The New EU MDR/IVDR

The Impact on Sterile Packaging and Global Sterile Packaging Standards

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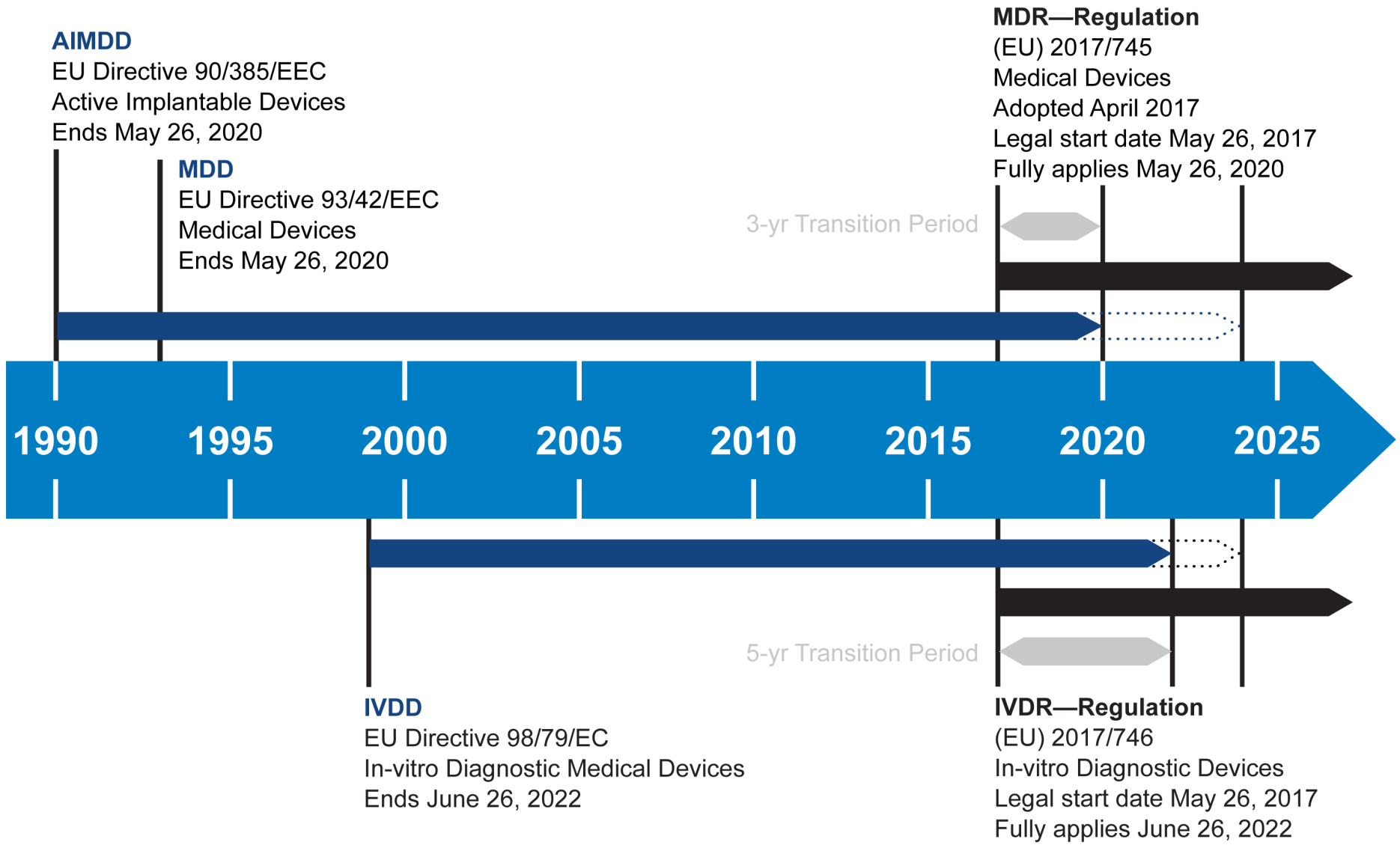
Disclaimer

