A summary of key changes to EU Regulations and harmonised standards for Sterile Medical Packaging (V2)

12 July 2023

Table of Contents

Purpose of the document

This document compares the General Safety and Performance Requirements (GSPRs) of the Regulation (EU) 2017/745 (MDR), that are relevant for packaging with the essential requirements (ERs) of the MDD. The changes are reviewed and discussed in relationship with the requirements of EN ISO 11607-1&2.

Introduction

Regulation (EU) 2017/745 on Medical Devices (MDR) and Regulation (EU) 2017/746 on *In Vitro* Diagnostic Medical Devices (IVDR) have been introduced in 2017 and are fully applicable since May 2021 repealing the preceding Directives (Directive 93/42/EEC on Medical Devices (MDD), Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD) and Directive 98/79/EC *In Vitro* Diagnostic Medical Devices (IVDD)). The MDD and AIMDD are still applicable for medical devices with existing certificates on the market under the MDR transition regime until they expire. The MDR and IVDR introduce rigorous risk and quality management requirements to ensure the safety and reliability of devices.

Under the MDR, sterilisation equipment is "deemed" to be a medical device. Packaging is extensively covered in the MDR with 73 instances of the word *"packaging"* or *"package"*, 21 instances of *"packaged"* and seven instances of *"sterile packaging"* while it is only covered 25 times in the MDD.

Preformed SBS sold to hospitals continue to be considered an accessory under the MDR in a similar way as with the MDD. SBS of sterile medical devices are a part or component of the sterile device indispensable for sterility assurance until the point of use and for the aseptic presentation of the sterile device to the sterile field. MDD or MDR requirements apply to both, accessories as well as components/parts.

Sealing equipment is neither an accessory nor a medical device.

Medical packaging standards

The EN ISO 11607 series *"specifies the requirements and test methods for materials, preformed sterile barrier systems, sterile barrier systems and packaging systems that are intended to maintain sterility of terminally sterilized medical devices until the point of use"*. It consists of two parts:

- EN ISO 11607-1:2020/Amendment 11: 2022 - Packaging for terminally sterilized medical devices - Part 1: *Requirements for materials, sterile barrier systems and packaging systems.*
- EN ISO 11607-2:2020/Amendment 11: 2022 - Packaging for terminally sterilized medical devices – Part 2: *Validation requirements for forming, sealing and assembly processes.*

In these standards, four key terms are defined.

A sterile barrier system (SBS) is defined as *"the minimum packaging configuration that provides a microbial barrier and allows aseptic presentation of the product unit at the point of use"*.

A **preformed sterile barrier system** is *a "partially assembled sterile barrier system prior to filling and final closure and sealing"*.

Protective packaging is the *"packaging configuration designed to prevent damage to the sterile barrier system and its contents from the time of their assembly until the point of use".*

The **packaging system** is the *"combination of the sterile barrier system and protective packaging*" and includes the transit packaging.

These definitions have been introduced in 2006 and today the terminology of "sterile barrier system" is also included in EN ISO 13485 since its latest revision published in 2016. Part one of EN ISO 11607 deals with materials and packaging design as well as design validation, while part two covers packaging process design, validation, and process controls. EN ISO 11607 parts 1 & 2 are considered general, semi-horizontal standards, but also process standards covering a wide range of sterile devices.

The harmonisation of EN ISO 11607 with the EU Medical Devices Regulations

After the first publication in 2006 by ISO, ISO 11607 parts 1 and 2 were published in 2009 by CEN as an EN ISO standard with an Annex Z for the MDD. Both standards were listed in the EU official journal as harmonised standards with the EU medical device directive. As such EN ISO 11607 provided a partial presumption of conformity with a few relevant essential requirements of directive 93/42/EEC (MDD) as they apply to sterile packaging.

After the 2014 amendments of the standards, Annex Z was revised in 2016 by CEN TC102/WG4 to also include the directive for active implantable devices (AIMDD) and the directive *for in vitro* diagnostic medical devices (IVDD). These new annex Z versions, however, were never formally accepted by the EU Commission, as efforts were underway to improve the harmonisation process and the work had started to develop the upcoming MDR which was published in 2017.

