APRIL 2021

HPRA MEDICAL DEVICES
NEWSLETTER

ISSUE 53

In this Issue

Contacting the HPRA

The vast majority of HPRA staff are currently working remotely. This is in line with Government advice aiming to slow down the spread of COVID-19.

During this period, please correspond with us by e-mail using existing HPRA staff e-mail contacts or via the devices mailboxes:

- Medical Device Adverse Incident Reporting, information regarding serious risk, falsified devices and any issue regarding device safety: devicesafety@hpra.ie
- Medical Device Registration and other queries: devices@hpra.ie

MDR TRANSITIONAL PROVISIONS

Key Dates and Considerations

The MDD and AIMD will be repealed and replaced by the MDR from 26 May this year. In order to support the continued supply of medical devices to the European market, the MDR has set out a number of transitional provisions for medical device manufacturers under Article 120 (see figure 1). These transitional provisions ensure that manufacturers of devices certified under the MDD/AIMD may continue to place their devices on the European market from 26 May, provided there are no significant changes in the design and intended purpose of the devices. A corrigendum adopted in 2019 clarifies that Class I devices 'up classified' under the MDR can also avail of these transitional provisions once a Declaration of Conformity has been drawn up. It is important to note that the requirements of the MDR relating to post-market surveillance, market surveillance, vigilance and registration of economic operators and of devices shall apply from 26 May. Furthermore, the reporting of serious adverse events and device deficiencies observed during clinical investigations shall also be carried out in accordance with the MDR from the date of application.

Article 123 of the MDR also sets out a number of soft transitional provisions. While these primarily relate to the use of Eudamed, transitional requirements for device labels are also addressed. For example, the staggered implementation associated with Article 27(4), which stipulates that UDI carriers must be placed on the label of devices and on all higher levels of packaging. In the context of this requirement, a higher level of packaging does not include shipping containers. Separate timelines will apply for reusable devices that are required to bear the UDI carrier on the device itself. For each class of these devices, Article 27(4) will apply a further two years after the dates given above, e.g. 26 May 2027 for reusable class I devices. The implementation of Article 27(4) will correspond to the risk class of medical devices and reusable devices, as outlined below:

Table 1: UDI Timelines

Device class	Deadline to include UDI on the device label	Deadline to include UDI on the label of reusable devices
Implantable devices Class III	26 May 2021	26 May 2021
Class IIb Class IIa	26 May 2023	26 May 2025
Class I	26 May 2025	26 May 2027

Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland.
T: +353 1 676 4971 E: devices@hpra.ie www.hpra.ie

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Further information relating to MDR transitional provisions may also be found in the following documents:

- The Competent Authorities for Medical Devices (CAMD) FAQ document for MDR transitional provisions.
- MDCG 2020-2 rev.1 provides additional information for class I transitional provisions.
- MDCG 2020-3 provides guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD.
- For a comprehensive timeline of the key transitional provisions and milestones in the MDR's application please our MDR Regulatory Timeline.

Management of Legacy Devices

Legacy devices are medical devices covered by a valid certificate under the existing Directives and can continue to be placed on the market after the date of application of the incoming MDR or IVDR. The definition of a legacy device applies to general medical devices, active implantable medical devices (AIMDs), and *in vitro* diagnostic medical devices (IVDs).

Article 120(3) of the MDR states that certain requirements of the MDR shall apply to legacy devices placed on the market after the date of application of the MDR. These requirements include those relating to post-market surveillance, market surveillance, vigilance, and registration of economic operators and devices in the European database on Medical Devices (EUDAMED). A corrigendum adopted in 2019 clarifies that Class I devices 'up classified' under the MDR can avail of these transitional provisions. This article will focus on the requirement for legacy devices to be registered on EUDAMED. An exception to these registration requirements for legacy devices is the assignment of a Basic Unique Device Identification system Device Identifier (Basic UDI-DI) and a UDI-DI. The UDI system will provide a harmonised method of identifying medical devices, as well as facilitating traceability and post-market monitoring of devices.