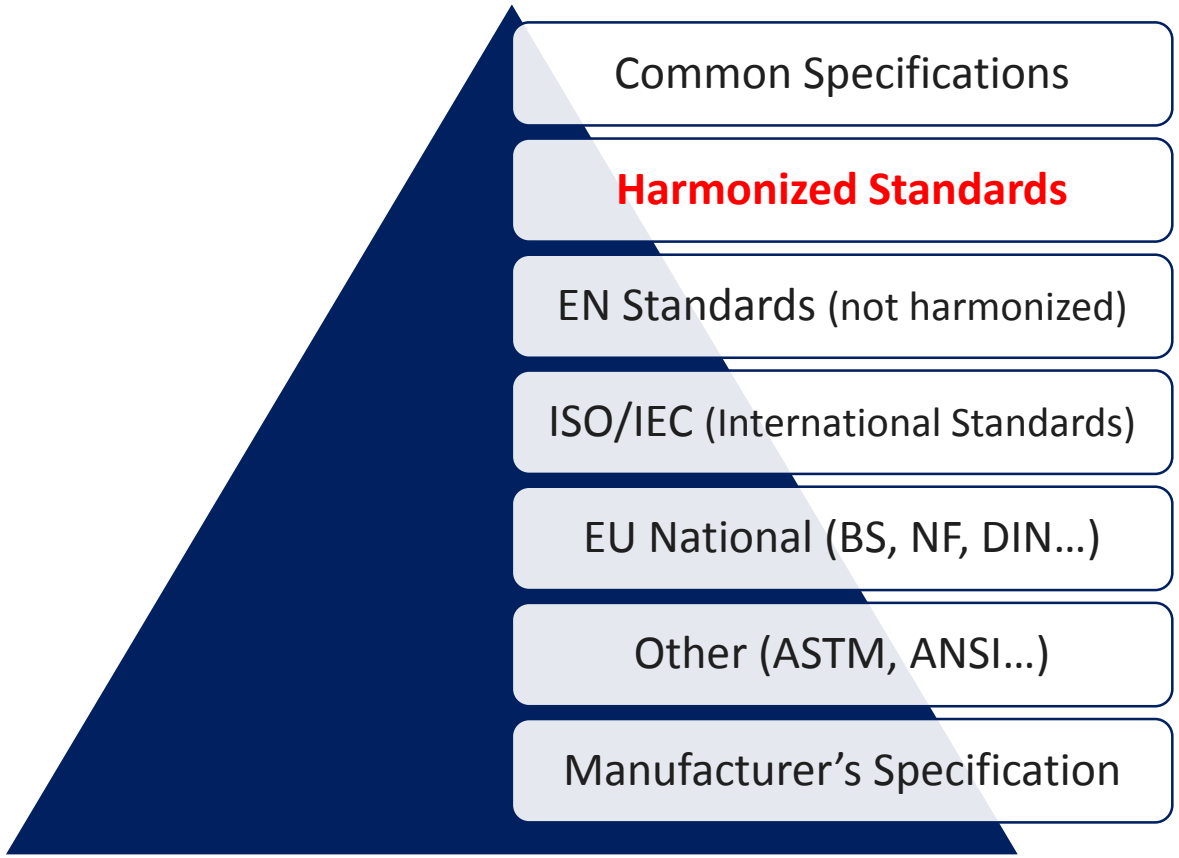
- The information and views set out in this presentation are those of the authors and do not necessarily reflect the official opinion of a specific company or organization.
- The information is based on the text of the medical device regulation as published on the 5th of May 2017 in the Official Journal of the European Union and titled "*REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 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*"
- Information on ISO 11607 is based on the draft of ISO/FDIS which may get edited before final publication
- Information in this presentation is provided without engagement for correctness nor completeness and does not represent legal advice.



···· *MDD Certificates can be valid up to 4 more years after date of application*

Hierarchy of Standards to comply with MDD ERs or MDR SPRs

MDR: “New Approach” legislation based on harmonized standard



> 300 Harmonized MDD Healthcare Standards

To be now harmonized with the new MDR/IVDR

Status of harmonization of standards with MDD

- **Last publication of references in the OJEU**: 17 November 2017
  - ✓ 10 standards cited
  - × 74 standards rejected (with justification provided)
- **Issues**:
  - Unprecise and too broad claims of conformity, lack of qualifying remarks
  - Undated normative references, reference chains, non EN standards
  - Wrong format
- **Context**: Legal concerns with harmonized standards
  - Elliot case: European court of justice ruled that hEN's are part of EU law
  - Other legal case: issues with transition dates of revised standards
  - Triggered redesign of harmonization process

