



Restricted Substances - EU MDR

Medical Devices placed on the EU market must comply with both the Medical Devices Regulation (MDR) 2017/745/EU and the Restriction of the use of certain Hazardous Substances (RoHS) Directive 2011/65/EU and its amendments. Both include substance restrictions but the approaches used are very different.

The medical industry has complied with the RoHS Directive since 2014 and report that this is very costly financially as well as administratively in terms of time occupied by employees who would otherwise be developing new medical technology.

The MDR Annex I section 10.4 requires substitution of carcinogens, reproductive toxins and mutagens (CMR) of category 1A and 1B as well as endocrine disrupting (ED) substances, of which the EU has two classifications, 1 and 2, unless the manufacturer can show that the use of the substance is justified from a benefit-risk analysis. The scope of these requirements is limited to materials that come into contact directly with patients or in contact with solids, fluids or gases that are administered or re-administered to patients.

At the same time manufacturers have to comply with requirements on substances from legislation worldwide and with specific black-lists coming from clients or purchasing organizations

EU MDR Restricted materials Scope

Let's explore first the differences in requirements that are applied under MDD & MDR:

MDD, ER 7.5	MDR, GSPR 10.4
<p>If parts of a device (or a device itself)</p> <ul style="list-style-type: none"> <input type="checkbox"/> intended to administer and/or remove medicines, body liquids or other substances to or from the body, or <input type="checkbox"/> devices intended for transport and storage of such body fluids or substances <p>Focus on phthalates; special attention to Carcinogenic, Mutagenic or toxic to Reproduction (CMR) (<i>Annex I, Council Directive 67/548/EEC</i>)</p>	<p>Devices, or those parts thereof or those materials used therein that:</p> <ul style="list-style-type: none"> <input type="checkbox"/> are invasive and come into direct contact with the human body, <input type="checkbox"/> (re)administer medicines, body liquids or other substances, including gases, to/from the body, or <input type="checkbox"/> transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body <p>Focus on phthalates, more on CMRs, Endocrine Disrupting Substances (EDs)</p>

Substance Compliance under MDR

Substances compliance required in the below sections of the MDR:

Section 10.4 Substances (Annex I)

- ☐ 10.4.1 Design and manufacture of devices
- ☐ 10.4.2 Justification regarding the presence of CMR and/or EDs
- ☐ 10.4.3 Guidelines on phthalates
- ☐ 10.4.4 Guidelines on other CMR and EDs
- ☐ 10.4.5 Labeling

Section 23.4(s) Information in the instructions for use, IFU (Annex I)

Section 6.2(d) Additional information required in specific cases (Annex II)

- ☐ Where a device incorporates, as an integral part, a substance, considered to be a medicinal product derived from human blood or human plasma
- ☐ Where a device is manufactured utilizing tissues or cells of human or animal origin, or their derivatives
- ☐ Devices that are composed of substances or combinations of substances that are intended to be introduced into the human body

Design and manufacture of devices (10.4.1)

- ☐ Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by substances or particles, including

- ✓ wear debris,
 - ✓ degradation products and
 - ✓ processing residues, that may be released from the device
- ❑ A variety of **ISO standards** used in Identification and quantification of degradation products
 - ✓ ISO 10993-9:2009 - Framework
 - ✓ ISO 10993-13:2010 - Polymeric Devices
 - ✓ ISO 10993-14:2001 - Ceramics
 - ✓ ISO 10993-15:2000 - Metals and Alloys

Restricted Substances

Below are the restricted substances in concern:

- ❑ **Carcinogenic, Mutagenic or toxic to Reproduction (CMR) Category 1A & 1B**
 - ✓ Total CMR substances under CLP – 4249 (Last updated Sept 2018)
 - ✓ Out of them, CMRs Category 1A & 1B - **1124**
- ❑ **Endocrine Disrupting Substances (EDs)**
 - ✓ 65 unique substances assessment done Jan'2015 - Oct'18 (*Last updated Oct 2018*)
- ❑ Based on the recent update dated Jun 2018, **total 191 Substances of Very High Concern (SVHC)**

Justification Requirements if > 0.1% w/w

- ❑ **If presence of CMR and/or endocrine-disrupting substances:** The justification for the presence of such substances shall be based upon
 - ✓ An analysis and estimation of potential patient or user exposure to the substance;
 - ✓ An analysis of possible alternative substances;
 - ✓ An argumentation why possible substance and/or material substitutes, or design changes, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product;
 - ✓ where applicable and available, the latest relevant scientific committee guidelines in accordance with *Part 3 of Annex VI to Regulation (EC) No 1272/2008* (classification, labeling and packaging) and *Article 59 of Regulation (EC) No 1907/2006 (REACH)* or *Article 5(3) of Regulation (EU) No 528/2012* (making available on the market of and use of biocidal products)
- ❑ **If presence of phthalates:**
 - ✓ Provide the relevant scientific committee with a mandate to prepare guidelines that shall be ready before **26 May 2020**
 - ✓ The mandate for the committee shall encompass at least a benefit-risk assessment of the presence of phthalates
 - ✓ The benefit-risk assessment shall take into account
 - The intended purpose and context of the use of the device,
 - As well as any available alternative substances and alternative materials
 - Designs or Medical treatments
 - ✓ And the benefit-risk assessment should be updated every five years.

