HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

New EU Device Legislation Information Pack

Practical Application of New EU Device Regulations

Introduction

On 26th May 2017, Regulation (EU) 2017/745 on medical devices (MDR) and Regulation (EU) 2017/746 on *in-vitro* diagnostics (IVDR) entered into force. Both Regulations will have a staggered transitional period with some aspects, such as the notified body requirements, becoming legally binding after 6 months on 26th November 2017.

These new EU Regulations will replace the current Directives[1] which have been in place for over 25 years. The MDR will become fully applicable from 26th May 2020 while the IVDR will be fully applicable from 26th May 2022.

Changes to Scope

The scope of the Regulations has changed and now extends to all economic operators in the supply chain as well as broadening the range of products subject to the requirements of the Regulations. The MDR will now include certain aesthetic products without an intended medical purpose, commonly used in the beauty industry (outlined in Table 1). Medical devices incorporating non-viable human tissues and certain devices comprised of substances which are ingested to achieve their intended action will be included. The MDR also contains specific optional provisions for the reprocessing of single-use devices. The IVDR includes broader definitions relevant to genetic tests and, like the MDR, places additional requirements on medical devices manufactured within hospitals (e.g. laboratory developed tests).

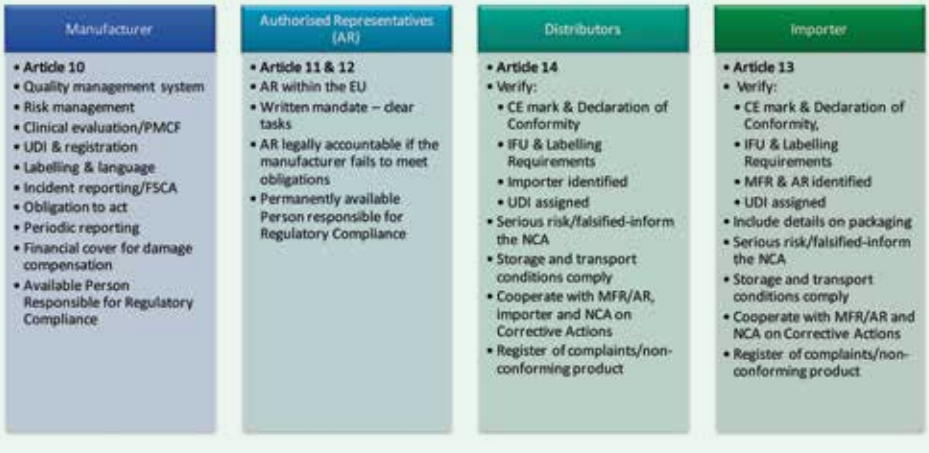
The new Regulations specify obligations and responsibilities for all economic operators including manufacturers, importers, distributors and authorised representatives. *Figure 1* illustrates some of the key obligations outlined in the Regulations. It is important that economic operators ensure that they have appropriate resources, processes and systems in place to fulfil their obligations under the new Regulations.

Table 1: examples of aesthetic products that will now be considered as a medical device (Annex XVI MDR)

Aesthetic Products
Liposuction equipment
Coloured contact lenses
Dermal fillers
Collagen implants
Laser hair removal equipment
Skin resurfacing equipment
Tattoo removal equipment

Note: tattooing and piercing products are excluded from this list.

Figure 1: Key obligations of Economic Operators



[1] *Directive 93/42/EEC, Directive 98/79/EEC and Directive 90/385/EEC*

Certificate Validity during Transition

The transition periods outlined in the Regulations are established to afford economic operators, notified bodies and competent authorities adequate time to put in place the appropriate resources, processes and systems by the dates of application to ensure devices placed on the market are in compliance with the new requirements. During this transition phase medical devices CE marked to the Directives[2] can continue to be placed on the market in accordance with the criteria specified in Chapter X of both Regulations.

Figure 2 illustrates the key timeframes for certificate validity. Certificates which have been issued under the existing Directives will be valid for the period specified on the certificate which can be up to a maximum of 5 years.