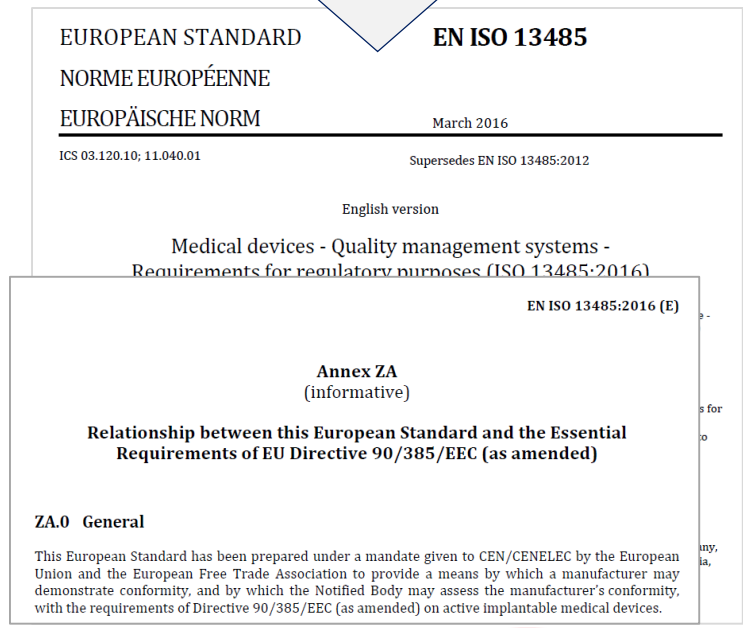
European harmonized standards

Need a new CEN/CENELEC mandate to create MDR harmonized standards

European Commission

MDR Standardization Request(s)

CEN CENELEC


EUROPEAN STANDARD
NORME EUROPÉENNE
EUROPÄISCHE NORM

EN ISO 13485

March 2016

ICS 03.120.10; 11.040.01

Supersedes EN ISO 13485:2012

English version

Medical devices - Quality management systems -
Requirements for regulatory purposes (ISO 13485:2016)

EN ISO 13485:2016 (E)

Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 90/385/EEC (as amended)

ZA.0 General

This European Standard has been prepared under a mandate given to CEN/CENELEC by the European Union and the European Free Trade Association to provide a means by which a manufacturer may demonstrate conformity, and by which the Notified Body may assess the manufacturer's conformity, with the requirements of Directive 90/385/EEC (as amended) on active implantable medical devices.

EU Commission **New** Formal Adoption Process

Official Journal of the European Union

Cited Harmonized Standards providing presumption of conformity with MDR/IVDR SPRs

DUPONT Tyvek.

EU Commission and Competent Authorities

- Have to establish MDR governance structure and resources
- Approve MDR Notified bodies… probably not before 2019
- 14 delegated acts with detailed provisions to be issued
- …
- …
- Need to stay within tight MDR transition timing
- Need to issue a mandate to CEN for standard development
  - Currently 50 standards + monitoring of 240 CEN TC62 standards (electro-mechanical devices)
  - Timing ??

- **Industry is worried**

What is the impact of the MDR on sterile packaging?

MDR Annexes

I. **General safety and performance requirements**

II. **Technical documentation**

III. Technical documentation on post-market surveillance

IV. EU Declaration of conformity

V. CE marking of conformity

VI. Information to be submitted upon the registration of devices and economic operators …core data elements to be provided to the UDI database …

VII. **Requirements to be met by notified bodies**

VIII. Classification rules

IX. Conformity assessment based on a quality management system and assessment of the technical documentation

X. Conformity assessment based on type examination

XI. Conformity assessment based on product conformity verification

XII. Certificates issued by a notified body

XIII. Procedure for custom-made devices

XIV. Clinical evaluation and post-market clinical follow-up

XV. Clinical investigations

XVI. List of groups of products without an intended medical purpose referred to in Article 1(2)

XVII. Correlation table

MDR Annexes

- **Annex I**
  MDD Essential Requirements (ERs) become General safety and performance requirements (GSPRs) under the MDR
- **Annex II**
  Technical documentation must include “validation reports, with respect to packaging, sterilization and maintenance of sterility”
- **Annex VII**
  Requirements to be met by Notified Bodies: Quality management system auditing: … draw up and keep up to date, for Class IIa and Class IIb devices, a sampling plan for the assessment of technical documentation
- **Annex VII**
  Requirements to be met by Notified Bodies: Specific qualification criteria shall be defined at least for …packaging,…and the different types of sterilization processes

