the manufacturer's instructions are met and documented for each container used in the validation (e.g. condition of gasket, container, etc.).

3.3.2.9.1 Installation Qualification

Although filling and closing of containers is typically a manual process, the following IQ aspects should be considered: environmental conditions such as cleanliness, temperature, humidity; documented/operated training; operating manual or procedure. If equipment is used, then IQ should be performed in accordance with ISO 11607-2:2006, 5.2.

3.3.2.9.2 Operational Qualification

There should be documented procedures for assessment for damage, filling and closing of the containers. These procedures should consider [3.2.2.3](#) and [3.2.2.6.4](#). Details should be obtained from the manufacturer.

Operators should be trained and assessed for competency. The SOP has to be written and approved prior to beginning the process qualification.

Containers should be cleaned and inspected, loaded and closed with a tamper evident system in accordance with the manufacturer's instructions and facility's documented procedure. In determining or choosing the contents of these containers the worst-case configuration of content should be included, (e.g. container loading with respect to weight, volume, and material). Sterile barrier systems where typical adjustments such as filter changes have been made by the operator should also be included. All samples should pass the acceptance criteria. For guidance on sample size see [3.3.2.2 h](#)). For this qualification the samples may be assembled at one time or over time using the same container(s), depending on the conditions of use. Depending upon the test methods used for the evaluation of the closure(s) multiple sets per batch should be prepared.

Assembled sterile barrier systems should be evaluated for sterile barrier system integrity and proper closure. Acceptance criteria should include, but are not limited to checking:

- a) the sealing, mating surfaces, and edges of the container system and lid to ensure that they are not dented or chipped;
- b) that filter retention mechanisms and fasteners, such as screws and rivets, are secure and not distorted or burred;
- c) that securing mechanisms are functioning properly;
- d) that the integrity of the filter media is not compromised;
- e) that gaskets are pliable, securely fastened, and without breaks or cuts;
- f) that valves work freely;
- g) closure continuity and integrity;
- h) no damage of filters, mechanical valve elements, or sterilant port;
- i) ability to open container without damage to contents;
- j) the container should allow for aseptic presentation of the contents;
- k) tamper evident mechanism is effective and intact;
- l) sterilization parameters are achieved;
- m) drying parameters are achieved.

In addition to the evaluation of the closed sterile barrier systems the containers should be opened and assessed for conformance to the documented cleaning, inspection and loading portion of the assembly procedure.

NOTE The OQ checklist in [F.3](#) can be used.

3.3.2.9.3 Performance Qualification

The manufacturer of the container should provide evidence to demonstrate the suitability of the container with a specified sterilization process and of the ability of the sterilized container to maintain sterility of its contents. The PQ demonstrates that the process of loading, filling and closing will consistently produce acceptable sterile barrier systems under specified operating conditions.

Evaluation of the sterile barrier system should be performed after the sterile barrier system has been closed and sterilized. The following points need to be considered:

- a) The batch documentation for batches used during the validation studies should form part of the validation records. The batch identification should include, but is not limited to:
 - 1) operator identification;
 - 2) time and date;
 - 3) sterilization process, parameters and cycle number;
 - 4) sterile barrier system materials used;
 - 5) any tamper evident closure used;
 - 6) contents of sterile barrier system;
- b) Three batches or sets of closed sterile barrier system(s) should be assembled in accordance with the facility's documented procedures. These three batches should encompass the potential significant sources of variation such as operator, time of day, material (size, source, lot), sterile barrier system contents. The contents that present the greatest challenge (worst-case) should be included. If the same sterile barrier system is intended to be used in several different sterilization processes each should be validated.
- c) All samples should pass the acceptance criteria. For guidance on sample size see [3.3.2.2 h](#)).
- d) The sterile barrier systems should be evaluated after exposure to the sterilization process and after the expected worst-case handling, distribution, and storage conditions until the point of use, using acceptance criteria from OQ. In addition to the OQ acceptance criteria contents should be assessed after sterilization to ensure that sufficient drying has occurred in moist heat sterilization process.
- e) Three batches of test samples should be exposed to the same sterilization process in three separate cycles to demonstrate reproducibility.
- f) All evaluation results should be documented.

