Demonstrating Conformity to General Safety and Performance Requirements (GSPR) under MDR

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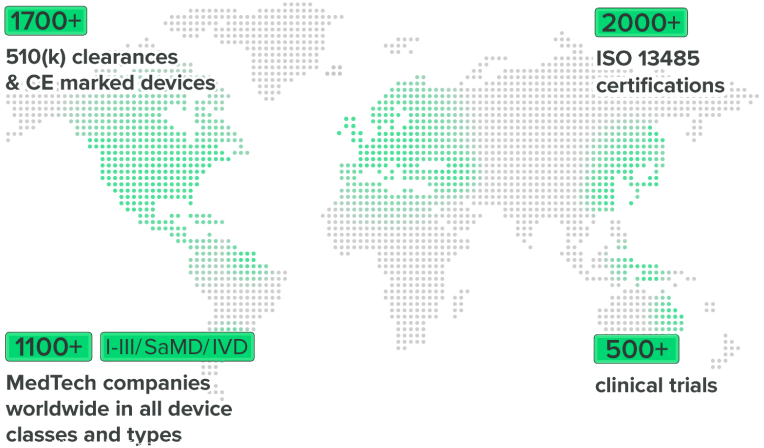

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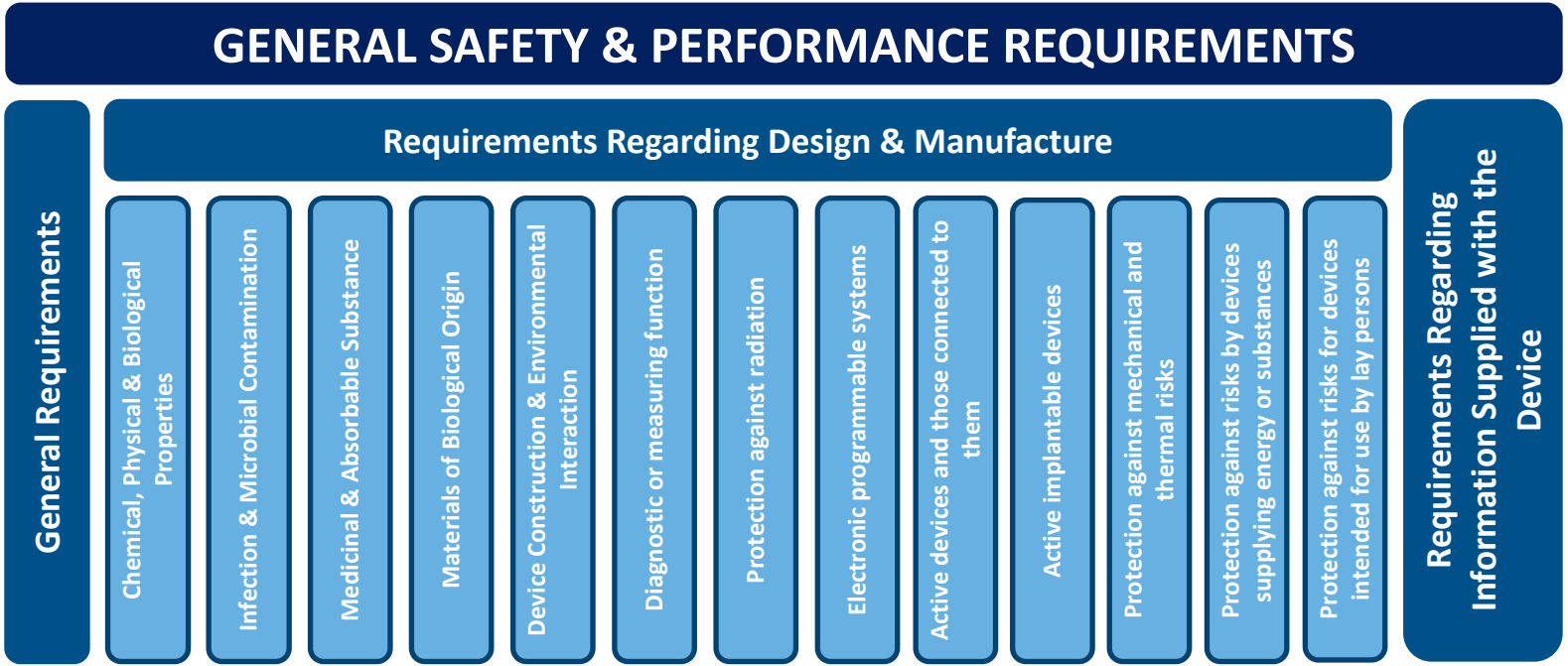
Introduction