Key MDD Essential Requirements for Sterile Medical Packaging as stated in Annex ZA of EN ISO 11607

In summary:

8.1 …eliminate, or reduce as far as possible, the risk of infection to the patient

- Design must allow for easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use

8.3 …remain sterile, under the specified storage and transport conditions until the protective packaging is damaged or opened

8.4 …manufactured and sterilized by an appropriate **validated method**

Note: In addition to the Essential Requirements (ERs) listed above, there are other ERs that must be met, such as general ERs 1-6, labeling, etc.

Key MDR Safety and Performance Requirements for Sterile Medical Packaging - EN ISO 11607

In summary:

11.1 …eliminate, or reduce as far as possible, the **risk of infection** to the patient

NEW Design shall allow for easy **and safe** handling and… **minimize microbial contamination**

11.4 …**remain sterile**, under the specified storage and transport conditions:

NEW **Until** that packaging is **damaged or opened at the point of use**

"That packaging" = "packaging that is intended to maintain its sterile condition"

NEW **It shall be ensured that the integrity of that packaging is clearly evident to the final user**

11.5 …processed, manufactured, **packaged and sterilized by an appropriate validated method**

Note: In addition to the Essential Requirements (ERs) listed above, there are other ERs that must be met, such as general ERs 1-6, labeling, etc.

Conclusions – New MDR Requirements

- **Validation of Packaging**, clear requirement, same level as sterilization! Packaging part of technical documentation (annex II), (see also EN ISO 13485:2016)
- Adding concepts of "***sterile up to the point of use***", "**easy and safe handling**"; "***integrity being evident…***" + New labelling requirements
- **Notified Body involvement growing**, unannounced audits… packaging part of NB qualification, expect more focus of NBs on packaging data
- Delegated acts, common specifications, MDCG… **more change expected**
- Focus on **life cycle** of the device includes the design and entire life time of the packaging

What is the impact of the MDR on ISO 11607?

Current version: ISO 11607-1:2006/Amd 2014

- EN ISO 11607-1: 2009 with annex ZA, published in OJ of EU → **harmonized with MDD**
- **EN ISO 2017 version published in July 2017 with new annex ZABC,**
  → harmonization pending, submitted by CEN to EU Commission in Jan 2018
- **Feb 2018 Copenhagen meeting – all ISO/DIS 11607 comments resolved → draft ISO/FDIS 11607**
- ISO FDIS **ballot 2 months probably period July-Sept 2018** + Parallel CEN ballot
- **4Q2018: expected publication of EN ISO 11607:2018**
- **EN ISO 11607 harmonization MDD/MDR → accepted within EU commission pilot !**

Requirements regarding design and manufacture

Medical Device Regulation	Medical Device 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 with impact on packaging:** (c) easy and safe handling (d) prevent microbial contamination of the device or **its content such as** specimens **or fluids**.

Caution: Draft for FDIS

5.2 Microbial barrier properties

5.5 Storage and transport of materials and preformed sterile barrier systems

6 Design and development for packaging systems

6.1 General

6.1.1 …

6.1.2 …allow the product to be presented in an aseptic manner.

NOTE: …can be demonstrated by completing a usability evaluation (see Clause 7).

6.1.3 …

6.1.4 …

6.1.5 …

Caution: Draft for FDIS

6.1.6 ..

6.1.7 …

6.1.8 **If the packaging system to be opened at the point of use consists of more than one packaging layer, the sterile barrier system(s) shall have an indication to be recognized as such.**

…

6.1.9 …

7 Usability evaluation for aseptic presentation

7.1 A documented usability evaluation shall be conducted …

7.2 …include an assessment of:

a) …identify where to begin opening;

b)…recognize and perform the technique required to open …without contaminating or damaging the contents; and

c) …subsequently present the contents aseptically.