Based on the paper from the SBA published in 2016, ISO 11607 parts 1 & 2 were revised to also address the new requirements of the MDR. A new ISO version was published in 2019 while an annex ZA for the MDR and ZB for IVDR had been developed for the EN ISO version. During 2019 it became apparent that harmonization was only possible by amending EN ISO 11607 to add more details for risk management. The EN ISO version of the standards was then published in 2020 without the annexes ZA & ZB and an amendment project was launched to work on packaging risk management.

The 2020 EN ISO revisions of ISO 11607 were amended with revised annexes ZA, ZB, and ZC covering the MDD, AIMDD and IVDD, ratified in April 2022, after being accepted for harmonization by the EU Commission.

CEN and the ISO working group in charge of medical packaging continued to pursue the harmonization of EN ISO 11607 with the MDR. The amendment to the standard to integrate additional requirements for risk management has been completed and accepted in August 2023. Upon publication in the Official Journal of the EU, the standard will then provide a partial presumption of conformity with the GSPRs as outlined in the respective annexes.

The GSPRs in Annex I of the MDR are in general based on the ERs in Annex I of the MDD, with a few important changes to be considered by manufacturers.

This document represents the views of the Sterile Barrier Association based on members' feedback.

Analysis of packaging changes: Regulation (EU) 2017/745[1] vs Directive 93/42/EEC[2]

Annex Z for the MDD providing a presumption of conformity includes only the following key essential requirements:

Essential Requirements (ERs) of Directive 93/42/EEC included in Annex ZA of EN ISO 11607
8.1 The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties. The design must allow easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use.
8.3 Devices delivered in a sterile state must be designed, manufactured and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market and remain sterile, under the storage and transport conditions laid down, until the protective packaging is damaged or opened.
8.4 Devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method.

When reviewing the MDR presumption of conformity, a much wider approach was taken by CEN TC102/WG4 by including all general safety and performance requirements that apply to sterile packaging. This was also a request from the Harmonised Standards (HAS) Consultants working for the EU Commission. In this paper, we will only include those requirements where EN ISO 11607 parts 1 and 2 provide a presumption of conformity, or which are in scope. Other standards like the EN ISO 10993 series or EN ISO 14971 for risk management will provide further presumption of conformity.

For simplification, the discussion will only cover the MDD and the MDR. A similar conclusion can be made for the IVDD and the IVDR.

Risk Management in the MDR

A key change of the MDR versus the MDD is the extended requirements for risk management. These requirements were further reinforced through the standardization request of the EU Commission to CEN/CENELEC asking standardisers to provide details on how to apply risk management. In the MDR, the key general risk management requirements are documented in GSPRs 1, 2, 3, 4 5 and 8 while the MDD covers risk management essentially in ER 1, ER 2, and ER 6. The MDR GSPR 7 and the MDD ER 5 cover transport and storage and a more detailed analysis is indicated:

[1] Regulation (EU) 2017/745 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (MDR).

[2] Council Directive 93/42/EEC concerning medical devices (MDD).

Medical Devices Regulation	Medical Devices Directive	Comments
6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.	4. The characteristics and performances referred to in Sections 1, 2 and 3 must not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the device as indicated by the manufacturer when the device is subjected to the stresses which can occur during normal conditions of use.	Applying this to the SBS which is a component or part of the sterile device necessary for the maintenance of sterility, is asking to make sure that the SBS is designed to withstand the hazards which can occur during normal conditions of use. EN ISO 11607-1 provides requirements to test for performance and stability to provide evidence. Subtle changes from the MDD to the MDR while highlighting that the device should be properly maintained.

This GSPR is included in Annex Z for the MDR.