GSPR – QMS – Clinical Evaluation

- General Safety and Performance Requirements (GSPR), Annex I
  - 'General' not specific, e.g., 11.2 '*Where necessary devices shall be designed to facilitate their safe cleaning, disinfection, and/or re-sterilization*.' → what is 'safe' in the context of the particular device?
  - Integrated into Quality Management System (QMS), Art. 10 (9), e.g.:
    - Art. 10(9b) 'identification of applicable general safety and performance requirements and exploration of options to address those requirements'
    - Art 10(9e) 'risk management as set out in in Section 3 of Annex I'
    - Even Art. 10(9) 'setting-up, implementation and maintenance of a post-market surveillance system, in accordance with Article 83', when considering lifecycle of device
  - Considers Clinical Evaluation (including clinical investigation), Arts 10(9f), 61 and 62, and Annex XIV and XV

GSPRs

GSPRs (23): General (9) + Design & Manufacture (13) + Label & Instructions for Use (1)



GSPR Chapter I. General Requirements

GSPR Chapter I: General Requirements

- GSPR 1 essentially ER 1 first paragraph, however, additions to the GSPR is that the devices "*shall achieve the performance intended by their manufacturer*" and "*shall be safe and effective*", and, acceptable risk / benefits and generally acknowledged state of the art
- GSPR 2 emphasizes need to reduce risks As Far as Possible (AFAP) without impacting the benefit-risk ratio
- GSPR 3 clear expectation that manufacturers develop an RMS (compliant to ISO 14971): establish, implement, document, and maintain

GSPR Chapter I: General Requirements, continued

- GSPR 4 risk control measures generally specified (assumed per ISO 14971), more explicit requirement that both the overall residual risks and the residual risk associated with each hazard is evaluated and judged to be acceptable, with respect to the benefits; note content about manufacturer managing risks and also risk control following order of priority - (c) new to ISO 14971:2019 "*provide information for safety* (warnings/precautions/contra-indications) *and where appropriate, training to users*"
- GSPR 5 related to reducing risk of use error AFAP for ergonomic features and environment of use, consider intended user and their technical knowledge, experience, education, training and use environment – requirements now explicitly included in the MDR
- GSPR 6 essentially ER 4, and requires that performance not be affected when subjected to stresses from normal conditions of use and properly maintained according to the IFU

GSPR Chapter I: General Requirements, continued

- GSPR 7 devices designed, manufactured, and packaged, that performance and intended use is not affected during transport and storage, ER 5
- GSPR 8 more detailed and elaborate than ER 6a, "*all known and foreseeable risks, and any undesirable side-effects, shall be minimized and 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*"
- GSPR 9 - related to Annex XVI, products without an intended medical purpose (Art. 1(2)) – clarifies that these products shall not present a risk at all or present a risk that is no more than the maximum acceptable risk related to these products' use as described in state-of-the-art

GSPR Chapter II. Requirements regarding Design and Manufacture

GSPR Chapter II: Design and Manufacture requirements

- GSPR 10 chemical, physical and biological properties of devices, this is ER 7, though more requirements are delineated
- GSPR 11 infection and microbial contamination of devices, largely ER 8, there is the consideration of AFAP for “unintended cuts and pricks, e.g. needle-stick (11.1a)”
- GSPR 12 devices incorporating medicinal product or composed of substances absorbed or locally dispersed in the body – scope significantly changed compared to ER 7.4 (on medicinal products only) – requirement for absorbed substances no longer limited to biocompatibility but also to absorption/distribution/metabolism/excretion/local tolerance/toxicity/interaction
- GSPR 13 devices incorporating materials of biological origin – expanded scope for devices utilizing non-viable tissues or cells of human origin, or their derivatives

GSPR Chapter II: Design and Manufacture requirements, continued

- GSPR 14 construction of devices and interaction with the environment, largely ER 9, 14.2(d) inserts the risks associated with possible negative interaction between software and IT environment within which it operates and interacts
- GSPR 15 devices with diagnostic or measuring function, ER 10
- GSPR 16 devices with radiation, ER 11
- GSPR 17 devices that incorporate electronic programmable systems or programmable electronic systems (PES), this is part of ER 12 (ER 12.1 and 12.1a). The GSPR introduces 17.3 and 17.4 related to software used with mobile computing platforms and setting requirements for hardware, IT networks, and IT security measures needed to run the software.

