Regulatory Oversight of Patient Safety in Medical Devices

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To Mum and Dad,

my first teachers, my lifelong inspiration

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Addendum – *Ensuring Patient Safety through Medical Device Regulatory Science: A Regulatory Framework for Competent Authorities* [*MD-PMSV-RF01*]

List of Abbreviations

AI	Artificial Intelligence
AIMDD	Active Implantable Medical Devices Directive
ANVISA	Agência Nacional de Vigilância Sanitária
ASCA	Accreditation Scheme for Conformity Assessment (US)
BPAP	Bi-Level Positive Airway Pressure
CAB	Conformity Assessment Bodies
CAMD	Competent Authorities for Medical Devices (EU)
CAPA	Corrective and Preventive Action
CDRH	Center for Devices and Radiological Health (US)
CE	Conformitèe Européenne mark
CEAR	Clinical Evaluation Assessment Report
CER	Clinical Evaluation Report
CHMP	Committee for Medicinal Products for Human Use (EMA)
CPAP	Continuous Positive Airway Pressure
DMRC	Defective Medicines Report Centre (UK)
DOC	Declaration of Conformity
DSCA	Division of Standards and Conformity Assessment (US)
EC	European Commission
ECG	Electrocardiogram
EEA	European Economic Area
EHDS	European Health Data Space Regulation
EMA	European Medicines Agency
EPSCO	Employment, Social Policy, Health and Consumer Affairs Council (EU)
EU	European Union
EUDAMED	European Database for Medical Devices

FDA	Food and Drug Administration (US)
FFDCA	Federal Food, Drug and Cosmetic Act (US)
FREC	Faculty of Research Ethics Committee (Malta)
FSCA	Field Safety Corrective Action
FSN	Field Safety Notice
GDPR	General Data Protection Regulation
HaDEA	Health and Digital Executive Agency
HIPAA	Health Insurance Portability and Accountability Act
IDAP	Innovative Devices Access Pathway (UK)
IMDRF	International Medical Device Regulators Forum
IRIS	Incident Reporting and Investigation Scheme (Australia)
ISO	International Organisation for Standardisation
IVD	*In vitro* Diagnostic Device
IVDMD	*In vitro* Diagnostic Medical Devices Directive
IVDR	*In vitro* Diagnostic Medical Device Regulation [(EU) 2017/746]
JAMS 2.0	Joint Action on Reinforced Market Surveillance of Medical Devices and In Vitro Medical Devices
MDCG	Medical Device Coordination Group
MDD	Medical Devices Directive
MDR	Medical Device Regulation [(EU) 2017/745]
MDSAP	Medical Device Single Audit Program
MHLW	Minister of Health, Labour and Welfare (Japan)
MHRA	Medicines and Healthcare Products Regulatory Agency
MIR	Manufacturer Incident Report
ML	Machine Learning
MORE	Manufacturer’s On-line Reporting Environment portal (UK)
NEST	National Evaluation System for health Technology (US)

OECD	Organisation for Economic Co-operation and Development
PMCF	Post-Market Clinical Follow Up
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
PMPF	Post-Market Performance Follow Up
PMS SI	Post-Market Surveillance Statutory Instrument (UK)
PMS	Post-Market Surveillance
PRAC	Procedure for Recalls, Product Alerts and Product Corrections (Australia)
PSUR	Periodic Safety Update Reports
QMS	Quality Management System
RCB	Registered Certification Bodies (Japan)
SaMD	Software as Medical Device
SF	Substandard and Falsified Medical Devices
SMEs	Small and Medium Sized Enterprises
SWOT	Strengths, Weaknesses, Opportunities and Threats
TGA	Therapeutic Goods Administration (Australia)
UDI-DI	Unique Device Identifier – Device Identifier
UK	United Kingdom
US	United States of America
WHO	World Health Organisation

Abstract

The increasing reliance on medical devices and *in vitro* diagnostic technologies has improved healthcare outcomes but also raised the need for robust regulatory oversight to ensure patient safety. The aims of this study were to identify weaknesses in medical device patient-centred regulatory sciences, and to develop a post-market surveillance regulatory framework focused on providing a strategic oversight approach to ensure long-term patient safety.

The methodology consisted of three phases. Phase I identified procedures across EU and non-EU countries related to the oversight of post-market surveillance and vigilance, coupled with a review of global standards and guidelines. Insights were captured in a data collection tool disseminated to European surveillance and vigilance regulatory experts. Findings from this phase informed the design of a regulatory framework in Phase II. Phase III included pilot testing of the framework on a sample of incident reports from the Malta Medicines Authority medical device vigilance database, and a SWOT analysis to refine the framework. Data from each incident report was collated using a developed evaluation template. An adapted CASP-based tool was used to assess application of the developed framework to incident reports to evaluate regulatory performance in real-world scenarios for pilot testing.