NOTE 1: …consider conditions of use, including utilizing personal protective equipment …

NOTE 2: …contact of the presented sterile contents with the opened seal or closure is avoided to reduce the risk of contamination of the sterile contents by the external edge of the seal …

NOTE 3: …presentation technique where exposure of presented sterile contents to potential contaminants (eg airborne particles, dust etc.) is minimized.

7 Usability evaluation for aseptic presentation… cont'd

…

7.3 ..real or simulated conditions of use.

7.4 …may be leveraged between sterile product families and packaging families based on worst case considerations or other valid rationales.

7.5 …

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Requirements regarding design and manufacture

Medical Device Regulation	Medical Device 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."**

Requirements regarding design and manufacture

Medical Device Regulation	Medical Device 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**

8 Packaging system performance and stability

8.1 General

...

Caution: Draft for FDIS

9 Packaging system validation and changes

9.1 Packaging systems that meet the requirements of design, usability, performance testing and stability testing shall be considered validated if the sterile barrier system conforms with ISO 11607-2.

9.2 …change-control procedure for documenting, verifying and authorizing change.

9.3 Packaging systems shall be revalidated if changes are made …

Caution: Draft for FDIS

9 Packaging system validation and changes… cont'd

…

9.4 The need for revalidation shall be evaluated …. If the situation does not require that all aspects of the original validation be repeated, this revalidation does not have to be as extensive …

…

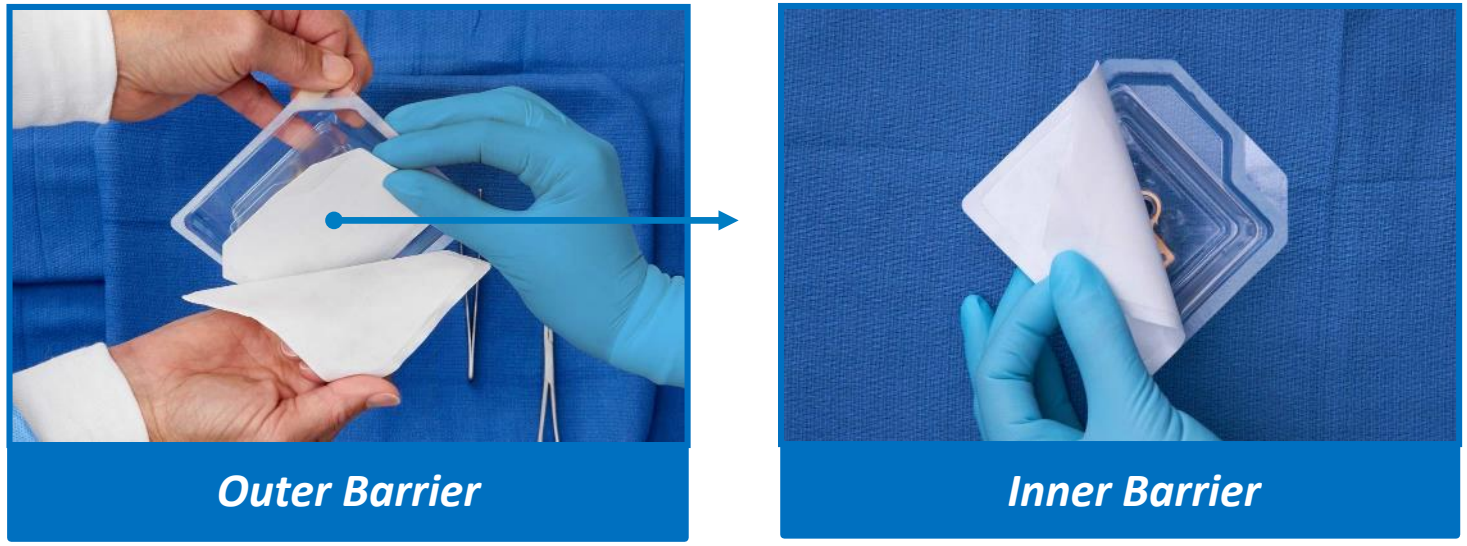
9.5 …

Requirements regarding the information supplied with the device

Medical Device Regulation	MDD	Comments
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) → 13.3 (c) (c) → 13.3 (m) (d) → 13.3 (a) (e) → 13.3 (b) but changes to language (f) → 13.3 (h) (g) → 13.3 (g) (h) → 13.3 (l) only for active devices (i) → 13.3 (f) but changes to language	**New specific requirement for sterile packaging labelling**