However in the event that a certificate is issued under the Directives just before the new Regulation comes into full application it will become void after 4 years for the MDR and 2 years for the IVDR. Devices covered by such certificates (becoming void in May 2024) can continue to be made available once in the supply chain up until May 2025. These devices will be subject to the new post market surveillance requirements (e.g. reporting requirements) specified under the MDR/ IVDR.

Once a notified body has been designated under the new Regulations it can begin to certify devices to the new Regulations.

Figure 2: Timeline for certificate validity

[2] *Directive 93/42/EEC, Directive 98/79/EEC and Directive 90/385/EEC*

Incoming Process Changes

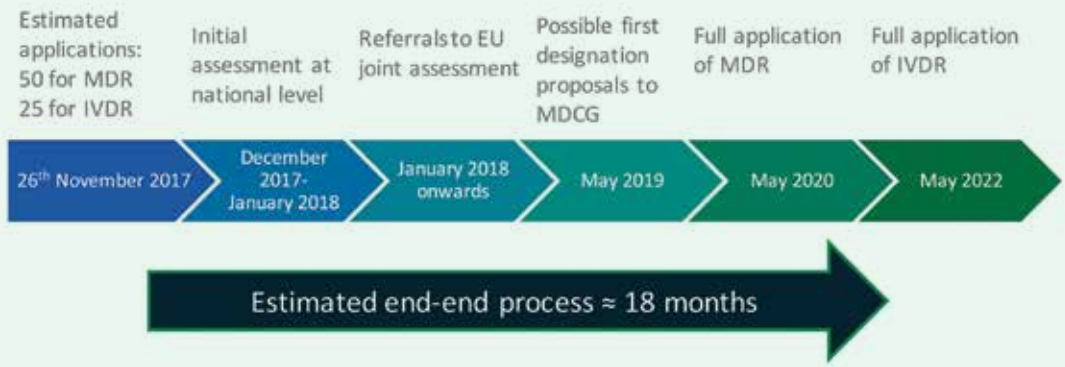
While the fundamental principle of the regulatory framework has not changed, the two Regulations bring increased clarity, definition and enhanced assessment procedures to a dynamic medical device sector. Some of the key process changes are outlined in the following section.

1. Notified Body Designation

The requirements in the new Regulations build on the work already carried out under the European Commission's Joint Assessment Scheme to help ensure that notified bodies across Europe perform to a consistent and high standard. Obligations have also been introduced for national authorities to ensure effective oversight of notified bodies based in their territory on an on-going basis.

From the 26th November 2017, a conformity assessment body can submit an application to the authority responsible for notified bodies (the HPRA) to be designated under the new Regulations as a notified body in Ireland. The designation process, which involves national and European assessments, is expected to take a minimum of 18 months after which notified bodies can begin to certify devices to the new requirements *(Figure 3)*.

Figure 3: Timeline for the notified body designation process



Until the date of full application of the new Regulations, 26th May 2020 for medical devices and 26th May 2022 for IVDs, devices can continue to be certified and placed on the market according to the current Directives. Alternatively manufactures can, on a voluntary basis, certify their devices to the new Regulations in advance of the date of full application.

It is recommended that manufacturers talk with their notified body to ensure they understand the process for re-certification and are fully prepared for the MDR and IVDR. Both IVD manufacturers and IVD designated notified bodies will be particularly impacted by the IVDR. Under the new Regulation the majority of IVDs will now be subject to assessment and certification by a notified body prior to being placed on the market. IVD manufacturers should review their product portfolios to determine which devices will now require a Notified Body assessment.

2. Scrutiny

Novel high risk devices, Class III implantable devices and devices intended to administer or remove a medicine that do not have common specifications identified, will now be subject to an extra layer of scrutiny, or pre-market assessment, by an expert panel during the notified body assessment *(Figure 4)*. The scrutiny process will provide an additional independent review of the manufacturer's clinical data to ensure the performance and safety of these devices. This process will ensure safe patient access to new and innovative therapies, however, it may result in an additional premarket review process step for manufacturers. Manufacturers should examine their product portfolio to identify devices that may be subject to this new scrutiny process.