Guidance published by the European Medical Devices Coordination Group (MDCG) in 2019 outlines details on how legacy devices should be registered in EUDAMED. Although legacy devices are exempt from strictly requiring the above identification elements, this guidance clarifies that the design of EUDAMED should be adapted to allow the registration of legacy devices in the absence of a Basic UDI-DI. Therefore, in order to keep the same structure and identification elements for all devices registered on EUDAMED, an identification element EUDAMED DI will be required. Further information on how this identification element will work is available on the 'Management of Legacy Devices in Eudamed' MDCG document.

Following on from the 2019 guidance, and in light of the recent announcement that implementation of EUDAMED Module 2 (UDI/device registration) and Module 3 (notified bodies and certificates) will be delayed until September 2021, the MDCG has also published guidance regarding alternative technical solutions that may be utilised until EUDAMED becomes fully functional. This document provides guidance on how to apply certain MDR provisions prior to the full functionality of EUDAMED. It aims to allow Member States and other relevant parties to meet their obligations under the MDR, whilst minimising any potential extra burden. This guidance calls out that the alternative technical solutions given should also apply to legacy devices where appropriate, whilst taking into account the availability of the various EUDAMED modules. Registration of certificates issued in accordance with the existing Directives should take place in Module 2 of EUDAMED once it is launched. In the meantime, registration at a national level with the HPRA is required for Irish economic operators. Additional information on the HPRA's national registration requirements will be available on our website shortly.

Preparing for May 2021

While the above articles aim to raise awareness of the MDR transitional provisions and to assist our stakeholders in their planning for MDD/AIMD certified devices, the HPRA has also received a number of queries relating to the manufacturer obligations and requirements that must be fulfilled by 26 May 2021. In anticipation of the date of application of the MDR manufacturers must fulfil the MDR conformity assessment and CE-marking requirements. Manufacturers must also have a number of processes and systems in place. While it is not possible to provide an exhaustive list of these obligations and requirements, the tables to the right aim to support manufacturers as they finalise MDR implementation plans.

Manufacturer requirements: Are the following processes & systems in place?

- Quality Management System (QMS)
- Risk Management system, established, documented, implemented & maintained
- Liability for defective products/financial coverage (this also applies to ARs)
- Post-Market Surveillance in place and documented, including a post-market surveillance plan, PSURs
- Reporting system; incidents, FSCA, trend reporting
- Person Responsible for Regulatory Compliance identified within the organisation
- Clinical Evaluation planned, conducted and documented

This is not an exhaustive listing but provides some examples of the key essential requirements; this document is for guidance purposes only

Manufacturer requirements: Conformity Assessment & CE Marking

- Verify MDD/AIMDD certificate is still valid and expiry date
- Identify MDR classification rules applicable
- Identify appropriate conformity assessment and notified body requirements
- Clinical Evaluation planned, conducted and documented
- Update technical documentation
- Assign UDI and plan for label updates
- Supply health institutions with implant cards to accompany implantable devices

This is not an exhaustive listing but provides some examples of the key essential requirements; this document is for guidance purposes only

Medical Device Coordination Group (MDCG) Update

The Medical Devices Coordination Group (MDCG) met on 4 and 5 March to discuss the continued implementation of both the MDR and the IVDR. During this session, particular focus was placed on IVDR implementation, which remains a high priority for the Commission and competent authorities. The IVD Working Group also provided an overview of their ongoing implementation tasks. The WG has a number of specific task forces established to look at implementation issues such as the Common Specification for CMV(cytomegalovirus), Chagas, Syphilis etc., assays in clinical trials (joint with medicines) as well as in-house manufacturing. The EU Commission is currently processing the results of the survey circulated to IVD stakeholders. This survey was launched to gather quantifiable information on the readiness of the market specifically for IVDR implementation.

An IVD Question & Answers document (MDCG 2021-4) specifically covering how the IVDR transitional provisions will apply to Class D IVDs was endorsed by the MDCG during the March session. This guidance document has now been published on the Commission website.