GSPR Chapter II: Design and Manufacture requirements, continued

- GSPR 18 active devices, this is part of ER 12 (ER 12.3- 12.6). 18.1, 18.6, and 18.8 are newly-introduced and relate to non-implantable active devices in single-fault condition - eliminate or reduce AFAP risks, level of intrinsic immunity to electromagnetic interference, and protection against unauthorized access that could hamper the device from functioning.
- GSPR 19 requirements for active implantable devices – due to merging of the MDD and AIMDD requirements into the single MDR – generally mapped to ERs from the AIMDD
- GSPR 20 protection against mechanical and thermal risks of devices, this is generally ER 12.7: 20.1 (12.7.1), 20.3 (12.7.3), 20.4 (12.7.4), and 20.6 (12.7.5). 20.5 relates to errors made when fitting or refitting parts which could be a source of risk should be made impossible or by information given on the parts themselves.
- GSPR 21 protection against risk posed to the patient or user by devices supplying energy or substances, this appears to be ER 12.8.1, 12.8.2, and 12.9

GSPR Chapter II: Design and Manufacture requirements, continued

- GSPR 22 protection against risks posed by medical devices intended for lay person use, this is clearly a new GSPR. The MDD did not really consider lay use (ER1 device design appropriate user).
  - 22.1 requires lay person be able to understand and apply information and instructions related to the device--compliance to EN 62366 critical
  - 22.2 includes requirements addressed in the RM process related to usability and reducing AFAP risk of error in the handling of the device
  - 22.3 requires a procedure that allows the lay person, at the time of use, to verify that the "*device will perform as intended by the manufacturer*"

GSPR Chapter III. Requirements regarding the Information Supplied with the Device

GSPR Chapter III: Requirements regarding The Information Supplied with the Device

- GSPR 23 product labels and IFU – entire chapter – requirements significantly developed compared to MDD/AIMD
  - 23.1 general requirements - requires the general information needed to identify device/manufacturer and S&P related information to the users available on manufacturer's website
  - 23.2 information on the label - includes new requirement that label shall bear an indication that the device is a medical device
  - 23.3 information on the sterile packaging – separation of requirements is new compared to MDD but requirements are similar

GSPR Chapter III: Requirements regarding The Information Supplied with the Device, continued

- 23.4 info in the IFU – requirements generally expanded and some new general requirements

23.4(b) clear specification of indications, contraindications, the patient target groups and the intended users

23.4(c, d) expected clinical benefits to be specified + link to the publicly available Summary of Safety and Clinical Performance

23.4(g) MDR now explicitly requires that residual risks are identified in the IFU

GSPR Chapter III: Requirements regarding The Information Supplied with the Device, continued

23.4(w) “for use by lay persons” information on circumstances when the user should consult with a healthcare professional

23.4(x) device without a medical purpose – absence of clinical benefit and risks to be disclosed

23.4(z) notice to report serious incident to manufacturer/competent authority

23.4(aa) “implant card”

GSPR - Summary

- GSPR scope significantly increased compared with MDD ERs
- Manufacturer must be able to demonstrate compliance to relevant GSPRs

Identification of applicable standards, CS and demonstrating compliance

Many Types of Standards

- Globally recognized vertical standards, e.g., ISO 7886 on sterile hypodermic syringes for single use
- Globally recognized horizontal standards, e.g., ISO 13485 on quality management systems for medical devices
- Professional standards, e.g., ACC/AHA 2008 Guidelines for the management of adults with congenital heart disease
- National standards, e.g., Dutch standard on use of UDI on devices used in hospitals

Standards are Voluntary

- Standards are not law
- Compliance to a standard may result in a presumption of conformity to a legal requirement if this is explicitly stated (e.g., harmonized standards)
- Compliance to a standard may still result in a legal non-compliance
- Non-compliance to a standard may still result in a legal compliance

Create an Overview of Applicable Standards

- Search the list of harmonized standards as published in the *Official Journal of the European Union* (OJEU)
- Some organizations offer tools in which to search for applicable standards
- Search literature for professional standards, if appropriate
- Create a rationale for each applied standard why it has been applied

Common specifications (Technical Req's for Products)

Article 9

*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, ……*

3. **Manufacturers shall comply with the CS referred to in paragraph 1** unless they can duly justify that they have adopted solutions that ensure a level of safety and performance that is at least equivalent thereto.