Figure 4: The scrutiny process defined in the MDR, Chapter V

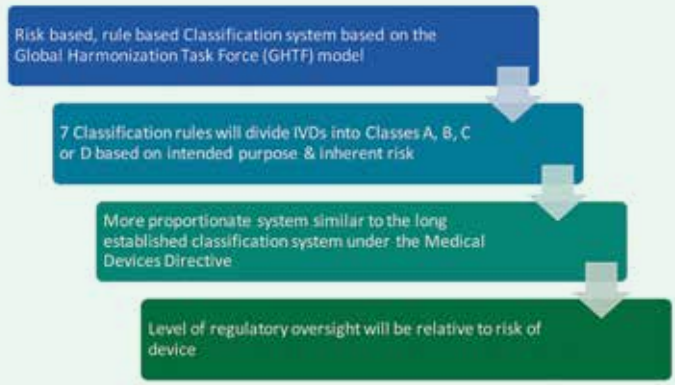
A similar process has been introduced for IVDs in the case of Class D IVDs where no common specifications are available and where it is also the first certification for that type of device. In such cases, the notified body consults the expert panel on the performance evaluation report of the manufacturer and the timeframe for the expert panel to deliver an opinion is the same as that specified in the MDR (i.e. 60 days). In the conformity assessment procedure for Class D IVDs, at the same time, a designated EU reference laboratory verifies the performance claimed by the manufacturer who shall provide an opinion within 60 days.

3. IVD Classification

The IVDR introduces a rule-based classification system for IVDs. IVDs will now be classified into four different classes from class A (low risk) to class D (high risk).

IVDs in accordance with the IVDR will be subject to conformity assessment based on the classification of the device. In line with the new classification system additional classes of IVDs will be required to undergo assessment and certification by a notified body (appropriately designated for IVDs) prior to being placed on the market. This is a significant change as most IVDs are currently self-declared without assessment by a notified body.

Figure 5: Classification summary for IVDs

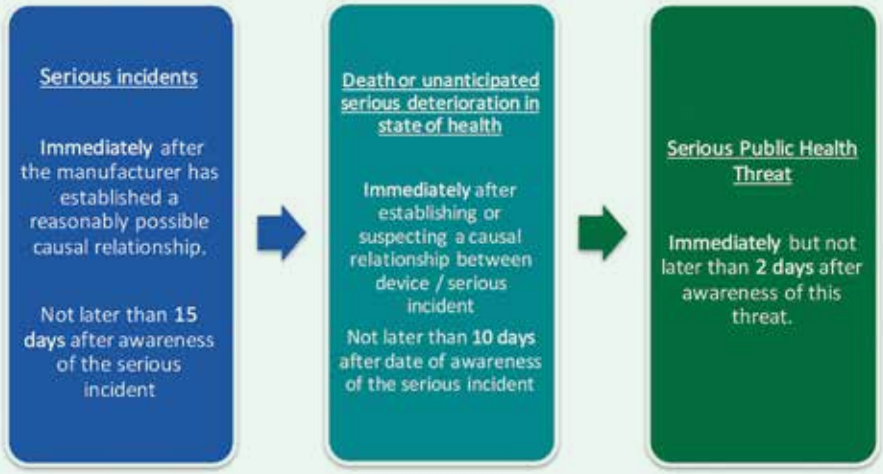


4. Vigilance Reporting

The new Regulations set out specific requirements for manufacturers to establish and maintain a post market surveillance and vigilance system. As part of their system there is a requirement to report serious incidents and Field Safety Corrective Actions to the relevant Competent Authority (the HPRA in Ireland) through the centralised database. As a general rule, the time period for reporting shall take account of the severity of the serious incident (see *Figure 6*). It is important to note that the timeframe for reporting serious incidents has been reduced compared to that specified in the European Commission guidelines on a medical devices vigilance system[3]. If after becoming aware of a potentially reportable incident, the manufacturer is uncertain about whether the incident is reportable, the manufacturer should submit a report within the timeframes required as set out in *Figure 6*. Medical device users are also encouraged to report incidents. Suspected incidents or complaints may also be reported to the importer or the distributor of the device. This information shall be shared with the manufacturer of the device.