NOTE The checklist for the PQ in [G.3](#) can be used for documentation purposes.

- g) If packaging failures are found, investigation should be made to identify a root cause, see [Annex R](#).

3.4 Quality system

ISO 11607-1:2006, 4.2 and ISO 11607-2:2006, 4.2 require a formal quality system and no further guidance is given.

4 Guidance for industry

4.1 General guidance

4.1.1 Quality systems

4.1.1.1 The application of ISO 11607-1 should be performed within a formal quality system (ISO 11607-1:2006, 4.2).

4.1.1.2 A critical element of this quality system is design control. Design control procedures are intended to ensure that the design of the packaging system and any modifications or revisions meet the specified design requirements ISO 11607-1:2006, 6.2.1.

For further information on developing the specified design requirements see [4.3](#) and [Annex J](#) on design inputs.

4.1.1.3 The design history file typically provides documentation of the packaging system development process and any later modifications or revisions (ISO 11607-1:2006, 4.5 and 6.2.5).

4.1.1.4 A fundamental requirement of many quality systems is risk management. A formal risk analysis should be conducted to anticipate the possible failures that can occur in the packaging process and their effects on the safety and efficacy of the medical device. The key requirement is to design the packaging system to minimize the safety hazard to the patient and user under the intended specified conditions of use (see ISO 11607-1:2006, 6.1.1). ISO 14971 describes the requirements and applicability of risk assessment within the scope of medical devices. Tools for conducting risk analysis are described in [Annex K](#).

4.1.1.5 For references on regulatory frameworks, design controls and other quality system aspects see [Annex N](#).

4.1.2 Test methods

ISO 11607-1 and ISO 11607-2 require that all test methods used to show compliance with this standard are validated (see [Annex O](#)). For guidance on the requirements on test methods in ISO 11607-1 and ISO 11607-2, see [Annex A](#) of this document.

Test methods that have been subjected to systematic inter-laboratory studies are preferred since the repeatability, reproducibility, and in some cases the sensitivity have been determined. When incorporating these methods into a specific laboratory it is important to demonstrate the accuracy and repeatability of the method are at least as good as the reproducibility from inter-laboratory studies.

Test methods developed independently or from the scientific literature can be used. However it is important to determine if the test method meets the required sensitivity and that the accuracy and repeatability meet predetermined criteria.

4.1.3 Sampling

Sampling plans should be applicable to packaging systems, reflective of risk tolerance, and be based on statistically valid rationale (ISO 11607-1:2006, 4.3). See [4.8.2](#) and [I.4](#) for further information.

4.2 Design inputs

Prior to considering materials and/or packaging system design, a set of design inputs should be developed (ISO 11607-1:2006, 6.2.2 and 6.2.3). These will be used in assessing the materials and/or design.

The design inputs will reflect user needs. This information will come from users engineering, manufacturing, marketing, regulatory, etc. Some examples of design inputs are medical device attributes,

medical device protection requirements, sales unit configuration, sterilization process, distribution, handling, and use environment (ISO 11607-1:2006, 6.1 and 6.2).

NOTE For guidance on developing these design inputs see [Annex J](#).

4.3 Selection and evaluation of materials

NOTE Information on these topics may be found in [Annex A](#).

4.3.1 Guidance on sterilization requirements (ISO 11607-1:2006, 5.1.6 e) and 5.3)

When assessing the material characteristics important to the medical device, process, and end use, it is critical to keep in mind that the material possesses characteristics appropriate for the sterilization process (e.g. porosity for gaseous sterilization) as well as be able to withstand the rigors of the sterilization process. There are further details on sterilization in [Annex B](#).

4.3.2 Guidance on safety requirements (ISO 11607-1:2006, 5.1.5 and 5.1.6)

When choosing a material for a sterile barrier system there are basic safety requirements that should be met. The source, history and traceability of materials should be known and controlled. Chemical properties should be evaluated. This will typically include toxicity and an evaluation of possible chemical interactions between material and medical device. Testing for the presence of toxic heavy metals is often included. Further details are provided in [Annex A](#).