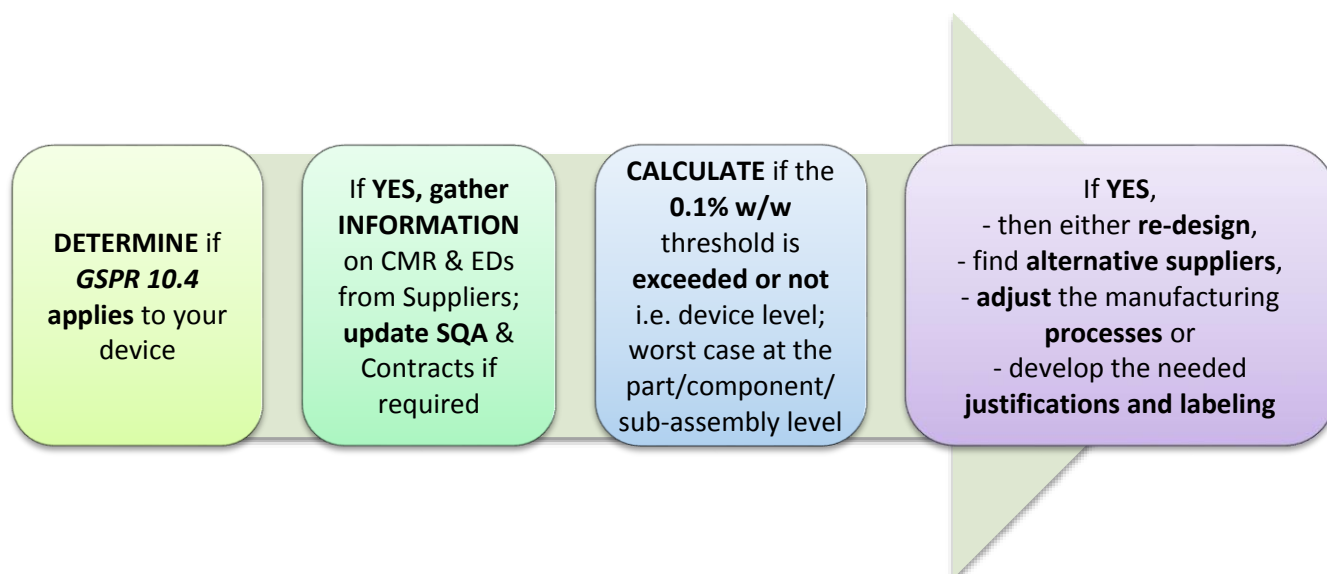
Labeling Requirements

- ❑ Presence of those substances shall be labeled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging, with the list of such substances.
- ❑ Appropriate precautionary measures shall be given in the instructions for use (If the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials, information on residual risks for those patient groups)
- ❑ **Labeling Summary Requirement**
 - ✓ Substances that require justification require labeling on either the device, the device packaging, or where appropriate, on the sales packaging
 - ✓ Label
 - ✓ List of applicable cat 1 CMRs or endocrine disruptors
 - ✓ Historical (EU MDD)
 - ✓ DEHP Label
- ❑ **Information in the IFU**
 - ✓ Information regarding any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device
 - ✓ Precautions related to materials incorporated into the device that contain or consist of CMR substances or endocrine disrupting substances, or that could result in sensitization or an allergic reaction by the patient or user

Manufacturer – Steps & Action Items

All medical devices will need to be converted to the MDR/ retired; timelines are very short

- ✓ Legacy - **till 2022**
- ✓ New designs – **till 2024** Compliance Challenges



- ❑ **Labeling challenges** for reproductive toxicants and endocrine disrupting chemicals
- ❑ There are sufficient details in the BoM to perform the final “*roll-up*” *calculations* is potentially a very large task
- ❑ Suppliers have reasonable data, but are significantly *lacking in extended requirements*
- ❑ A lot of complexity to explain to a large range of internal stakeholders

Approach for Legacy Medical Devices

- ✓ Test representative products for different product families to extended requirements
- ✓ Learn and apply findings to a wider range of products
- ✓ Primary focus on business affecting results

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MakroCare can assist if any of your products need Restricted materials consulting or analysis.