Two CS published to date (related to the MDR):

The first that was published is for the reprocessing of single-use devices-Aug 2020: https://eur-lex.europa.eu/eli/reg_impl/2020/1207/oj

The second is on devices without medical purpose (Annex XVI): https://eur-lex.europa.eu/eli/reg_impl/2022/2346/oj

Harmonized Standards (Articles 2(70) and 8)

- CEN (European Committee for Standardization) / CENELEC (European Committee for Electrotechnical Standardization)
  - European standardization organizations
  - Can propose standards to be harmonized
- Conformity with a Harmonized Standard (HS) presumes conformity with relevant requirements
  - Harmonized standards are published in the Official Journal of the European Union (OJEU) and the European Commission publishes the list of recognized standards: https://ec.europa.eu/docsroom/documents/55101
  - 'Annexes Z' are added to standards where compliance with the standard by itself does not provide a presumption of conformity with the Directive / Regulation, therefore, additional provisions must be taken to ensure conformity (e.g., EN ISO 14971:2019/A11:2021, EN ISO 13485:2016/A11:2021)
  - For the MDR, new Annexes Z must be made (where currently present)

Harmonized Standards (Articles 2(70) and 8), continued

- Until MDR HS widely available, current HS can be presumed the best available alternative, although current Annexes Z (for compliance to Directives) may not fully apply
- Even HS are voluntary standards

EN ISO 14971
Z-Annex - example

Annex ZA
(informative)

Relationship between this European standard and the General Safety and Performance Requirements of Regulation (EU) 2017/745 aimed to be covered

This European standard has been prepared under a Commission's standardisation request M/575 to provide one voluntary means of conforming to the General Safety and Performance Requirements of Regulation (EU) 2017/745 of 5 April 2017 concerning medical devices [OJ L 117].

Once this standard is cited in the Official Journal of the European Union under that Regulation, compliance with the normative clauses of this standard given in Table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding General Safety and Performance Requirements of that Regulation, and associated EFTA regulations.

For application of this European standard under Regulation (EU) 2017/745,

1. the scope is limited to medical devices and accessories for a medical device as defined in that Regulation and to products regulated as a device under that Regulation;
2. in case of differences between terms defined in this European standard and terms defined in that Regulation, the terms defined in the Regulation shall prevail;
3. the manufacturer's policy for establishing criteria for risk acceptability (see 4.2 of this European standard) shall ensure that the criteria comply with the General Safety and Performance Requirements of that Regulation.

Explanation on the correspondence of the standard and the General Safety and Performance Requirements is included in Table ZA.1.

NOTE 1 — Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Regulation (EU) 2017/745. This means that risks have to be 'reduced as far as possible', 'reduced to the lowest possible level', 'reduced as far as possible and appropriate', 'removed or reduced as far as possible', 'eliminated or reduced as far as possible', 'removed or minimized as far as possible', or 'minimized', according to the wording of the corresponding General Safety and Performance Requirement.

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Use of harmonized standards (Technical Req's for Products)

- MDR HS Commission Implementing Decision (EU) 2021/1182 of 16 July 2021 on the harmonised standards for medical devices drafted in support of Regulation (EU) 2017/745 of the European Parliament and of the Council

ANNEX

No	Reference of the standard
1.	EN ISO 10993-23:2021 Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)
2.	EN ISO 11135:2014 Sterilization of health care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 11135:2014) EN ISO 11135:2014/A1:2019
3.	EN ISO 11137-1:2015 Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 11137-1:2006, including Amd 1:2013) EN ISO 11137-1:2015/A2:2019
4.	EN ISO 11737-2:2020 Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process (ISO 11737-2:2019)
5.	EN ISO 25424:2019 Sterilization of health care products - Low temperature steam and formaldehyde - Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 25424:2018)