4.3.3 Guidance on barrier requirements (ISO 11607-1:2006, 5.1.4 and 5.1.6)

The barrier requirements of the medical device and the chosen sterilization method will help define the appropriate sterile barrier and packaging system materials. Various methods can be used to assess the material characteristics and evaluate the barrier or barrier levels required to protect the medical device. Some of the areas to consider include porosity, microbial barrier, air (oxygen), moisture, temperature and light transmission. These are detailed in the section on barrier in [Annex A](#).

4.3.4 Guidance on visibility and appearance requirements

Visibility and appearance requirements, if applicable, will be determined by the desired aesthetics (for example a sterile barrier system with high gloss versus one with a matte finish), labelling approach (for example, a label insert may require a sterile barrier system with good clarity), and the desire to see (or mask) the device. Areas to consider are haze, gloss, opacity, and clarity; further information is in [Annex A](#).

4.3.5 Guidance on physical property requirements (ISO 11607-1:2006, 5.1.6 c), 5.1.7 e), and 6.3.2)

The sterile barrier system should be capable of protecting the medical device's sterility, efficacy, and/or functionality until time of use. The sterile barrier system or preformed sterile barrier system physical property requirements will depend on the mass and profile of the contents, the type of protective packaging (if applicable), storage conditions and the distribution system. There are several factors that impact material performance. Examples include resistance to puncture, abrasion, and tear, flexural durability, thickness, and basis weight. These factors are detailed further in [Annex A](#). Test methods to assess physical properties will characterize the material, but are not directly predictive of completed sterile barrier system performance and further evaluation, such as laboratory simulated packaging system performance tests, frequently need to be performed to assess material performance of the sterile barrier system for a specific medical device.

4.3.6 Guidance on heat sealability requirements [ISO 11607-1:2006, 5.1.6 d) and 5.1.8 c)]

Seals should be tested for tensile peel strength and reviewed to determine if the results meet the desired seal strength for the sterile barrier system. Other criteria include peelability, seal visual attributes, and

failure of material(s) during opening. A tensile test of the seal is typically used as a screening tool for selection of material combinations and can be used to evaluate heat seals pre and post sterilization. A number of different test methods for seal strength can be used. See Annex B of ISO 11607-1. ASTM F88 contains details of some of these methods and also includes information on the effect of differences in technique.

4.3.7 Guidance on processing requirements (ISO 11607-1:2006, 5.1.2 to 5.1.9)

As packaging materials are evaluated for compatibility with equipment and processing conditions, consideration needs to be given to predetermined requirements which ensure consistent and reliable production of sterile barrier systems. Common methods used to assess process requirements and conditions are dimensional measurements, coefficient of friction (COF), sealability, and coat weight: these are discussed in more detail in [Annex A](#).

4.3.8 Guidance on printing requirements (ISO 11607-1:2006, 5.4)

It is important to keep in mind the attributes of the packaging materials when designing the print. Font sizes or styles may be inappropriate for specific substrates, print colour(s), artwork placement and copy should also be considered. Evaluations of new substrates need to consider the ability to be printed. Printed ink properties need to ensure physical and chemical resistance to degradation, and printed process indicators function for the intended exposure or sterilization process(es). Thought should be given to printing before and/or after forming to guarantee that the graphical appearance is not significantly altered and the information to be conveyed is not rendered illegible. For further information on evaluating materials for specific printing requirements see [Annex A](#).

4.3.9 Guidance on cleanliness and particulate requirements [ISO 11607-1:2006, 5.1.7d)]

Typical cleanliness expectation is that packaging materials should be adequately free of dirt, dust, grease, and other forms of contamination. Particulates may be embedded or loose, foreign or bits of parent material. For further information on particulates see [Annex A](#). The level of particulate inherently present will be dependent upon the packaging material chosen. Size of particulate is frequently estimated using a TAPPI Dirt Estimation Chart.

4.3.10 Device-packaging system interaction

Material stiffness, sticking, discoloration or other attributes could interact with the medical device use.

Sterile barrier system components could migrate into the medical device (leachables) and interact with its contents, which could lead to adverse effects. In the same way, medical device materials could migrate into the packaging system materials resulting in adverse effects. The risk needs to be assessed and compatibility studies should be performed as appropriate.