Medical Devices Regulation	Medical Devices Directive	Comments
7. Devices shall be designed, manufactured and **packaged** in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.	5. The devices must be designed, manufactured and **packed** in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage taking account of the instructions and information provided by the manufacturer.	**Adding examples of** fluctuations in temperature and humidity during transport and storage

EN ISO 11607 requires manufacturers to validate their packaging designs by doing performance testing to demonstrate that the packaging system *provides "adequate protection to the product through the hazards of handling, distribution and storage"* intending to show that the integrity of the sterile barrier system is maintained to ensure sterility. It is best practice to use standards such as ASTM 4169, ISTA 1, 2 and 3 series or ISO 4180-1 to define test cycles based on the distribution cycle defined by the manufacturer that will also include environmental challenges like fluctuations of temperature and humidity. These standards are listed in Annex B of EN ISO 11607-1.

SBA Proposal: The SBA recommended that GSPR 7 will be considered for inclusion into the future annex Z of EN ISO 11607 with the comment that the GSPR is partly covered for the function of maintenance of sterility assuming that the manufacturer has included environmental challenges in their test program.

GSPR 8 covers the requirement that all known and foreseeable risks, and any undesirable side-effects, shall be minimised and be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use. It is not possible to apply GSPR 8 to

packaging alone, it can only be done together with a medical device which will be used to treat the patient. GSPR 8 is not included in annex Z.

GSPR 9 is only applicable to devices referred to in Annex XVI.

GSPR 10 applies to packaging in combination with the device, however, EN ISO 11607 parts 1 and 2 do not provide direct support for the presumption of conformity with these requirements.

Medical Devices Regulation	Medical Devices Directive	Comments
11. Infection and microbial contamination 11.1. Devices and manufacturing processes shall be designed in such a way as to **eliminate or to reduce as far as possible the risk of infection** to patients, users and, where applicable, other persons. The design shall: (a) reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries, (b) allow easy and safe handling, (c) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use, and (d) prevent microbial contamination of the device or its content such as specimens or fluids.	8. Infection and microbial contamination 8.1. The devices and manufacturing processes must be designed in such a way as to **eliminate or reduce as far as possible the risk of infection** to the patient, user and third parties. The design must allow easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use.	Added requirements a, b, c, d, New Requirement: b) easy **and safe** handling (d) prevent microbial contamination of the device or **its content such as** specimens **or fluids**.

A sterile barrier system is an essential part of a sterile medical device and plays an essential role in the fight against healthcare-associated infections. Sterile barrier systems in their function to maintain sterility and to allow for aseptic presentation are one of the elements contributing to the elimination or reduction of the risk of patient infections. GSPR 11.1 takes over the idea of ER 8.1 and extends it with further specific requirements for the design. Applying this requirement to sterile packaging is straightforward. Presenting a product in an aseptic manner requires the application of a proper **Aseptic Technique** adapted to the specific design of the sterile barrier system. The current version EN ISO 11607-1 introduces a normative usability evaluation to assess the ability of proper aseptic technique in the intended clinical environment. This usability evaluation allows for confirmation that 11.1, 11.1a) and 11.1d) are fulfilled for the packaging function.

SBA comments: The SBA supports the inclusion of requirements for usability evaluation of aseptic presentation in the current revision of EN ISO 11607. The SBA has developed a guidance document for the usability of sterile barrier systems that can be used as supporting documentation for such evaluation (link).

GSPR 11.2 are outside of the scope of EN ISO 11607 parts 1 and 2.

GSPR 11.3 is applicable only for reusable sterilization containers and reusable materials.

Medical Devices Regulation	Medical Devices Directive	Comments
11.4. Devices delivered in a sterile state shall be designed, manufactured and packaged in accordance with appropriate procedures, to ensure that they are sterile when placed on the market and that, unless the packaging which is intended to maintain their sterile condition is damaged, they remain sterile, under the transport and storage conditions specified by the manufacturer, until that packaging is opened **at the point of use**. It shall be ensured that the integrity of that packaging is clearly evident to the final user.	8.3. Devices delivered in a sterile state must be designed, manufactured and **packed** in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market and remain sterile, under the storage and transport conditions laid down, until the protective packaging is damaged or opened.	**Deleted "**non-reusable pack**"**. **Added "**at the point of use**".** Added requirement: "It shall be ensured that the integrity of that packaging is clearly evident to the final user."