The MDCG working groups provide an overview of their work packages for 2021 as well as MDR implementation, such as the activities of the NBO working group, the Market Surveillance working group and the UDI working group. The EU Commission also presented the ongoing work in the area of expert panels. Experts have been formally appointed, trained and a series of 'kick off' meetings have taken place. It was anticipated that the thematic panels would start to meet in March, with expert panels accepting submissions from Notified Bodies from 1 April. Further information on expert panels is available on the Commission website.

An overview of the progress of designation of notified bodies was also provided with the Commission reporting that 49 applications for the MDR and 16 for the IVDR have been received.

In addition, the MDCG also endorsed a number of guidance documents during the March meeting, which were recently published and are provided below.

Recently Published Documents

- MDCG Document 2021-4 (April 2021): Application of transitional provisions for certification of Class D in vitro diagnostic medical devices according to Regulation (EU) 2017/746
- MDCG Infographic (March 2021): Is your software a Medical Device?
- MDCG Document 2021-3 (March 2021): Questions and Answers on Custom-Made Devices
- MDCG Document 2021-2 (March 2021): Guidance on State of the Art of Covid-19 rapid antibody tests
- MDCG Document 2021-1 (February 2021): Guidance on harmonised administrative practices and alternative technical solutions until EUDAMED is fully functional
- Commission Rolling Plan (Updated 9th April): Implementation Rolling Plan Regulation (EU) 2017/745 and Regulation (EU) 2017/746
- MDCG Document 2021-5 (April 2021) Guidance on Standardisation for Medical Devices

Regulatory Considerations for Custom-Made Devices

As medical device manufacturing processes continue to improve, so too does our ability to meet the individual needs of patients. Custom-made devices (CMDs) such as dental crowns and prostheses may play an increasingly important role as patient care continues to shift towards a more personalised approach. With this in mind, manufacturers and suppliers should be aware of the regulatory requirements associated with CMDs. In this article, the HPRA will outline some of the important information for CMD manufacturers. Further information can be found in the MDCG Q&A document MDCG 2021-3 (March 2021).

What is a custom-made device?

A CMD is a medical device that is specifically designed, based on a written prescription, for a patient to meet their individual conditions and needs.[1]

1 Article 2(3) of the Medical Devices Regulation (EU) 2017/745

At a minimum, a written prescription should contain the name of the patient and the specific design characteristics, which are unique to the patient's anatomic/physiological features and/or pathological condition. By definition, CMDs cannot be mass-produced. While manufacturers can use state of the art industrial manufacturing processes such as 3-D printing and CAD/CAM, not all 3D printed devices are CMDs.

What are the obligations of CMD manufacturers according to the MDR?

While CMD manufacturers are exempt from certain requirements under the MDR, for example assigning a Unique Device Identifier, all medical device manufacturers should review Article 10 of the MDR to ensure that the applicable obligations such as the establishment of a quality management system are fulfilled. CMD manufacturers should consider the applicable requirements outlined in Annex I of the MDR and in Annex XIII, which describes the conformity assessment procedure for all types of CMDs. In accordance with section 1 of Annex XIII, and in place of a declaration of conformity, CMDs must be accompanied by an Annex XIII statement. This statement must be made available to the particular patient or user identified by a name, an acronym or a numerical code. High-risk CMD such as Class III implantable devices may also require Notified Body oversight. If you intend to manufacture Class III implantable devices, please refer to Article 52(8) for the additional requirements.

The MDR requires all device manufacturers to implement a post-market surveillance system. CMD manufacturers should therefore establish appropriate communication channels with relevant healthcare professionals and patients to receive feedback on the quality, performance and safety of their devices. In accordance with Article 87(1) of the MDR, CMD manufacturers must also report any serious incidents and/or field safety corrective actions to the competent authorities as soon as they learn of them. The HPRA would encourage all manufacturers to review the reporting requirements and identify the reports that must be developed for their specific devices.

If you are changing a part or component on a CE-marked device it is important to ensure that the performance and safety characteristics of the device are not adversely affected and that the intended purpose of the device is not altered. Supporting evidence shall be kept available for the competent authority (HPRA). If the part or component significantly changes the intended purpose of the device or the performance and safety characteristics of the device, the part or component will be considered a device in its own right and will have met the requirements of the MDR, including CE marking and general safety and performance requirements. Should you have any additional questions, please refer to MDCG 2021-3.