4.4 Sterile barrier system and protective packaging design (packaging system development)

4.4.1 Key elements in the design

Use documented procedures for the design and the development of the sterile barrier system and protective packaging (ISO 11607-1:2006, 6.2.1).

A key component of the packaging system design process is gathering and assessing the design inputs (ISO 11607-1:2006, 6.2.2 and 6.2.3), these have been previously covered in [4.3](#) and [Annex J](#).

The package development function should be included in the design control system or process. The process of designing a packaging system for a terminally sterilized medical device should begin very early in the overall development cycle for the medical device. It is important to be engaged in the medical device development process and have a keen understanding of all of the attributes of the medical device, including all relevant medical device, sterilization and manufacturing specifications.

Sterile barrier system and protective packaging (i.e. packaging system) design may be performed in conjunction with a contract packager. Guidance on the use of contract packagers may be found in [Annex P](#).

4.4.2 Steps in packaging system design

4.4.2.1 Design the sterile barrier system

4.4.2.1.1 The goal of the package design process is a sterile barrier system which allows the medical device to be sterilized, maintains sterility to the point of use or expiry date and allows the medical device to be presented in an aseptic manner at the point of use (ISO 11607-1:2006, 6.1 and 6.2).

4.4.2.1.2 Select the type of sterile barrier system and the materials of construction based on the information (design inputs) gathered through participation in the medical device development process. Some common preformed sterile barrier system types and sterile barrier system types are:

- a) preformed tray and lid (ISO 11607-1:2006, A.3.2);
- b) preformed pouch (ISO 11607-1:2006, A.3.3);
- c) preformed sterilization bag (ISO 11607-1:2006, A.3.4);
- d) preformed header bag (ISO 11607-1:2006, A.3.5);
- e) reusable containers (ISO 11607-1:2006, A.3.12);
- f) self-contained products with tortuous path closures (ISO 11607-1:2006, A.3.11);
- g) those requiring fabricating of sterile barrier system and making all seals – form/fill/seal and four-side-sealing (ISO 11607-1:2006, A.3.6 and A.3.7).

4.4.2.1.3 Specify and document the materials, dimensions, tolerances, geometry and physical characteristics of the sterile barrier system, in accordance with the procedures outlined in the quality system.

NOTE Assure tolerances are reasonable for the supplier capabilities and the equipment being used.

4.4.2.2 Design the protective packaging

The protective packaging provides physical protection to the sterile barrier system and its contents.

Specify and document the materials, dimensions, geometry, and physical characteristics of the protective packaging, in accordance with the procedures outlined in the quality system.

4.4.2.3 Prototype the packaging system

- a) If assessment is successful, proceed to feasibility testing;
- b) If the prototype packaging system is unacceptable, return to the design phase;

NOTE Guidance for packaging system design feasibility testing may be found in [S.2](#).

4.4.2.4 Labelling considerations for the packaging system design

NOTE The design and printing of labelling is a critical and time-consuming activity in the medical device industry. The responsibility for specifying the labelling content is not generally the sole responsibility of the packaging area or group. Assuring that this specified labelling is incorporated into the packaging system is usually the responsibility of the packaging area or group.

4.4.2.4.1 The completed labelling system should remain intact and legible at the point of use, be compatible with all materials and processes, and not transfer to the medical device or react with the packaging system in a way that impairs the utility of the packaging system.

4.4.2.4.2 Determine if labelling will be accomplished by printing directly on the packaging materials or by affixing labels to the packaging system.

4.4.2.4.3 If labels are used, specify the dimensions of die cut label stock, materials, coatings, and adhesives.

4.4.2.4.4 If labels are used, determine whether they will be pre-printed or printed on the manufacturing floor.

4.4.2.4.5 Specify the type of printing to be used. Printing types include but are not limited to laser, ink jet, and thermal transfer.

4.4.2.4.6 If necessary, specify system of printing variable medical device information on the labels. Variable information includes but is not limited to lot or serial number, manufacturing date, and expiry date.

4.4.2.4.7 Incorporate instructions for use (IFU) and any included medical device literature into the packaging system design.

4.5 Packaging process feasibility evaluation

NOTE Feasibility is not a requirement of ISO 11607-1 or ISO 11607-2. This section is used to assess the feasibility of the packaging system.

