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Health Science Network

Regulatory Considerations Fact Sheet

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This is part of a series of fact sheets designed for innovators by the Eastern AHSN Innovation and Industry team.

1. Intellectual Property
2. Product Development
3. Market Assessment
4. Commercialisation Models
5. Regulatory Considerations

Download a digital edition from the Innovation Pathway hub on the Eastern AHSN's website:

www.eahsn.org/our-work/innovation-and-industry/the-innovation-pathway

Each fact sheet forms a comprehensive but not exhaustive source of information outlining the intricacies of the Innovation Pathway and are designed to help you navigate your way to a successful outcome. At the end of each fact sheet you will find the hyperlinks to referenced organisations.

You can also access Funding Resources directory at www.eahsn.org/our-work/innovation-and-industry/funding-resources

Introduction

A medical device can be broadly defined as an instrument, apparatus, implant, in vitro reagent, or similar or related article that is used to diagnose, prevent, or treat disease or other conditions, and does not achieve its purposes through chemical action within or on the body. The latter would make it in a medicinal product which falls under a separate set of regulatory requirements and is not explored further here.

Within the EU, regulations for the control and supply of medical devices are governed by a series of two recently adopted regulations, Regulation (EU) 2017/745 and Regulation (EU) 2017/746.

These regulations update and replace three previous medical device directives.

- (EU) 2017/745 combines the previous Medical Devices Directive 93/42/EEC and the Active Implantable Medical Devices Directive 90/385/EEC.
- (EU) 2017/746 replaces the previous In Vitro Diagnostic Medical Device Directive 98/79/EC.

These connected regulations harmonise controls within a single system, ensuring manufacturers do not need to comply with different sets of rules for each individual country within the EU. They also reassure purchasers and users that devices manufactured within the EU meet common performance and safety standards.

The move from a Medical Device Directive to a Medical Device Regulation creates a binding legislative act that must be applied in its entirety across the EU to unify the regulatory system with respect to medical devices.

This new Medical Device Regulation will have a broader scope of products, including those without an intended medical purpose but which are similar to medical devices in terms of their characteristics and risks. It places a greater onus on post-market surveillance, increased traceability of devices and stricter rules on clinical data requirements and safety and performance. It is anticipated this new regulatory framework will have significant implications for those developing medical technology with costs likely to increase to meet the new, more stringent regulations that are to be introduced.

The new rules will only apply after a transitional period. Namely, three years after entry into force for the regulation on medical devices (spring 2020) and five years after entry into force (spring 2022) for the regulation on in vitro diagnostic medical devices.

As the United Kingdom voted to leave the EU in 2017 and current regulations are determined by agreements at the European level, it is possible that there will be further changes to the regulatory environment. An innovator can connect with the Eastern AHSN and the associated regulatory bodies through our on-line tool at Hyperlink to keep you up to date https://www.eahsn.org/our-work/innovation-and-industry/nhs-clinical-trials-webkit/.

The CE mark, the sign of regulatory approval, states that the manufacturer declares the product meets the requirements of all the applicable regulations and confirms the **efficacy** and **safety** of the device.

In the UK, the Medicines and Healthcare Products Regulatory Agency (**MHRA**) are the government agency responsible for ensuring that medicines and medical devices work, and are acceptably safe. The MHRA is the UK's **Competent Authority** and audit the performance of manufacturers and **Notified Bodies** (accredited organisations that evaluate manufacturer's compliance to the regulations), and is responsible for granting CE marks. The MHRA should be contacted in the first instance if an innovator is unsure of whether a product would be considered a medical device.

Definitions

Determining how to progress to meet the regulatory requirements.

Step 1: Is the idea a medical device?

A **medical device** (2017/745) is defined as "any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means. The following products shall also be deemed to be medical devices:
    - devices for the control or support of conception;
    - products specifically intended for the cleaning, disinfection or sterilisation"

Example: Femoral Head & Cup for Hip Replacement.

An **in vitro diagnostic medical device** (IVD) (2017/746) is defined as "any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:

(a) concerning a physiological or pathological process or state

(b) concerning congenital physical or mental impairments

(c) concerning the predisposition to a medical condition or a disease

(d) to determine the safety and compatibility with potential recipients

(e) to predict treatment response or reactions

(f) to define or monitoring therapeutic measures

Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices"

Example: Chorionic Villus Sampling (CVS)

Classification of Medical Technologies

Step 2: What are the different classes of medical device?

Medical devices can be classified into one of four risk categories depending on the device's potential to cause harm to the patient, user or other person. The classes are I, IIa, IIb and III ranging from low to high risk.

The higher the class the greater time and financial investment required to gain regulatory approval. Classification of a device will determine the conformance route and is dependent upon a series of factors, based on a series of 22 rules outlined in Annex VIII of 2017/745. The manufacturer has the legal responsibility for correctly classifying the device. Compliance of class I devices is based on self-declaration by the manufacturer, all other devices require use of a Notified Body (list of such organisations: www.gov.uk/government/publications/medical-devices-uk-notified-bodies/uk-notified-bodies-for-medical-devices) to assess compliance.