How do CMDs differ from patient matched and adaptable medical devices?

Unlike CMDs, adaptable medical devices (AMDs) are mass-produced and must be adapted at the point of care, typically by a healthcare professional, to suit a particular individual's needs prior to use. Examples of AMDs include patient-fitted wheelchairs, hearing aids, orthotic braces and certain spectacle frames or optical glasses.

Unlike CMDs, patient-matched devices (PMDs) do not require a written prescription by an authorised person. These devices may often be produced in batches through a process that is capable of being validated and reproduced. Examples of PMDs include plates used to fix a broken bone, which are made by 3D printing, based on a template model and DICOM files/ images of the patient or cutting guides used in procedures such as knee arthroplasties, or guides used for pedicle screw placement, that are made by 3D printing based on MR or CT data to match a specific patient.

Table 2: Qualification of Custom-Made, Patient-Matched, and Adaptable Medical Devices

	Custom-Made Devices	Patient-Matched Devices	Adaptable Medical Device
Mass produced or batch produced	✘	✓	✓
Written prescription required	✓	✘	✘
Adaptions required at point of care	✘	✘	✓

Carcinogens, Mutagens and Reproductive Toxins: Rules and Regulations

The MDR represents a significant strengthening of the existing regulations and advancement in public health protection. In keeping with this, it introduces new requirements and restrictions on the inclusion of carcinogens, mutagens and reproductive toxins (CMRs) included in medical devices.

Annex I of MDR 2017/745 specifies the general safety and performance requirements of medical devices. This includes the requirements regarding CMRs in medical devices. Devices must be designed in a way that reduces the potential risk posed by the release of such substances, taking into account wear debris, degradation products and processing residuals. If these devices or parts of the devices are:

- Invasive and come into direct contact with the human body;
- Administer (or re-administer) medicines, body liquids, gases etc. to or from the human body;
- Or transport or store such medicines, body fluids etc. to be administered (or re-administered) to the human body;

And contain CMRs in concentrations above 0.1% w/w they must be justified in their presence. The basis for any such justification must be based upon:

a) an analysis and estimation of potential patient or user exposure to the substance;

b) an analysis of possible alternative substances, materials or designs, including, where available, information about independent research, peer-reviewed studies, scientific opinions from relevant scientific committees and an analysis of the availability of such alternatives;

c) argumentation as to why possible substance and/ or material substitutes, if available, or design changes, if feasible, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product; including taking into account if the intended use of such devices includes treatment of children, pregnant women, breastfeeding women, or treatment of other patient groups considered particularly vulnerable to such substances and/ or materials; and

d) where applicable and available, the latest relevant scientific committee guidelines in accordance with Sections 10.4.3. and 10.4.4 of the MDR. These sections relate to phthalates and other CMRs and endocrine-disrupting substances, respectively.

These restrictions apply to:

- Category 1A and Category 1B CMRs listed in the Regulation on Classification, Labelling and Packaging (CLP)[2];
- Substances which have endocrine-disrupting properties for which there is scientific evidence of probable effects to human health and which are identified either:
  - in accordance with the procedure set out in the REACH legislation;[3] or
  - once a delegated act has been adopted by the Commission pursuant to the Biocidal Products Regulation.[4]

In December 2020, the European Commission amended[5] the REACH Regulation resulting in an exemption for medical devices (and accessories) to avoid 'double regulation'.

Where a device, parts of a device, or materials used therein contain CMRs or substances with endocrine disrupting properties above 0.1% w/w, the presence of those substances should be indicated on the device's labelling and/or packaging. If the device is intended to be used on or by children, pregnant/breastfeeding women or a group considered vulnerable, information on residual risks for those patient groups and, if applicable, on appropriate precautionary measures shall be given in the instructions for use.

The above does not circumvent other provisions of the MDR, such as Annex I 10.5, which requires all devices to be designed and manufactured in such a way as to reduce the risks linked to the unintentional ingress of substances, or the risks posed by size and properties of particles which are (or could be) released into the patient's or users body. These requirements apply accumulatively. Although provisions allow for the controlled and restricted inclusion of CMRs into medical devices, public health protection is central to the MDR and no such substances should be included in the absence of adequate justification.