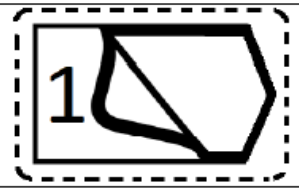
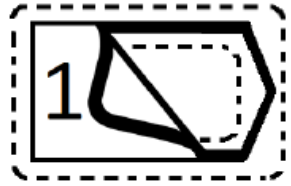
23.3 (a) an indication permitting the sterile packaging to be recognized as such

Where is the Sterile Barrier System (SBS)?
One or two validated SBS?



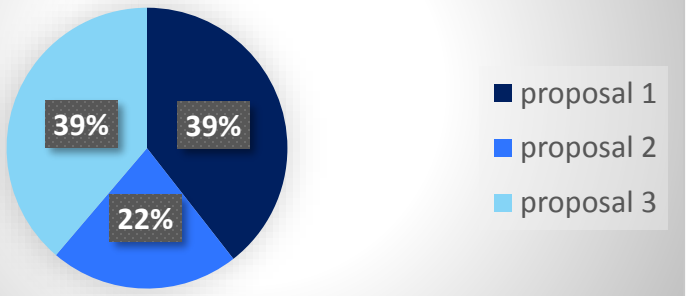
SBA Survey

Symbols: Three alternative proposals 1 – 2 – 3

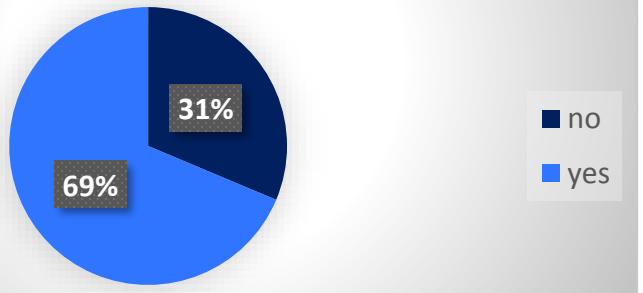
	Proposal 1 Use the abbreviation 'SBS' to indicate the sterile barrier system configuration	Proposal 2 Use the form of a blister to indicate the sterile barrier system configuration	Proposal 3 Use the form of a pouch to indicate the sterile barrier system configuration
Configuration A: Sterile barrier system /sterile packaging			
Configuration B: Sterile barrier system with an additional packaging layer inside to minimize the risk of contamination during aseptic presentation			
Configuration C: Non-sterile protective packaging with sterile barrier system inside			
Configuration D: Non-sterile protective packaging with sterile barrier system and an additional packaging layer inside			

Survey Results (150 participants):

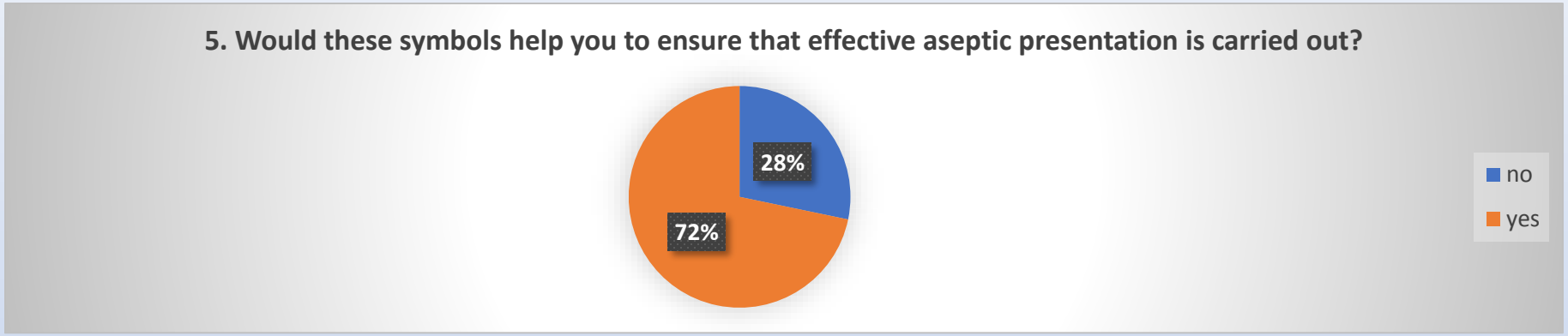
1. Which of these 3 symbols identifies the SBS most effectively?