Incoming Process Changes

Figure 6: Time frames for reporting serious incidents

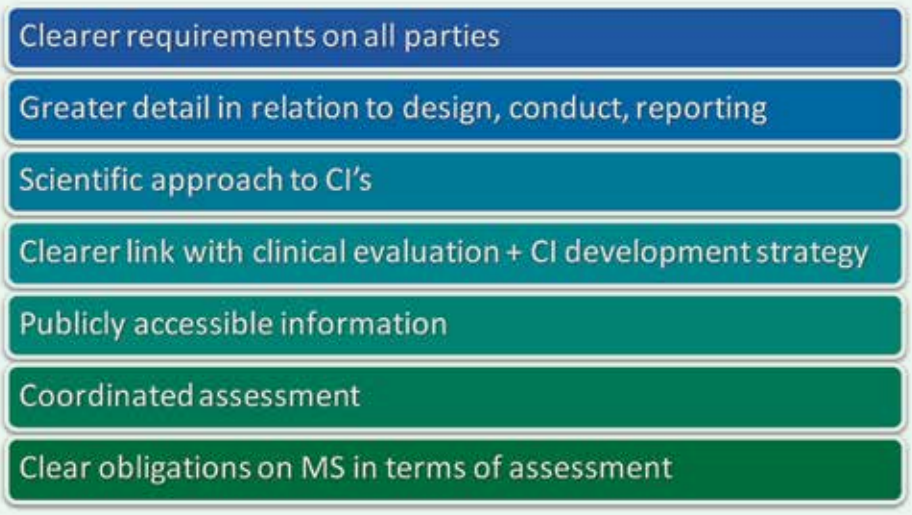


[3] *MEDDEV 2.12-1 REV 8*

5. Clinical Investigation Process

Clinical investigations are studies carried out in human subjects to verify the safety and/ or performance of a specific medical device. The purpose of a Clinical Investigation (CI) is to verify the performance claimed by the manufacturer under normal conditions and to determine any undesirable side effects and assess whether these constitute a risk when weighed against the expected benefits.
The CI process has been poorly defined in the Medical Device Directives[4]. The requirements for CIs are significantly enhanced in the MDR and include many specific provisions to ensure that people enrolled in clinical studies are appropriately protected. In addition a clinical investigation report summarising the study results will be available to the public to improve transparency. *Figure 7* outlines some of the key changes for CIs in the MDR and includes clear requirements on the application and assessment process (with defined timelines), the conduct of the study and on all stakeholders involved in CIs such as subjects, sponsors, competent authorities and for the principal investigator.
For multi-site investigations, the MDR introduces a voluntary coordinated procedure where the sponsor submits a single application which is transmitted via an electronic system to all Member States in which the CI is to be conducted. The coordinated procedure means that there is one lead or coordinating member state responsible for coordinating the assessment of the CI application.

Figure 7: Key changes in the Clinical Investigation process in the MDR



[4] *Directive 93/42/EEC and Directive 90/385/EEC*

Stakeholder Communication and Engagement

The HPRA's implementation plan for both of the new regulations is currently in the final drafting stages.

An essential part of this implementation plan is engagement with all stakeholders to clearly communicate the relevant requirements of these new Regulations to ensure they are correctly understood and implemented in a timely manner.

The HPRA is committed to working closely with stakeholders throughout the sector on implementation and will continue our regular dialogue with all stakeholder groups within the regulated sector. The HPRA will, through a variety of events and methods of communication seek to deliver relevant and timely communications to each group within the regulated sector. We encourage engagement from all stakeholders on the new legislative requirements.

Stakeholders wishing to receive legislative updates including regular communication on the new Regulations can sign up by emailing eudr@hpra.ie.

All planned future stakeholder events will be published in the "News and Events section" of our website.