2 Annex VI Part 3 of Regulation 1272/2008, which amends Regulation 1907/2006 (REACH)
3 Article 59 of Regulation 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)
4 Pursuant to Article 5(3) of Regulation 528/2012 on biocidal products
5 Commission Regulation 2020/2096

IVDR Introductory Reference List for Class A Manufacturers

The HPRA's Medical Devices department has developed an introductory reference list for Class A medical device manufacturers. From 26 May 2022, Regulation (EU) 2017/746 on In Vitro Diagnostic Devices (IVDR) will become fully applicable and manufacturers will be required to comply with the regulations in their entirety.

Although not an exhaustive list, this introductory list aims to help Class A device manufacturers plan and coordinate their regulatory activities, helping to ensure compliance in advance of May 2021.

The Medical Devices section of the HPRA website contains further guidance and helpful resources as well as information on IVD Classification.

HPRA Clinical Investigation Process

In advance of 26 May 2021, the date of application of the MDR, the HPRA is now pleased to be in a position to accept applications to conduct clinical investigations of non-CE marked medical devices under the MDR. However, whilst applications are being accepted, authorisations cannot be issued until after the date of application, at the earliest. The MDR introduces a number of key changes related to the conduct of clinical investigations, and sponsors should make sure they are aware of these changes in advance of making an application to the HPRA. An updated guide has recently been published by the HPRA to help in understanding the implications of the MDR for clinical investigations. This guide, along with further information regarding clinical investigations, is available from the HPRA website.

For post-market clinical follow-up investigations of CE marked devices in Ireland, the HPRA expects to be in a position to receive notifications for relevant studies in line with Article 74 of the MDR shortly before the date of application of the MDR. Further information and the notification form will be available from the HPRA website in due course.

One of the key areas where sponsors will see a significant change in the conduct of clinical investigations in Ireland is related to the assessment of applications by an ethics committee. Under the new National Research Ethics Office, a national research ethics committee for medical devices will soon be established. Further information on this important new aspect of health research in Ireland can be found on the national research ethics office website (www.nrecoffice.ie).

Sponsors considering undertaking a clinical investigation of a non-CE marked medical device in Ireland are strongly encouraged to request a pre-submission meeting with the HPRA. This meeting is a useful opportunity to discuss your plans for a clinical investigation with assessors in the HPRA medical device department. Further information is available on our clinical investigations webpage.

Impact of Brexit on Medical Device Regulation

Although the UK formally left the European Union on 31 January 2020, the resulting transitional period only ended on 31 December 2021 with a trade agreement in place. Over the last number of years, the HPRA has produced several resources and communication initiatives to highlight the resulting changes to medical device economic operators, and to ensure the continued supply of medical devices to the Republic of Ireland. The HPRA has worked across national organisations to ensure the continued supply of medical devices, in addition to working with individual economic operators to help the sector understand the regulatory changes.

In addition to our guidance on the application of EU device legislation, the HPRA has compiled some information on recent guidance issued by Revenue on our website for ease of reference. Detailed guidance in relation to Brexit and the associated customs requirements is available on the Revenue website. While Brexit readiness has predominantly focused on the immediate onset of Brexit for many, the HPRA is encouraging our stakeholders to ensure they have planned for the medium/long term implications of Brexit. If you have any concerns or queries related to Brexit and medical devices, please contact devices@hpra.ie. Any questions relating to customs should be addressed to Revenue at brexitqueries@revenue.ie