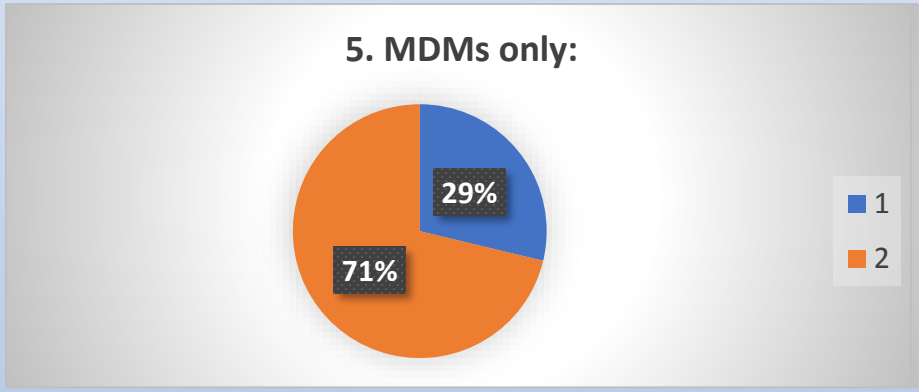


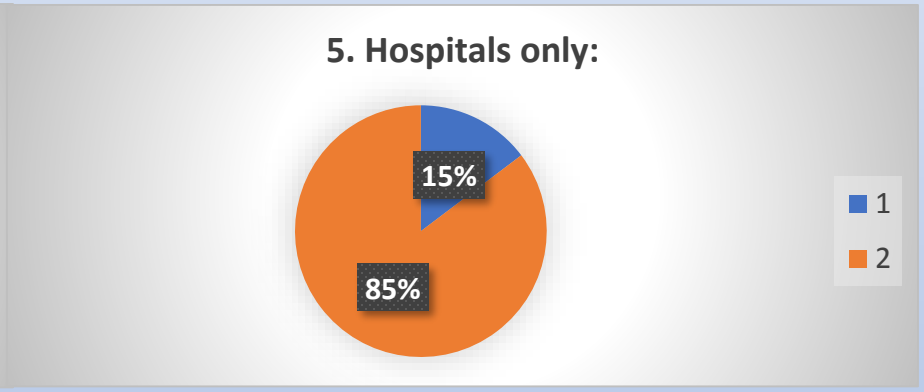
3. Is the difference between the SBS and the protective packaging clearly identified by using solid and dotted lines?



Survey Results





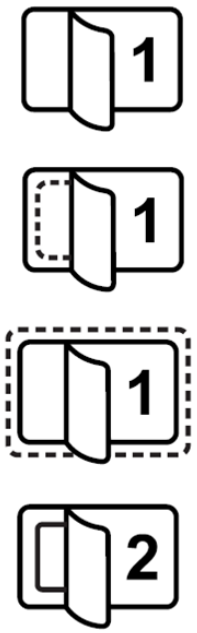


A vast majority of 76% confirms that the symbols help to ensure that effective aseptic presentation is carried out.
The group of healthcare professionals confirms with an even larger majority of 85%.

Symbol Proposal by the Sterile Barrier Association & Medtech Europe

Many Design Options being considered !!

- Feedback indicates preferences for a visual representation



	Option 1 Uses an oval in conjunction with the symbol 'sterile' to indicate the sterile barrier system	Option 2 Uses the form of a pouch to indicate the sterile barrier system	Option 3 Uses the form of a square to indicate the sterile barrier system	Option 4 Uses the symbol for package in combination with solid and dotted circles to indicate the sterile barrier system
Solid line indicates sterile barrier material				
Dotted line indicates an indicates an outer protective packaging layer or an additional inner packaging layer (without microbial barrier) to minimize the risk of contamination during aseptic presentation				
Configuration 1: Sterile barrier system /sterile packaging	STERILE EO			
Configuration 2: Sterile barrier system with an additional packaging layer inside to minimize the risk of contamination during aseptic presentation	STERILE EO			
Configuration 3: Non-sterile protective packaging with sterile barrier system inside	STERILE EO			
Configuration 4: Double sterile barrier system	STERILE EO			