Use of harmonized standards (Technical Req's for Products), continued

- Amendment of 4 January 2022 to Implementing Decision (EU) 2021/1182 : addition of #6 to #14 HS
- Amendment of 11 May 2022 to Implementing Decision (EU) 2021/1182: addition of EN ISO 13485:2016/AC:2018, #15 and #16 (EN ISO 14971:2019/A11:2021.
- Amendment of 4 July 2023 to Implementing Decision (EU) 2021/1182: replacement of #5 and addition of #17 (EN ISO 10993-10:2023)

Common Specifications (CS) (Articles 2 (71)and 9)

- If (harmonized) standards are not considered sufficient, or in case of public health concerns, the European Commission can adopt CS
- CS may relate to:
  - GSPR in Annex I
  - Technical documentation requirements in Annex II and III
  - Clinical Evaluation and PMCF in Annex XIV
  - Clinical Investigations in Annex XV
- CS are equally ‘voluntary’ as HS, except for Annex XVI devices

Demonstration of Compliance

- Auditing of QMS (not further discussed here)
- Testing
  - Related to device-specific requirements
  - Bench testing (e.g., verification of a single characteristic)
  - Use simulation (e.g., test in a usability laboratory)
  - Certification testing (e.g., EMC testing in accredited laboratory)
- Other types of evidence
  - Documented results of processes (e.g., risk analysis report)
  - Self-evident evidence (e.g., name and address of manufacturer on label)
  - Tests on healthy volunteers

Standards, CS - Summary

- Manufacturer must be able to demonstrate compliance to relevant GSPRs
- Technical documentation is mechanism by which the documented evidence stored/presented
- Compliance can be presumed if HS are used, for the specific requirements listed in Annexes Z of that standard, additional provisions must be taken to ensure conformity

GSPR Checklist

General Safety and Performance Requirements (GSPR)

- Demonstration of compliance to all applicable GSPR
- Explanation why certain GSPR may not apply
- Methods used to demonstrate compliance
- Harmonized standards, CS and other solutions applied
- Reference relevant documents
- Use a GSPR checklist template

GSPR Checklist

Checklist with all separate requirements split out into single lines

- 185 requirements in total:
  - Chapter I: 18
  - Chapter II: 98
  - Chapter III:68
- Requirement description
- Comply (Y/N/NA); if N or NA provide a strong justification
- Applied standards, specifications or guidelines + date/version
- Complying documents (test reports, certificates etc.)
- Location where these documents can be found (as specific as possible, e.g., ‘Chemical stability testing can be found in the Master Product File, Verification & Validation, section 10.2.3’)
- GSPR Checklist should be a controlled document

GSPR Checklist

PLACE ON MANUFACTURER LETTERHEAD

GENERAL SAFETY AND PERFORMANCE REQUIREMENTS Checklist – MDR

Product name:	Project or file number:	Project Revision #:

#	General Requirement	Comply (Y / N / NA)	Applied Standards Common Specifications or Guidance Documents	Complying Documents	Location
I.	**GENERAL REQUIREMENTS:**				
1.	Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.				
2.	The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.				
3.	Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall:				
(a)	establish and document a risk management plan for each device;				
(b)	identify and analyse the known and foreseeable hazards associated with each device;				
(c)	estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;				
(d)	eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4;				

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Other Directives/Regulations

Other Directives/Regulations

Other Directives or Regulations may also be applicable. For example:

- Machinery Directive 2006/42/EC
- Directive 2011/65/EU - Restriction of the use of certain hazardous substances in electrical and electronic equipment (RoHS Directive)
- Radio Equipment Directive 2014/53/EU (RED)
- Medicinal Products Directive 2001/83/EC
- General Data Protection Regulation (EU) 2016/679
- Regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (EC) 1907/2006 (REACH)

Focus on MDR only: GSPR

Other Directives/Regulations, continued

- Machinery Directive 2006/42/EC

- “Devices that are also machinery within the meaning of point (a) of the second paragraph of Article 2 of Directive 2006/42/EC of the European Parliament and of the Council (35) shall, where a hazard relevant under that Directive exists, also meet the essential health and safety requirements set out in Annex I to that Directive to the extent to which those requirements are more specific than the general safety and performance requirements set out in Chapter II of Annex I to this Regulation.” Source: Art 1(12) MDR

Questions?

Emergo can assist you in Europe and other markets worldwide.

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