4.5.1 Sterile barrier system manufacturing process

Define the manufacturing process for the chosen sterile barrier system. Establish a process map or flow chart for the manufacturing process. Show each stage of the fabricating, loading, sealing, and packing process. For each step, analyse potential risks for failure of the sterile barrier system or packaging system as well as sources of variation that could lead to quality issues. Evaluate risks, decide on ways to control and redesign the packaging process accordingly (for guidance see [Annex K](#)). Indicate packaging system material and medical device movement. For guidance on detailed analysis see [Annex S](#). For guidance on determining process parameters, see [Annex Q](#).

4.5.2 Equipment Installation Qualification guidance

Determine equipment IQ requirements for each stage/piece of equipment defined in the process map or flowchart. See ISO 11607-2:2006, 5.2 for discussion of IQ as well as [4.8](#).

- a) If using existing equipment, determine whether new or current tooling will be used and assess IQ accordingly.
- b) If using new equipment, perform IQ.

4.5.3 Prototype or trial runs

Producing prototype packaging for initial performance testing is recommended as it reduces the risk for failure during validation of the packaging process.

Prototype sterile barrier systems should be produced using process parameters that are to be used for sterile barrier system performance testing.

4.6 Sterile barrier system design feasibility evaluation

4.6.1 General considerations

4.6.1.1 This is an engineering evaluation in which the sterile barrier system (possibly only a prototype at this point) is subjected to testing. Results of this testing determine if the design is worth pursuing.

4.6.1.2 This testing typically assesses:

- a) Whether the sterile barrier system contained the medical device and protected it from being physically damaged.
- b) Possible interactions between sterile barrier system and contents.

4.6.1.3 While this step is frequently not a full-scale validation, useful guidance may be found in [Annex I](#), generating a final packaging system validation protocol.

4.6.2 Sterile barrier system test method

4.6.2.1 Use a documented test plan employing validated test methods (ISO 11607-1:2006, 6.3.2). See [Annex A](#) for further information on test methods.

4.6.2.2 This test plan should include pass-fail criteria.

4.6.2.3 Sterile barrier system tests should be conducted on samples that have been constructed considering the worst-case elements identified in [4.6.3](#) (ISO 11607-1:2006, 6.3.4).

4.6.2.4 Samples should be exposed to dynamic testing which simulates the expected distribution environment (ISO 11607-1:2006, 6.3.5).

4.6.3 Worst-case feasibility condition

NOTE Further guidance on addressing worst-case may be found in [Annex H](#).

To properly determine feasibility, determine worst-case conditions, or what at this point in the process are believed to be worst-case, for a number of factors related to the packaging system. These include but are not limited to:

- a) sterile barrier system manufacturing (sealing parameters, etc.);
- b) sterilization process (parameters, number of cycles, etc.): it may not be necessary for the samples to be sterilized for initial feasibility testing;
- c) shipping configuration: this requires an understanding of how the medical device will be shipped to the customer;
- d) distribution environment: this requires an understanding of how the medical device will be shipped to the customer;
- e) shelf life testing is usually not required at this point; however accelerated aging may be used. Accelerated aging testing allows the simulation of the effects of time on a packaging system by subjecting the fully processed protective packaging system to elevated temperatures in a controlled environment. Real time is generally estimated by assuming the degradation of packaging materials follows the kinetics described by the Arrhenius reaction rate function. For further guidance see ISO 11607-1:2006, Annex B.

4.6.4 Pass/fail status of packaging system

4.6.4.1 On completion of testing determine whether the packaging system met the acceptance criteria for the feasibility tests.

4.6.4.2 The packaging system passes the feasibility testing if the packaging system met all criteria set forth in the test plan. This establishes confidence that the design will work. Begin preparing for packaging system validation, typically performed on a validated manufacturing process as in [4.7](#).

4.6.4.3 If the packaging system failed to meet all of the criteria set forth in the test plan, the failure modes should be determined and investigated. Corrective action(s) for the failures should be put in place. This may include redesigning the concept and repeating feasibility. Guidance on determining failure mode and appropriate corrective action may be found in [Annex R](#).