Phase I revealed five key areas of patient-centric regulatory weaknesses. These areas formed the main domains of the data collection tool: (a) resources in regulatory authorities, (b) incident reporting, (c) legal requirements of legacy and custom-made devices, (d) the recall process, and (e) integration of artificial intelligence (AI) in surveillance and vigilance regulation. The twelve respondents of the data collection tool emphasised the need for training of economic operators on post-market surveillance

responsibilities and highlighted the lack of harmonisation and challenges with AI integration. The framework developed in Phase II mapped regulatory processes involved in ensuring safety and performance of medical devices across risk classes, including specific niches such as custom-made devices. It outlines the responsibilities of stakeholders to enhance collaboration and inform training modules, and provides guidelines on integrating the requirements of the newly-adopted AI legislation into regulatory processes. In Phase III, the SWOT analysis revealed opportunities, namely developing guidelines to align AI and medical devices regulations, and implementing training strategies to address threats like the outpacing of regulation by rapidly-evolving technologies.

The developed regulatory framework is intended to enhance post-market surveillance and vigilance oversight in medical device regulatory sciences. By addressing key weaknesses and supporting integration of AI-driven solutions, the framework aims to provide a proactive structured approach to mitigate risks while still fostering innovation, to maintain patient safety.

Keywords: *patient safety, post-market surveillance, vigilance, medical device, regulatory framework*

CHAPTER 1
INTRODUCTION

1.1 Background – Bridging gaps without re-inventing the wheel

Medical devices and pharmaceutical products are both an integral part of modern healthcare as we know it. Both contribute to the diagnosis, prevention and treatment of diseases (Contardi, 2019). Regulatory frameworks of medicinal products and medical devices differ from each other in terms of legal evolution, international harmonisation and assessment of risks involved with the different categories. Legislations controlling the use of pharmaceutical products for human consumption have been established for over half a century (Parvizi et al, 2014), and are continuously being revised and amended accordingly. The field of medical devices is more recent in comparison. The use of medical devices has been growing exponentially throughout these last few decades, and with currently more than 2 million different medical devices on the global market[1] (Bracciale et al, 2023), there is a progressively growing number of patients who depend on mechanical and electronic technologies (Morgenthaler et al, 2022) to improve, maintain, and even sustain, health. This extensive usage of medical devices results not only in enhanced benefits in healthcare (Babyar, 2017; Charlesworth and van Zundert, 2019) by impacting patients' health directly and indirectly (Seo et al, 2022), but also a critical need for market regulation (Oi Lam Ung, 2019).

Regulation of medical devices in the EU was initiated in the 1990s, with the Council Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD), the Council Directive 93/42/EEC on Medical Devices (MDD) and the Directive 98/79/EC of the European Parliament and of the Council on *In Vitro* Diagnostic Medical Devices

[1] World Health Organization. Health topics: Medical Devices. Geneva, Switzerland. [Internet] 2025. [cited 2025 February 14]. Available from: https://www.who.int/health-topics/medical-devices

(IVDMD)[2]. Having directives instead of regulations as legal instruments caused a lack of harmonisation between the Member States, because each diverse Member State had to transpose the provisions listed in the directives into individual national laws.

Between 2010 and 2012, there were two high-profile scandals that were highly publicised in the global media. One of these cases involved breast implants containing silicone which was non-compliant to manufacturing specifications causing a higher risk of ruptures and serious adverse reactions (Lampert et al, 2012; Antich-Isern, 2021). Due to poor post-market surveillance and record keeping, it was impossible to recall all the affected implants. The other case refers to metal-on-metal total hip prostheses initially designed for young osteoarthritis patients, that produced hypersensitivity adverse reactions, pseudo-tumours, and high levels of metal ions in the blood and soft tissues (Pane et al, 2020; Bitar et al, 2021). Other recalls that led to a global uproar include cases involving transvaginal polypropylene mesh implants to treat stress urinary incontinence and pelvic organ prolapse, that caused traumatic complications and pain in several women, leading to lawsuits that exposed the lack of informed consent and information regarding potential risks to the patient (Dyer, 2023). A recent global recall, in 2021, involved the emission of potentially carcinogenic chemicals and dangerous particles from the polyurethane foam inside continuous positive airway pressure (CPAP) devices, bi-level positive airway pressure (BPAP) devices, and other mechanical ventilatory devices manufactured by Philips Respironics. This recall was estimated to have impacted more than 16 million patients globally (Morgenthaler et al, 2022). Spinal cord stimulators, marketed for chronic pain relief, have caused thousands of injuries