Further information

See the 'New EU Device Legislation' tab in the Medical Devices section of www.hpra.ie for detailed information.

In addition, the HPRA has a dedicated email address (eudr@hpra.ie) for queries relating to the Regulations.

This is one in a series of information leaflets that you can get from the HPRA and from our website: www.hpra.ie.

What does the HPRA do?

As the regulatory authority, we monitor the safety and compliance of all medical devices available in Ireland. Our aim is to make sure that these products do not compromise the health and safety of the patient or the person using them. We are the designating authority for notified bodies in Ireland and we also work to ensure that medical device manufacturers are informed of and comply with the requirements laid down in the Regulations.

The Health Products Regulatory Authority (HPRA)

Our role is to protect and enhance public and animal health by regulating medicines, medical devices and other health products. We provide guidance to companies and individuals in relation to regulatory requirements particularly if they are developing new and innovative medical devices or diagnostics that will benefit patients.

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Economic Operators Obligations under the new EU Device Regulations[1] (EUDR) Legislation

The new EUDR elaborates and strengthens the responsibilities and obligations of all economic operators. For the first time distributors are included within the scope of the new EUDR and distributor obligations are specifically called out within the Regulations and confers additional obligations and responsibilities on all economic operators. The Regulations build on the New Legislative Framework for the Marketing of Products and provide economic operators with greater legal clarity, in particular, where they assume the manufacturers' obligations or when an operator is considered the manufacturer when certain activities are carried out.[2] This will help improve regulatory compliance by economic operators and help ensure the safety and performance of the device throughout the supply chain. The EUDR obligations range from ensuring proper storage and transportation of devices while under their care to greater verification, traceability and reporting requirements.

Who are Economic operators?

Economic operators under the EUDR refers to manufacturers, importers and distributors. It includes the manufacturers' authorised representative established within the EU who has received and accepted a written mandate to act on behalf of a manufacturer based outside of the EU. The manufacturer is ultimately responsible for ensuring that a device is compliant with the relevant legislation. A summary of other economic operators' responsibilities can be found below.

Summary of the responsibilities of Authorised Representatives, Distributors and Importers:

Economic operator	Authorised Representative	Distributor	Importer
Verify:			
Devices is CE marked	X	X	X
EU Declaration of Conformity & technical documentation are drawn up	X	X	X
Correct conformity assessment procedure has been carried out	X		
Labelling & accompanying information (IFU)		X	X
MFR has assigned the UDI		X	X
Importer has included name & contact details (Art. 13.3 EUDR)		X	X
MFR is identified & authorised representative has been assigned			X
Additional requirements:			
Have a person responsible for regulatory compliance in place	X		
Storage and transportation requirements fulfilled		X	X
Maintain a register of complaints	X	X	X
Inform MFR when device presents a serious risk or is not in conformity	X	X	X
Eudamed Registration obligations	X		X
Reporting requirements (serious incidents/serious risk) *Note: Reporting is encouraged by all Economic Operators*	X	X	X
Cooperation with Competent Authorities (preventative/corrective action)	X	X	X
Store UDI for Class III implantable devices	X	X	X
Identification within the supply chain (Art. 25 EUDR)	X	X	X

[1] *Regulation (EU) 2017/745 on medical devices [MDR] and Regulation (EU) 2017/746 on in vitro diagnostics [IVDR].*

[2] *Regulation (EU) 2017/745, Regulation (EU) 2017/746, Article 16.*

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Classification under the Medical Devices Regulation (MDR)

Regulation (EU) 2017/745

Medical devices are stratified according to risk into four classes with Class I being the lowest risk and Class III the highest:

RISK

DEVICE CLASS	EXAMPLES OF APPLICATION
Class III	Complex joint implants, drug eluting stents, coronary valves, breast implants, surgical meshes, active implantables
Class IIb	Peripheral Bare Metal Stents (BMS), bone fixation plates, dressings for chronic ulcerated wounds
Class IIa	Contact lenses (short-term), ECG machines, electronic BP monitoring, dental fillings
Class I *Sub-divided into sterile devices (Is) and those with a measuring function (Im)*	Wheelchairs, simple wound dressings, stethoscopes, ECG electrodes, syringes.