The current EN ISO 11607-1 proposes a requirement for SBS to be visually inspected prior to use. If instructions for use are required, they shall include instructions for visual inspection of integrity.

SBA comments: The requirement to protect until the point of use adds clarity in that sense that SBS have to be protected against loss of packaging integrity until they are opened at the point of use where healthcare is provided. Manufacturers have to consider this new requirement and need to provide guidance on how to handle units of products in the hospital environment as well as test for it. The SBA supports the clarity that is provided by adding the *"point of use"* and recommended upgrading EN ISO 11607 in that sense.

Visual inspection of packaging prior to use is important, however, the user will have only a short time to do this and the ability to detect small breaches of integrity is limited. This visual inspection will never be a 100% verification and should be considered an additional control rather than claiming it as only a risk control measure. For these reasons, a strong focus should be on design control and subsequent design validation. The SBA suggests that manufacturers consider the usability evaluation of packaging as an opportunity to seek feedback from users on their ability to assess the integrity of specific packaging designs. This step will allow to confirm that the design ensures that "*the integrity of that packaging is clearly evident to the final user*".

The new legislation refers to sterile barrier systems as *"the packaging which is intended to maintain their sterile condition"*. The SBA would welcome clarification from the EU Commission on the use of such language used in the MDR in one of their future guidance documents referring to the term *"sterile barrier system"*. The SBA believes that the use of this term adds significant clarity to requirements.

Medical Devices Regulation	Medical Devices Directive	Comments
11.5. Devices labelled as sterile shall be processed, manufactured, **packaged** and, sterilised by means of appropriate, validated methods.	8.4. Devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method.	"packaged" has been added

SBA comments: The SBA welcomes that more clarity has been added to this GSPR by explicitly adding packaging. The ER 8.4 is among those listed in the current annex ZA of EN ISO 11607. Packaging is to be considered part of *"manufactured"*, adding *"packaged"* to the new GSPR of the MDR leaves no room for interpretation. There are no further changes to be made since this has already been considered in EN ISO 11607 and EN ISO 13485.

Medical Devices Regulation	Medical Devices Directive	Comments
11.6. Devices intended to be sterilised **shall** be manufactured and **packaged** in appropriate and controlled conditions **and facilities**.	8.5. Devices intended to be sterilized must be manufactured and **packaged** in appropriately controlled (e. g. environmental) conditions.	"Facilities" added

In the 2016 revision of EN ISO 13485, the requirements for the control of the work environment have been strengthened. Clause 6.3 covers the infrastructure and clause 6.4 the work environment and contamination control. These requirements are not part of the EN ISO 11607 series.

SBA comments: More clarity has been added to this GSPR by explicitly adding the word "*facilities*". There is no recommendation for revision of EN ISO 11607. Adding new requirements for the work environment and facilities would be redundant with quality management system requirements.

GSPR 11.7 is outside of the scope of EN ISO 11607 parts 1 and 2.

Medical Devices Regulation	Medical Devices Directive	Comments
11.8. The labelling of the device shall distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition **additional to the symbol used** to indicate that devices are sterile.	8.7. The packaging and/or label of the device must distinguish between identical or similar products sold in both sterile and non-sterile condition.	Added requirement to include symbol and specific label

SBA comments: The current symbol 5.2.7 defined in EN ISO 15223-1 can continue to be used (see Appendix). Medical device manufacturers will need to find ways to add the required information in addition to the symbol to their label in order to comply with this GSPR. The SBA will support proposals clarifying this situation and standardising the approach taken by manufacturers.

Note: EN ISO 15223-1 addresses labelling requirements for medical devices.

GSPR 12 does not apply to packaging.

GSPR 13 on devices incorporating materials of biological origin can indirectly apply, packaging can include such materials, but the evaluation of the risks needs to consider that the risks are not the same as if such materials are incorporated into the medical device itself. EN ISO 11607-1 does not provide a presumption of conformity.