[2] Directorate-General for Health and Food Safety. Medical Devices – Sector – Directives. European Commission. [Internet] 2025. [cited 2025 February 14]. Available from: https://health.ec.europa.eu/medical-devices-sector/directives_en

including burns, shock, and paraplegia, with hundreds of fatalities (Deeksha et al, 2021). In 2020, the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK ordered a recall of around 750,000 COVID-19 testing kits because they were giving unreliable results[3]. Such reports expose limitations of the former directives, and also highlight the need for a regulatory framework (Antich-Isern, 2021; Shatrov and Blankart, 2022) that safeguards the patient under stricter regulations and reinstates trust in the safety of medical devices (Thienpont et al, 2020).

The recent, more robust, Medical Devices Regulation[4] (MDR) and *In vitro* Diagnostics Regulation[5] (IVDR) have both entered into force in 2017, and dates of application of both regulations were the 26 May 2021 and 26 May 2022 respectively. Implementation of these regulations is still a work in progress, and amendments are continuously being put forward by all stakeholders involved. An advantage of having these new regulations is that they are equally relevant and applied directly in every Member State, having direct implications and enforcement as a national legislation. The scope of the MDR [(EU) 2017/745], and the IVDR [(EU) 2017/746], requires intensive scrutiny of devices, and manufacturers need to re-evaluate, and if necessary, improve the technical documentation and clinical data available for their whole portfolio of medical devices and *in vitro*

[3] Medicines and Healthcare products Regulatory Agency. Results from laboratory-based tests for COVID-19 antibodies using capillary blood sample collection kits may not be reliable (MDA/2020/015). GOV.UK. [Internet] 2020. [cited 2025 February 14]. Available from URL: https://www.gov.uk/drug-device-alerts/results-from-laboratory-based-tests-for-covid-19-antibodies-using-capillary-blood-sample-collection-kits-may-not-be-reliable-mda-2020-015

[4] Official Journal of the European Union (EU). Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC [Internet]. Luxembourg: Official Journal of the EU; 2017 [cited 2025 February 14]. Available from URL: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745

[5] Official Journal of the European Union (EU). Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU [Internet]. Luxembourg: Official Journal of the EU; 2017 [cited 2025 February 14]. Available from URL: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0746&qid=1690896553203

diagnostics to be put on the European market (Egbosimba, 2019). Effective oversight of the post-market surveillance process by the regulatory bodies of each EU member state is fundamental to provide the necessary network needed to safeguard patients and public health (Gadotti Martins et al, 2021), and to provide an essential balance between safety and innovation (Maci et al, 2022).

International harmonisation is one of the pillars establishing pharmaceutical regulation. Organisations such as the World Health Organization (WHO), the Food and Drug Administration (FDA) of the United States (US) of America, and the European Medicines Agency (EMA) combine joint efforts to standardise processes like drug safety and quality globally. Regulations for medical devices are more variable and less harmonised, being well-established and centralised in some regions such as the US, and still emergent in regions such as the EU. The WHO recommends the use of the International Medical Device Regulators Forum (IMDRF) terminologies and codes when reporting medical device adverse events, to increase global harmonisation and minimise language barriers (Choi et al, 2024). These codes are proposed for amendments and updates in 2025. If stakeholders are adequately trained to use these IMDRF codes, the processes of vigilance and surveillance would become more standardised. When the European Database on Medical Devices (EUDAMED) is fully set up by the European Commission (EC), this should also provide a common hub of information on medical devices for all stakeholders involved, from the regulatory authorities to the end users (Malvehy et al, 2022), facilitating oversight of vigilance.

At EMA level, there is still an absence of a centralised department that has its own expertise in every clinical sector of medical devices and *in vitro* diagnostics (Fraser et al,

2021). This may be a cause of concern, considering that the European market for medical devices is the second largest in the world, estimated by *MedTech Europe Facts and Figures 2024*[6] to make up 26.1% of the global market, topped only by that of the US at 47.2%. Factors influencing the US dominance of the device market include the presence of key global manufacturers, an ever-growing healthcare infrastructure, a strong regulatory framework, and importantly, the rapid adoption of the most innovative medical technologies (Amaral et al, 2024). This does not indicate that the US market is without any flaws. In 2018, an international journalist investigation, under the name 'Implant Files', investigated more than eight million records such as recall notices, legal documents and adverse event reports sent to the FDA over a ten-year period, on flawed devices that contributed to a staggering 1.7 million injuries and around 83,000 deaths. These devices range from cardiac defibrillators to transcutaneous aortic valve replacements to permanent implanted contraceptives (Lenzer, 2018).