The MDR sets out 22 classification rules[1] which are used to classify devices based on risk criteria:

Degree/type of invasiveness
Duration of contact
Site of contact/anatomical locations
Specific characteristics- active/non-active, single use/reusable; combined with medicinal substance; incorporating animal tissues.

The application of these rules will depend on the intended purpose of the device and will replace the 18 rules[2] currently used under the General Medical Devices Regulation. This rule based classification system covers 30,000 difference types of medical device and influences: pre-market requirements, the conformity assessment route, clinical data requirements as well as post-market obligations.

The new rules primarily relate to:
Software
Nanomaterials
Ingested products
Non viable human tissues, cells & derivatives

In addition, certain existing devices have been up-classified due to the nature of risk associated with the specific devices. Examples of up-classifications can be found in Rule 8.

Devices used together (e.g. same procedure) are classified in their own right. Device accessories are classified in their own right and separately to the device with which they are used.

Software which drives or influences a device falls automatically into the same class as the device.

[1] *Regulation (EU) 2017/745, Article 51 & Annex VIII*

[2] *Directive 93/42/EEC, Article 9 & Annex IX*

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Classification under the *In-Vitro* Diagnostics Regulation (IVDR)

Regulation (EU) 2017/746

The classification system for IVDs in accordance with the IVD Directive differs from the medical devices classification system as it is list based rather than a risk based rules approach. This list based system is provided in Annex II of the IVD Directive.[3]

With the introduction of the IVDR the classification system has been modelled on the Global Harmonisation Task Force (GHTF) Guidelines with some modifications. IVDR classification adopts a similar system to the MDR risk based rules approach with four distinct classes now introduced. Class A is the lowest risk and Class D is the highest.

IVD CLASS	EXAMPLES
Class D	HIV, ABO blood grouping, Rhesus testing
Class C	Companion diagnostics, tests for screening, diagnosis & staging of cancer
Class B	Pregnancy or fertility self-test
Class A	Products for general laboratory use & Specimen receptacles

Annex VIII of the IVDR sets out the 7 classification rules based on intended purpose & inherent risk:

7 IVD Classification Rules
Blood/Tissue screening & high risk, life-threatening diseases
Blood/Tissue compatibility, high risk blood groups
Pre-natal screening, cancer, companion diagnostics, genetic tests, congenital screening
Devices not covered by Rule 1-5
Products for general laboratory use, general culture media, instruments, specimen receptacles
Self-testing devices, exceptions listed, near- patient tests classified in their own right
Controls without a quantitative or qualitative assigned value.

The new classification system and the broadening of the scope of the IVDR means that approximately 90% of IVDs will be subject to review by a notified body to some degree for the conformity assessment process under the IVDR. This includes, for example, genetic tests that provide information on predisposition to a medical condition or disease and tests that provide information to predict treatment response or reactions (companion diagnostics). The conformity assessment for each device class is set out in Chapter V of the IVDR.

[3] *Directive 98/79/EC on in vitro diagnostic medical devices*

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Innovation in the MedTech sector

What is medical device innovation?

The European medical technology sector is globally recognised as highly innovative. Medical device innovation plays an important role in the enhancement of public health by allowing new diagnostic and treatment options to be developed while simultaneously increasing the practical benefits for patients and health providers. While much medical technology innovation is iterative, new technologies frequently emerge offering new possibilities and addressing unmet or underserved clinical needs.

The European regulatory system for medical devices has always facilitated a suitable environment to promote high levels of innovation. Indeed based on the number of patents filed on an annual basis at the European Patents Office, the medical technology sector exceeds innovation levels in comparison to other health products and related sectors. The new European Regulations on medical devices (detailed below) will preserve and nurture this innovation-friendly environment through initiatives like: coordinated EU assessment of clinical investigation applications (research), clearer and better defined requirements for clinical data and EU level advisory services for new product and clinical development strategies. These new Regulations will further protect and enhance public health by ensuring the safety and performance of medical devices throughout their lifecycle while supporting innovation and facilitating market access in an appropriate and timely manner.