GSPR 14-21 do not apply to packaging.

GSPR 22 on protection against the risks posed by medical devices intended by the manufacturer for use by lay persons can apply. EN ISO 11607-1 does not include specific requirements for laypersons. Since the revision of 2019, it includes requirements to evaluate the usability of packaging which can also be applied to lay persons. Specific requirements for lay persons could be considered for inclusion in the next revision of ISO 11607-1.

GSPR 23.1 and 23.2 provide general requirements regarding the information supplied by the manufacturer and information on the label.

Medical Devices Regulation	Medical Devices Directive	Comments
The 23.3. Information on the packaging which maintains the sterile condition of a device ('sterile packaging') The following particulars shall appear on the sterile packaging: (a) an indication permitting the sterile packaging to be recognized as such, (b) a declaration that the device is in a sterile condition, (c) the method of sterilization, (d) the name and address of the manufacturer, (e) a description of the device, (f) if the device is intended for clinical investigations, the words: 'exclusively for clinical investigations', (g) if the device is custom-made, the words 'custom-made device', (h) the month and year of manufacture, (i) an unambiguous indication of the time limit for using or implanting the device safely expressed at least in terms of year and month, and, (j) an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use.	(b) à 13.3 (c) (c) à 13.3 (m) (d) à 13.3 (a) (e) à 13.3 (b) but changes to language (f) à 13.3 (h) (g) à 13.3 (g) (h) à 13.3 (l) only for active devices (i) à 13.3 (f) but changes to the language	Modified text and new specific requirement for sterile packaging labelling (a), (h), (j)

SBA comments: The SBA welcomes the added requirement to provide an indication permitting the sterile packaging to be recognised as such. Indeed, there is a potential risk of confusion when additional packaging layers are used in order to reduce the risk of loss of sterility during aseptic presentation or in the case of double sterile barrier systems.

The SBA developed and validated a symbol for such labelling in the annex of this document which has been accepted by the standardization community and included in EN ISO 15223-1.

The SBA recommended that ISO TC198/WG7 and CEN TC102/WG4 address the situation of double sterile barrier systems and additional layers of packaging that are part of the design in order to reduce the risk of loss of sterility during aseptic presentation. In a future revision, Annex E of ISO 11607-1 could be revised to reflect the current situation.

The SBA has developed extensive guidance on the use of symbols.

Medical Devices Regulation	Medical Devices Directive	Comments
23.4. Information in the instructions for use (l) If the device is supplied sterile, instructions in the event of the **sterile packaging being damaged or unintentionally opened** before use. (m) If the device is supplied non-sterile with the intention that it is sterilised before use, the appropriate instructions for sterilisation. (n) If the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, **packaging** and, where appropriate, the validated method of re-sterilisation **appropriate to the Member State(s) where the device is placed on the market.** Information **shall** be provided to identify when the device should no longer be reused, e.g., signs of material degradation or the maximum number of allowable reuses.	13.6. Where appropriate, the instructions for use must contain the following particulars: (g) the necessary instructions in the event of damage to the sterile packaging and, where appropriate, details of appropriate methods of resterilization; h) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, **packaging** and, where appropriate, the method of sterilization of the device to be resterilized, and any restriction on the number of reuses.	Adding case of "unintentionally opened sterile packaging" Extended requirements in case the device is supplied non-sterile for sterilization or reusable devices

EN ISO 11607-1:2019 includes a list of requirements for reusable containers and fabrics including the requirement to establish processing procedures and acceptance criteria for inspection prior to reuse.

SBA comment and proposal: The SBA welcomes information on appropriate processes for reuse including the aspects of packaging. This is in line with the concept of EN ISO 11607-1 since packaging designs have to be validated with the device and sterilisation has to be validated with its specific sterile barrier system.

Conclusion

The SBA welcomes the update of MDR to include critical considerations for sterile packaging.