A significant drawback to global harmonisation arises from the US requirement that manufacturers must comply with 21 CFR Part 820, which is the FDA's Quality System Regulation, rather than to ISO 13485:2016, which is the internationally recognised standard for medical device quality management systems (Wright, 2023). Both these standards have similarities, such as considering the entire lifespan of the device to improve efficiency and minimise risks, but key differences exist in areas such as risk management and documentation, increasing the burden on manufacturers if these want to comply with both standards. As of February 2025, the FDA has issued a final rule to

[6] MedTech Europe. Facts and Figures 2024. [Internet] Belgium. 2024 [cited 2025 February 14]. Available from URL: https://www.medtecheurope.org/resource-library/medtech-europes-facts-figures-2024/

amend 21 CFR Part 820 to align it with ISO 13485:2016.[7] This amendment, the Quality Management System Regulation, is set to take effect in 2026, aiming to streamline compliance for manufacturers who operate in multiple markets and to represent a move towards global harmonisation.

When it comes to risk assessment, medicines undergo extensive clinical trials before receiving marketing authorisation, where they are already being tested on a large number of patients to demonstrate their safety, efficacy and quality before approval. On the other hand, in the field of medical devices, clinical evidence is usually generated in both pre-market and post-market surveillance studies (Craig et al, 2019; Fraser et al, 2021). The generation of real-world evidence from real clinical data may be easier and more cost-effective for manufacturers when compared to complete clinical investigations (O'Neill et al, 2019). The inclusion of safety data in the risk management processes lacks uniformity (Pane et al, 2017). The clinical development phases and the clinical design of devices are not highly standardised and randomised as in the pharmaceutical industry, but are dependent on the type of product and are more individualised to each device (Oi Lam Ung, 2019; Fraser et al, 2021). Irreversible effects on the patient may be more common with the use of medical devices, rather than with medicines (Fraser et al, 2021). Medical devices are subject to a risk-based classification. Class I devices would have less stringent regulatory requirements than Class III devices. Under the older directives, clinical data was not adequate, if at all present, and this data was not sufficiently verified by notified

[7] US Food and Drug Administration. Quality Management System Regulation: Final Rule Amending the Quality System Regulation – Frequently Asked Questions [Internet] USA. 2024 [cited 2025 February 14]. Available from URL: https://www.fda.gov/medical-devices/quality-system-qs-regulationmedical-device-current-good-manufacturing-practices-cgmp/quality-management-system-regulation-final-rule-amending-quality-system-regulation-frequently-asked

bodies (Egbosimba, 2019). In this regard, the new regulations aim to become stronger tools for enhancement of patient safety and assurance of conformity in device performance requirements to safeguard public health. Standards and requirements for clinical investigations of medical devices and performance evaluations of *in vitro* diagnostics are relatively new. The regulations still have shortcomings, such as generic rules with lack of comprehensive details on methodologies which can lead to different and inconsistent interpretation by different manufacturers and notified bodies (Fleetcroft et al, 2021; Fraser et al, 2021).

A major challenge lies with applying the new regulations to innovative devices. Innovation in the medical device sector is often driven by small and medium enterprises (SMEs). These companies are more vulnerable when compared to large industries. The administrative costs that come with development of devices can be so burdensome that SMEs are forced out of business (Maresova, 2020). By finding means to address this challenge, regulatory efforts can yield broader benefits for the smaller enterprises and, ultimately, for the patient (Peñarrubia-Ortiz et al, 2025).

Rather than re-inventing the wheel, the evolving regulation of medical devices presents an opportunity for adaptation on well-established principles and structures that have successfully founded the regulation of pharmaceuticals for years. This would ensure efficiency besides enhancing public health outcomes.

1.2 Beyond Approval – The Current State of Affairs in Post-Market Surveillance and Vigilance Regulation

Post-market surveillance (PMS) is the systematic process of monitoring the safety, performance, and quality of devices after they have been placed on the market. It involves real-world data collection of adverse events, risk management, implementation of corrective and preventive actions, and analysis of other periodic updates that ensure the safety and performance of devices throughout their lifecycle (Ren et al, 2023).