Medtech Europe - Proposed symbols

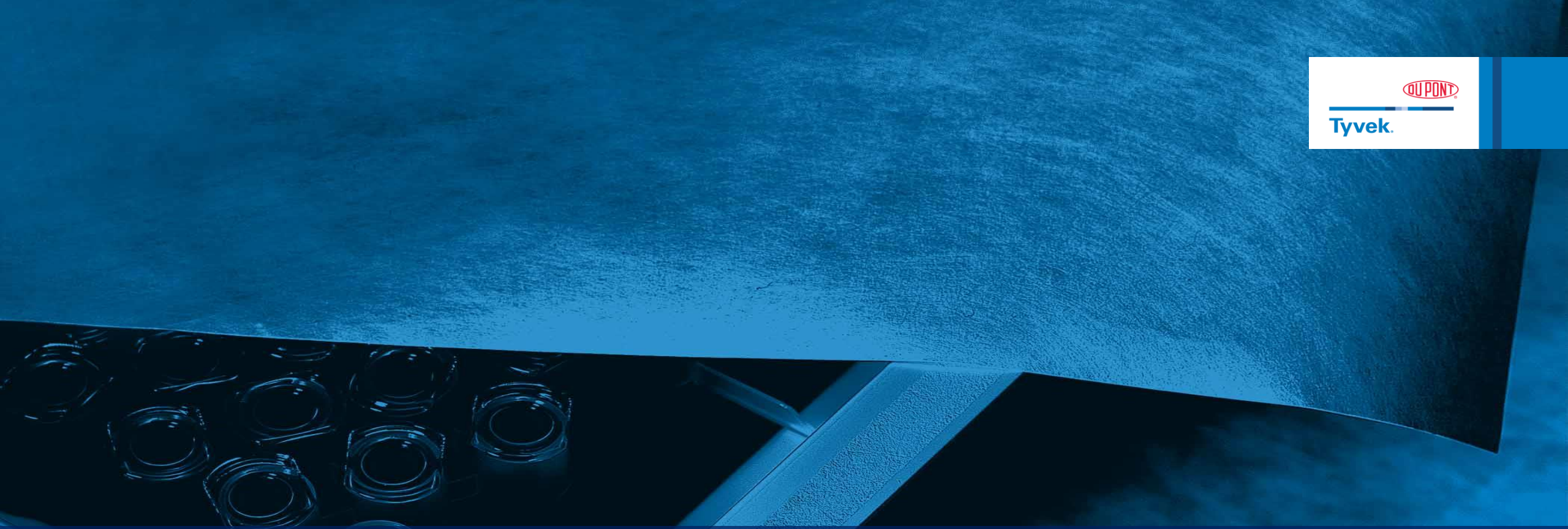
In addition to harmonised standards….Article 9 - Common specifications

1. *… where no harmonised standards exist or where relevant harmonised standards are not sufficient, or where there is a need to address public health concerns,* ***the Commission, after having consulted the MDCG, may, by means of implementing acts, adopt common specifications (CS) in respect of the general safety and performance requirements*** *set out in Annex I, the technical documentation set out in Annexes II and III*

EN ISO/FDIS 11607:2018 Revision —Key Focus Areas

- Editorial changes for clarity and better flow of the document
- Alignment of **definitions** with other standards and ISO/DIS 11139
- **Evaluation to assess aseptic presentation (usability evaluation)**
- **New annex:** guidance on ways to differentiate a SBS from protective packaging
- **Visual inspection** of SBS prior to use
- New section on **design changes and revalidation**
- Process validation section – introduction of a formal **process specification**
- New annex D on **environmental aspects** following ISO and CEN guidance
- Considerations of recent changes to regulatory requirements (i.e., MDR)
  - EN ISO version: Annex ZABC (MDD, AIMDD & IVDD) + **Annex Z-MDR/IVDR**

Next meeting: February 2018—review DIS comments, finalize DIS (target is FDIS)



Questions?