Classes:

- Class I [Class I non-sterile e.g. tongue depressor; Class I sterile e.g. surgical instruments; Class 1 measuring e.g. dosing spoon]
- Class IIA e.g. blood pressure measuring
- Class IIB e.g. ventilators
- Class III e.g. heart valve

Rules for determining classes:

- Rules 1-4: Non-invasive devices – how long is device to be used for and is use continuous?
- Rules 5-8: Invasive devices – is the device invasive or surgically invasive?
- Rules 9-13: Active devices – is the device implantable or active?
- Rules 14-22: Special rules – e.g. does the device contain or use a medicinal substance?

In vitro diagnostic medical devices (IVDs) are classified into four categories of risk: A, B, C and D. Seven classification rules will direct which of the four classes the IVD will fall into and are outlined in Article 47 and Annex VIII of 2017/746. The conformity assessment procedure for lowest-risk Class A devices will be the sole responsibility of the manufacturer. Class B, C, and D devices are characterised by increasing risk levels and will all require notified body involvement.

Conformity Assessment

Step 3: Establish a plan to achieve and maintain regulatory approval for medical device

The manufacturer must decide on the conformity assessment route to meet the essential requirements of the appropriate regulation to gain regulatory approval and a CE mark for said medical technology. An overview of the process is summarised below. However, it should be noted that this process and the information required will predominantly depend upon the classification of the device.

1. Define the **Intended Use** of the device
2. **Classify** the device
3. Establish **Quality Management System** to support device – ISO 13485 is the harmonised standard for medical devices.
4. Establish **Post Market Surveillance** systems – May include: vigilance process, FSCA (Field Safety Corrective Action) process, User/Patient feedback, input from Scientific Advisory Boards and post Market Clinical Follow Up.
5. Choose a **Conformity Assessment** procedure – Refer to Articles 52-60 of 2017/745 or Articles 48-55 of 2017/746 to determine appropriate assessment procedure (as will depend on classification of device).
6. Conduct **Risk Assessment** – ISO 14871 is the harmonised standard for risk assessment of medical devices. Risks need to be eliminated or reduced as far as practicable and carried out throughout the product life cycle (pre- and post- market).
7. Prepare **Technical File** and submit to **Notified Body** if required – A technical file holds all the information that verifies that the testing of the medical device was conducted properly and that the device complies with applicable standards. It is a legal requirement and is applicable for all medical devices irrespective of the Conformity Assessment route taken. The technical file must be always available for the regulatory authorities and must be kept up to date and retained for the lifetime of the device, and at least five years from the date of last production. The manufacturer's notified body will review and assess the submitted technical file prior to recommendation to the MHRA. A typical technical file will contain: (a) device description (b) labelling including Instructions for Use (c) design and manufacturing specifications and processes (d) essential requirements checklist (e) risk analysis and control (f) clinical data (g) product verification and validation.
8. Sign **Declaration of Conformity** – A declaration by the manufacturer that the product concerned meets the provisions of the Regulation. Submitted once technical file is complete.
9. Affix the **CE mark** and place on EC market (European Community) – CE mark affixed to device and associated packaging/materials – refer to Annex V of both Regulations for specific requirements.
10. **Register Product** – For Class I devices only which have not required involvement of notified body, device is registered with MHRA by the manufacturer.

Summary

- The higher the class of medical device, the greater expense, time and clinical evaluation that is required to gain regulatory approval.
- Regulatory approval must be sought in a country-by-country manner. The EU is however harmonised through shared regulation. Acquiring regulatory approval (CE mark) in the EU does not give a manufacturer the right to make sales in the USA, however it may make process of regulatory approval in the USA easier.
- Medical device apps and related software are becoming a significant growth area in the healthcare management market. If an app is being used for a medical purpose it is important that it is CE marked. Examples of such apps include those that calculate medical doses for you to take/inject or those that tell you that you have a medical condition or disease or give you a percentage risk score of having one.
- With the changes expected through Britain's departure from the EU there may be changes to the regulatory environment that you will need to take account of.

Useful links

EU Regulatory Framework for Medical Devices (2017/745 and 2017/746)

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L:2017:117:TOC

https://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework_en#current_legislation

Directives for Medicinal Products

http://ec.europa.eu/health/human-use_en

The Organisation of Professionals in Regulatory Affairs (TOPRA)

www.topra.org

NHS National Innovation Centre Guidance on 'Regulatory Procedures for Medical Devices Under European Directives'

http://knowledge.nic.nhs.uk/documentDetails.aspx?docId=31

Guidance on whether your app is a medical device:

www.gov.uk/government/publications/medical-devices-software-applications-apps

Guidance on whether your product is a medicine or a medical device

www.gov.uk/guidance/decide-if-your-product-is-a-medicine-or-a-medical-device