4.7 Validation of sterile barrier system manufacturing process

Validation of the sterile barrier system often means the involvement of additional functional elements of the medical device manufacturer, and/or contract packagers and packaging suppliers. For preformed sterile barrier system, the medical device packager's process is often limited to the filling and application of a sterile barrier system closure seal. In the event a form-fill-seal method is employed, the medical device packager typically performs the validation of the sterile barrier system formation and the closure following insertion of the medical device. It is recommended to review this guidance along with ISO 11607-2.

4.7.1 Development of written process validation protocol

4.7.1.1 Validation protocols may be written for sterile barrier system families. The rationale for determining the sterile barrier system families to evaluate should be documented.

4.7.1.2 Often historical data exists for specific material combinations. This information should be evaluated to determine if it is appropriate for use. Document the rationale.

4.7.1.3 IQ activities need to be planned and documented. If an IQ has been previously performed on the equipment of interest, this work should be assessed to determine if it meets the needs of the current validation activities.

4.7.1.4 OQ activities need to be planned and documented. The acceptance criteria need to be detailed. These predefined requirements generally include dimension, seal strength, seal integrity, opening features, and material integrity.

4.7.1.5 PQ activities need to be planned and documented. The acceptance criteria need to be detailed. These predefined requirements generally include dimension, seal strength, seal integrity, opening features, and material integrity.

4.7.1.6 The process validation protocol needs to be reviewed and approved by appropriate personnel.

4.7.2 Performance of validation activities detailed in protocol

4.7.2.1 Installation Qualification (if not satisfied from previous IQ work) (ISO 11607-2:2006, 5.2)

IQ activities may include:

- a) establishing an installation checklist:
 - equipment design features;
 - installation conditions;
 - safety features;
 - supplier documentation, prints, drawings, and manuals;
 - spare parts list;
- b) verifying that the equipment operates within design parameters;
- c) performing software validation;
- d) establishing environmental conditions;
- e) establishing approved SOP's for equipment operation and documenting operator training;
- f) verifying that critical process parameters are controlled and monitored, such as
 - temperature;
 - pressure or gauge pressure;
 - dwell;
- g) establishing calibration procedures and schedules;
- h) establishing preventive maintenance cleaning procedures and schedules.

4.7.2.2 Operation Qualification (ISO 11607-2:2006, 5.3)

4.7.2.2.1 Perform engineering studies to establish a worst-case operating window. Typically, this is the extremes of the operating window (e.g. lowest and highest temperature, lowest and highest pressure, and shortest and longest dwell.) This window should be assessed to verify that it is appropriate given the capability of the process. The conclusions drawn should be documented.

4.7.2.2.2 Samples produced under worst-case conditions need to be included in the performance testing protocol, which will make sure that the entire process window is validated (see ISO 11607-1:2006, 6.3.4 and Annex H). Samples for performance qualification can be built during the OQ if manufactured under conditions confirmed under PQ.

NOTE Further guidance on addressing worst-case conditions can be found in [Annex H](#).

4.7.2.2.3 Verify that all control measures defined in the risk management process are in place and operate effectively.

4.7.2.2.4 Verify that the sterile barrier system produced at operating extremes will reliably meet the acceptance criteria defined in the protocol.

4.7.2.3 Performance Qualification (ISO 11607-2:2006, 5.4)

Three successful production runs are typically evaluated. These runs are produced at normal operating conditions and the runs can be interrupted by other manufacturing processes on the equipment. However, all three production runs for PQ need to be successful without a failed run in between. Considerations should be given to sufficient run time, and the effects of changeovers, breaks, and multiple shifts. Verify that the sterile barrier system produced meets the acceptance criteria defined in the protocol.

4.7.3 Assessment of validation results

Assess validation results (ISO 11607-2:2006, 5.4.7). Assess the activities performed in [4.7.2](#) to verify that they meet the acceptance criteria detailed in [4.7.1.4](#) and [4.7.1.5](#). Any deviations from the protocol need to be documented, and reviewed and assessed to determine if the intent of the validation protocol has been met.

4.7.4 Approval of process validation

The process validation needs to be reviewed and approved by appropriate personnel (ISO 11607-2:2006, 5.5).