The primary function of the HPRA is the protection, and enhancement of public health. The interplay of this responsibility with the need to ensure that innovative medical device technology is made available to European patients is a key focus for us as regulators.

Why is medical device innovation important?

Innovation plays an important role in medical device development for a number of reasons:

- Medical devices tend to develop through iterative change – i.e. they evolve and are often modified.
- The lifecycle for a typical medical device is less than 2 years.
- The technology is rapidly changing.
- The medical device industry drives innovation.

The interplay between the new Regulations and innovation

The Medical Devices Regulation 2017/745 (MDR) and In Vitro Diagnostic Devices Regulation 2017/746 (IVDR) were formally published in the Official Journal of the European Union on 5th May 2017. These Regulations incorporate a number of important improvements to the regulatory system in Europe. The importance of innovation is recognised in both the MDR and IVDR which note that a revised regulatory framework can ensure a high level of safety and health whilst supporting innovation.

How does the HPRA support Medical Device innovation?

Supporting innovation is a strategic priority for the HPRA. This reflects both the high density of innovative companies across the life sciences sector in Ireland and the presence of an extensive research, development and innovation sector within academia and other areas. Strong links between academia, industry and regulators will help to encourage and support innovation.

The HPRA offers support to medical device innovation in the form of:

- Preliminary meetings with device innovators. In these meetings, the HPRA offers general regulatory support to SMEs / academic research groups or spin-outs etc. as these groups are often scientifically focussed and may have a limited knowledge of regulations.
- Pre-submission meetings. In these meetings, the HPRA offers general advice to sponsors of clinical investigations planning a submission to HPRA in the near future.
- The HPRA accepts requests from manufacturers for the classification of a medical device, drug- device combination or borderline product prior to the intended submission of an application for CE marking to a notified body or prior to notification regarding the register of Class I devices. All classification requests are subject to a fee.

- The HPRA Innovation office. This is a facility whereby a question can be submitted to the HPRA Innovation Office relating to any of the healthcare products which the HPRA regulates.
- The Innovation Office will also publish general updates and information about regulatory and scientific issues related to innovation.
- The medical devices team at the HPRA can be contacted to discuss specific questions or queries about the Regulations and requirements for medical devices at any time.

How do I submit an innovation query to the HPRA?

- Anyone developing an innovative product can submit a query to the HPRA.
- Our Innovation Office will act as an initial point of contact for such queries and requests for advice in relation to innovative health products or technologies.
- Queries related to innovative medical technology or other health products should be submitted using our online enquiry form. This is available via the Innovation Office webpage which can be accessed through our website www.hpra.ie
- Alternatively you can e-mail us at innovationoffice@hpra.ie
- We aim to respond to all queries as soon as possible and within 20 working days. If a longer review period is necessary, we will contact you to inform you of the expected timeline for responding.
- All queries will be treated as confidential.

The Health Products Regulatory Authority (HPRA) - What we do?

Our role is to protect and enhance public and animal health by regulating medicines, medical devices and other health products.

We use our scientific and clinical expertise to review and monitor health products available in Ireland or exported abroad. Our aim is to make sure that the health products we regulate are as safe as possible and do what they are intended to do.

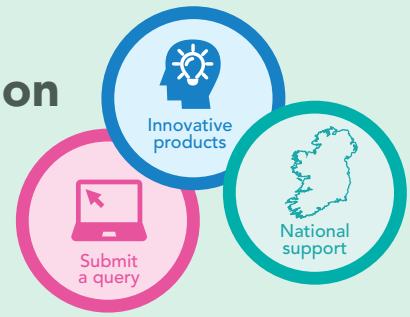
Further information

If you have any questions about the innovation supports available from the HPRA, please e-mail: innovationoffice@hpra.ie

Specific queries relating to medical device legislative requirements, clinical investigations (research) or other HPRA device services please contact devices@hpra.ie.