About the Sterile Barrier Association (SBA)

The SBA is the European trade association for companies who produce Sterile Barrier Systems (SBS) and associated equipment and accessories for the healthcare industry. Sterile barrier systems are made from sophisticated materials and allow single use and reusable medical devices to be sterilised after manufacture or after reprocessing. Sterilisation may take place at a medical device manufacturer or in the Central Sterile Supply Department (CSSD) of a hospital. In both cases the critical function of the SBS is to maintain product sterility up to the point of use.

Our **mission** is to be the recognised expert association in the healthcare industry, promoting best practice and providing education in the use of use sterile barrier systems to enhance patient safety.

For more information about the SBA, please visit: www.sterilebarrier.org.

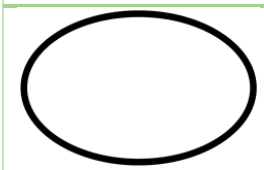
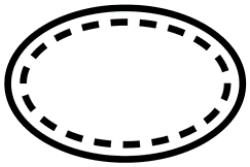
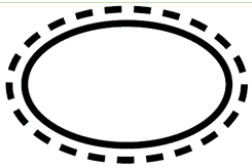
For more information about this document, please contact:

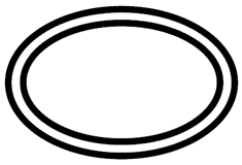
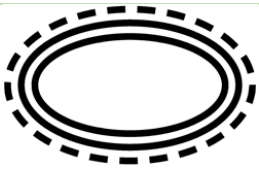
Patrick Sparkes
SBA Director General
director.general@sterilebarrier.org

Appendix: Current and Proposed Symbols for Sterile Products

Current symbols according to EN ISO 15223-1

Description	Symbol	Title of Symbol
5.2.3 Indicates a medical device that has been sterilized using ethylene oxide “single sterile barrier system”		Sterilized using ethylene oxide
5.2.8 Indicates a medical device that should not be used if the package has been damaged or opened. NOTE: This symbol may also mean "Do not use if the product sterile barrier system or its packaging is compromised”.		Do not use if package is damaged
5.2.7 Indicates a medical device that has not been subjected to a sterilization process. This symbol should only be used to distinguish between identical or similar medical devices sold in both sterile and non-sterile conditions.		Non-sterile
5.2.9 Indicates the presence of a sterile fluid path within the medical device in cases when other parts of the medical device, including the exterior, might not be supplied sterile.		Sterile Fluid Path

Symbol	What it represents	Recommended handling / usability
	Ref: ISO 7000 - 3707 Single sterile barrier system	Aseptic presentation technique requires opening by an assistant nurse. (Sterile) Scrub nurses or surgeons must not touch the outer surface of the packaging. Pack must not be placed on sterile surfaces.
	Ref: ISO 7000 - 3708 Single sterile barrier system with protective packaging inside	Aseptic presentation technique requires opening of the outer packaging by an assistant nurse. Sterile nurses or surgeons must not touch the surface of the outer packaging. The inner layer with the sterile product may be handled by sterile personnel. Product in inner layer can be placed on sterile surfaces.
	Ref: ISO 7000 - 3709 Single sterile barrier system with protective packaging outside	Aseptic presentation technique requires opening by an assistant nurse. Sterile nurses or surgeons must not touch the outer surface of the sterile packaging. Pack must not be placed on sterile surfaces.

	Ref: ISO 7000 - 3704 Double sterile barrier system	Aseptic presentation technique requires opening of the outer sterile packaging by an assistant nurse. Sterile nurses or surgeons must not touch the outer surface of the sterile packaging. Outer packaging must not be placed on sterile surfaces. The inner sterile packaging may be handled by sterile personnel and can be placed on sterile surfaces.
	Double sterile barrier system with protective packaging outside	Aseptic presentation technique requires opening of the outer protective packaging and the outer sterile packaging by an assistant nurse. Sterile nurses or surgeons must not touch the outer surface of the sterile packaging. Outer packaging must not be placed on sterile surfaces. The inner sterile packaging may be handled by sterile personnel and can be placed on sterile surfaces.