Table 3 – Important Regulatory Changes for Economic Operators

Changes for Manufacturers	Changes for Distributors and Importers
• All UK manufacturers must have an authorised representative located in the EU-27 (or Northern Ireland in accordance with the Northern Ireland protocol).	• If continuing to source medical devices from the UK (excluding Northern Ireland), economic operators should be aware they may take on the role of an importer and the responsibilities incumbent upon an importer come May.
• For non-EU based manufacturers, the authorised representative should be clearly identifiable on the labelling.	• Importers should affix their details on the labelling, packaging or accompanying documentation (in accordance with the MDR which is applicable from May 2021) before they place the device on the market.
• In order to place a medical device on the EU market it must meet the requirements for labelling, packaging and accompanying documentation set out in the current medical devices Directives. From May 2021, the requirements of the new Medical Devices Regulation will apply. While there may be additional information on the device label (such as a UKCA mark in addition to the CE mark), this must not obscure or replace the required EU details.	• Distributors sourcing devices from UK distributors or UK manufacturers (with the exception of Northern Ireland) will become EU-27 importers for devices they place on the EU-27 market. • Devices transitioning through the UK en route to Ireland from another Member State would not be considered imported devices within the meaning of the MDR). Please visit the Revenue's website for further details on the custom's transit provisions.

Medical Device Regulation

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Reference list for Class A in-vitro diagnostic medical device manufacturers

Introductory reference list for Class A medical device manufacturers under IVDR[1]*

** This guide does not purport to be an interpretation of law and/or regulations; it is not an exhaustive listing and provides some examples of the key essential requirements; this document is for guidance purposes only. All medical device manufacturers must comply with the entirety of Regulation 2017/746 on medical devices as per specifications laid down in the regulation and associated implementing acts/ regulations.*

Qualification and Classification	Regulation 2017/746
☐ Is the product an in-vitro diagnostic medical device under the IVDR?	Article 2
☐ Is the product a Class A in-vitro diagnostic medical device under the IVDR?	Article 47 Annex VIII

Processes and Systems	Regulation 2017/746
☐ Is there a Quality Management System (QMS) established, documented, implemented and maintained?	Article 10 (8)
☐ Is there a risk management system established, documented, implemented and maintained?	Article 10 (2) Annex 1 section 3
☐ Is there a performance evaluation planned, conducted and documented	Article 10 (3) Article 56 Annex XIII
☐ Is there a Person Responsible for Regulatory Compliance (PRRC) identified within the organisation?	Article 15
☐ Is there financial coverage/liability for defective devices put in place?	Article 10 (15)
☐ Is the device and manufacturer registered in EUDAMED (once available) and with the relevant national authority and UDI obligations fulfilled?	Article 24 Article 26 Article 28
☐ Is there a post-market surveillance system documented and in place including a post-market surveillance plan?	Article 10 (9) Article 78 Article 79
☐ Is there a system for reporting incidents and Field Safety Corrective Actions (FSCA) in place?	Article 10 (12) Article 82 Article 83

1 Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR)

Medical Device Regulation

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Conformity Assessment and CE marking	Regulation 2017/746
☐ Are the General Safety and Performance Requirements (GSPR) fulfilled?	Annex I
☐ Is the technical documentation drawn up and requirements fulfilled?	Article 10 (4) Annexes II and III
☐ Are the Instructions For Use (IFU), packaging and labelling requirements fulfilled?	Annex 1, Chapter III
☐ Is clinical evidence, a performance evaluation or performance study required?	Article 56, 57, 58 Annex XIII Part A Annex XIV
☐ Have you specified and justified the level of clinical evidence required to demonstrate conformity with the GSPR's?	Article 56
☐ Is Notified Body assessment required?	Article 48 (10)
☐ Has the IVD undergone the correct conformity assessment procedure by an IVDR designated notified body if applicable?	Annex IX Annex XI
☐ If the device is placed on the market in a sterile condition, has a notified body certificate been issued?	Article 48 (10)
☐ Is the Declaration of Conformity drawn up?	Article 10 (5) Article 17 Annex IV
☐ Is the CE mark affixed?	Article 10 Article 18 Annex V

Other Requirements	Regulation 2017/746
☐ Is your distributor/importer informed the device is on the market under the new Regulations? Therefore, Economic Operator obligations as defined in IVDR apply.	Article 13 Article 14
☐ Is there appropriate traceability within the supply chain?	Article 22 (1)
☐ Is there an EU-27 Authorised Representative designated and mandated? (if manufacturer is located outside the EU)	Article 11 (1)(2)

Additional guidance

MDCG Guidance	EU Commission Factsheets