Specific queries on the new medical device Regulations on medical devices can be submitted to eudr@hpra.ie

HPRA Innovation Office



www.hpra.ie/innovation-office

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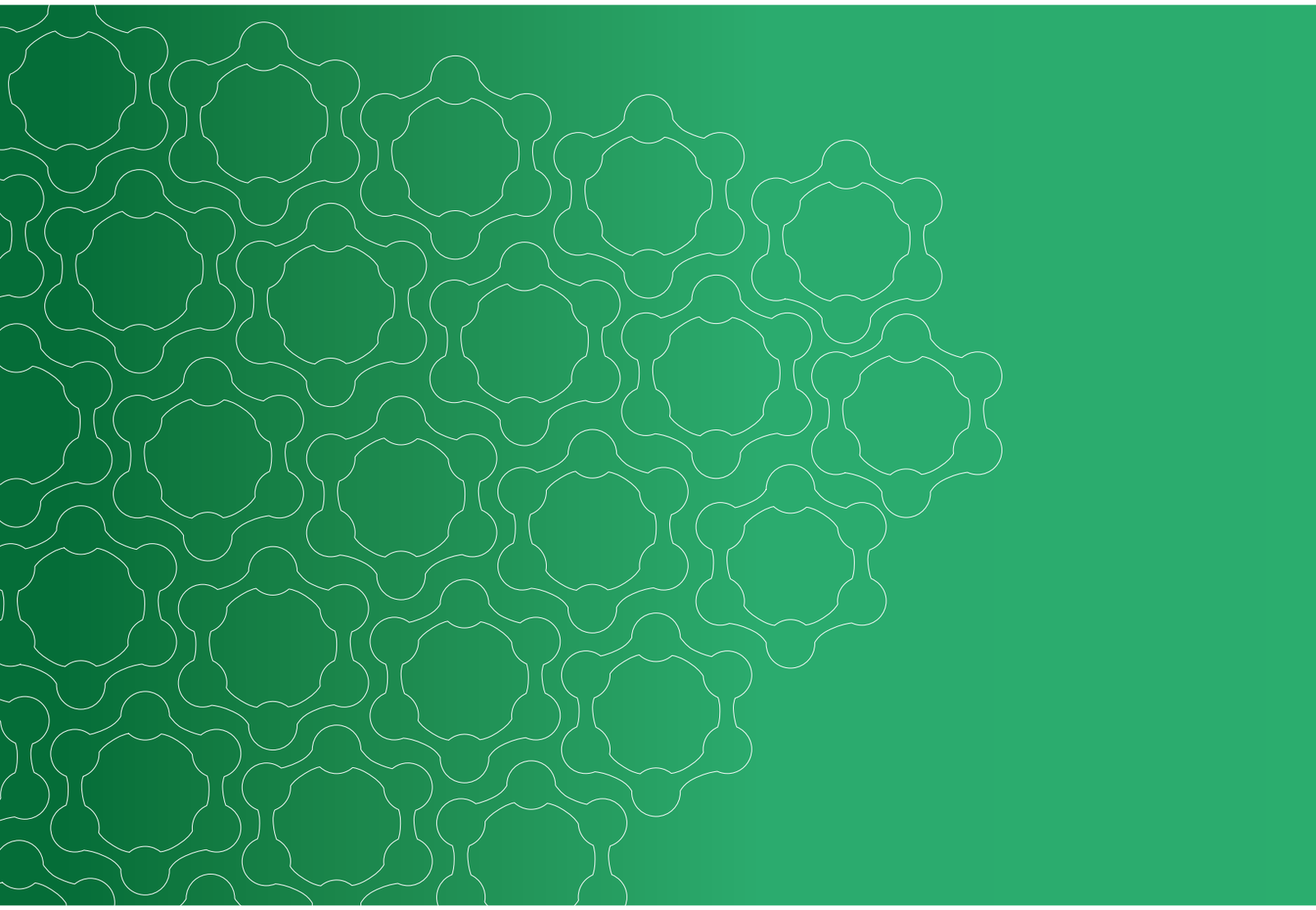

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