4.7.5 Establishment of documented ongoing process control and monitoring

Establish documented ongoing process control and monitoring (ISO 11607-2:2006, 5.6). This typically includes:

- a) monitoring and recording critical process parameters, and
- b) in process testing of sterile barrier systems in accordance to the quality system.

NOTE Selected monitors must be suitable for monitoring the process. Use data and process knowledge to choose monitor(s) suitable for the process as reflected in the Quality System.

4.8 Packaging system design validation

4.8.1 General

The packaging system design validation (ISO 11607-1:2006, 6.3, 6.4) includes:

- a) developing a validation protocol, which is the plan by which the packaging system will be tested,
- b) performing the conditioning and testing defined in the protocol,
- c) assessing whether the test results obtained meet the acceptance criteria detailed in the protocol, and
- d) obtaining formal approval of the validation.

4.8.2 Validation protocol

The validation protocol should include detailed information on the following subjects:

- a) Establish the plan objectives, which may include physical testing to see if the sterile barrier system has maintained its integrity after life cycle events such as sterilization, packaging system simulated distribution testing, and stability testing. Alternatively, stability testing may be performed during the feasibility portion of the design activities and should be conducted separately.

NOTE Microbial testing methods may be necessary for tortuous path closures.

- b) Establish the packaging system details and specification, for both the sterile barrier system and any additional layers of protective packaging. Ensure specifications are controlled prior to finalization test protocol.

If using the same packaging system for multiple medical devices or a family of medical devices, then a rationale should be developed indicating that the other included medical devices provide a less severe challenge than the specific configuration to be validated.

- c) Establish the sampling plan to be used: sample sizes need to be large enough to provide for statistically significant analysis to provide a high degree of reliability, and will be dependent on corporate risk policy, economics, and regulatory requirements. For further guidance see [1.4](#).

Prepare the packaging system as follows:

- the sterile barrier system used in the packaging system to be tested should be manufactured in a validated process or a process that will be validated. Samples for testing should be production or production equivalent to those made in the validated process;
 - the sterile barrier system or packaging system should be sterilized in the anticipated medical device/ packaging configuration and in a validated sterilization process. If specified, the sterilization process may be performed multiple times to simulate worst-case conditions;
 - packaging systems to be tested should contain the sterile barrier system with medical devices or a medical device surrogate inside, labelling, IFU's, and all additional packaging layers.
- d) Define the accelerated aging to be performed, for a discussion of accelerated aging see [1.8](#) and [A.12](#) and for stability testing see [Annex M](#).
- e) Define the handling, distribution, and storage testing to be performed; for a discussion of these see [1.7](#) and [A.12](#).
- f) Select appropriate test methods for the packaging systems to be tested, for guidance on test methods see [Annex A](#).
- g) Establish the acceptance criteria based on risk policy and a measured result such as maintenance of sterile barrier system/packaging system integrity and/or medical device functionality.
- h) Review and approve all documentation by the appropriate personnel.

For further guidance on these subjects, see [Annex I](#), generating a packaging system validation protocol.

4.8.3 Performing testing

Tests should be performed according to the protocol. Any deviations to the protocol should be documented and a rationale provided.

4.8.4 Documenting validation results

Results of testing should be compared to the acceptance criteria defined in the protocol and this assessment of passing or failing the protocol should be documented.

Validation reports and gathered data should be maintained in accordance with the quality system requirements. The last step is the formal approval of the final report.

4.9 Revalidation

4.9.1 Revalidation is required when changes have been made to the medical device, packaging system, process, or equipment that will affect the original validation. Some examples are changes in physical characteristics of medical device contained in the sterile barrier system, process locations,

methods of formulation or type of equipment, component manufacturer, and analytical techniques used (ISO 11607-2:2006, 5.7).

4.9.2 Revalidation concerns are frequently addressed in the quality system procedures or in the original validation protocol.

4.9.3 Revalidation is often affiliated with design control and the associated change control procedure, the extent of the revalidation chosen will depend on the nature of the change and how it affects the process or medical device. For further references on design control see [Annex N](#).

4.9.4 Review of the process, medical device, packaging system should be considered periodically to ensure that multiple minor changes, which did not require revalidation, have not affected the packaging system (ISO 11607-2:2006, 5.7.4).