A PMS system that is consistent with the risk class and type of the device needs to be incorporated into the quality management system (QMS) of the manufacturer. Practical details on implementing PMS activities, such as complaint handling, risk management, and regulatory reporting, can also be found in ISO 13485:2016 - *Medical Devices Quality Management Systems* and ISO/TR 20416:2020 – *Medical devices – Post-market surveillance for manufacturers.*[8] While the ISO standards focus on the general quality management of devices, the MDR / IVDR include additional requirements for a robust risk management system (Sheffer, 2018), and hold the manufacturer responsible for its implementation and maintenance (Simunovic, 2023). A well-conceived post-market surveillance is critical in ensuring the safety and performance of medical devices (Pane et al, 2019), and in ensuring that corrective actions are carried out when the risks of using a device outweigh the benefits.[9]

[8] International Organization for Standardization. Medical Devices Quality Management Systems (ISO Standard No. 13485:2016). [Cited 2025 January 10]. Available from URL: https://www.iso.org/standard/59752.html

[9] World Health Organization. Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics. 2020. [Cited 2025 January 10]. Available from URL: https://www.who.int/publications/i/item/9789240015319

While PMS is a continuous requirement for all devices from Class IIa upwards in the EU, PMS studies are ordered on a case-by-case scenario under section 522 of the Federal Food, Drug and Cosmetic (FFDCA) Act in the US. A manufacturer is only required to do post-market surveillance of a class II or a class III device in special cases, such as in implantable devices, in life-support devices used outside clinical facilities, in paediatric devices, and where it is possible to have serious incidents through device failure. The FDA has a database with these 522 PMS studies, where reporting status is provided, and this is updated weekly with any new requirements.[10] Conversely, the UK government has introduced the draft of the Post-Market Surveillance Statutory Instrument (PMS SI) in October 2024, with a transition period expected to extend till 2030. Once this is implemented, it will introduce more stringent PMS requirements for medical devices in the UK, and there will be more alignment with the EU regulations.[11]

The manufacturer is responsible for all conformity procedures leading to obtaining the Conformitèe Européenne (CE) mark (Shermilan and Kamaraj, 2021) which certifies that the device conforms with all the relevant EU laws and standards, and could be put on the market within the EU and the European Economic Area (EEA) (Hancher and Foldes, 2013). A notified body is nevertheless required to demonstrate that the device is compliant with the requirements of the regulations. The higher the class of the device, the higher would be the level of assessment carried out by the notified body (Mishra,

[10] U.S. Food and Drug Administration. Medical Devices. Postmarket Requirements (Devices). 522 Postmarket Surveillance Studies Program [Internet]. Silver Spring: U.S. FDA [cited 2025 January 10]. Available from URL: https://www.fda.gov/medical-devices/postmarket-requirements-devices/522-postmarket-surveillance-studies-program

[11] Cowlishaw S, Spivey D, Mitchell M. UK's Medical Device Post-market Surveillance Statutory Instrument Laid Before Parliament – What are the Key Changes for Medical Device Regulation? [Internet]. Global Policy Watch. 2024. [Cited 2025 January 10]. Available from URL: https://www.covingtonblogs.com/?s=uk+medical+device+post-market+surveillance

2017). The role of conformity assessment bodies (CAB) goes beyond the EU. In Australia, the Therapeutic Goods Administration (TGA) also authorises CABs based on requirements aligned with the EU and IMDRF standards to ensure international compliance.[12] In the US, the Division of Standards and Conformity Assessment (DSCA) plays a central role in ensuring FDA recognition.[13] In September 2024, the FDA introduced the voluntary Accreditation Scheme for Conformity Assessment (ASCA) Program, to streamline regulatory processes by leveraging accredited testing laboratories to assess the conformity of devices to specific FDA-recognised standards and international frameworks such as the IMDRF. In Japan, Registered Certification Bodies (RCB) are registered by the Minister of Health, Labour and Welfare (MHLW) to grant certification to manufacturers (Badnjević et al, 2022) and are then assessed by the Pharmaceuticals and Medical Devices Agency (PMDA).[14] The United Kingdom (UK) has UK Approved Bodies[15], designated by the MHRA, to do third-party conformity assessments. Several UK Approved Bodies, previously designated as notified bodies under the EU directives before the UK withdrew from the EU in 2020, retained their designations.

[12] Therapeutic Goods Administration. How we regulate - Australian Conformity Assessment Bodies (Australian CABs). [Internet] Australia. 2025 [cited 2025 February 14]. Available from URL: https://www.tga.gov.au/how-we-regulate/australian-conformity-assessment-bodies-australian-cabs

[13] US Food and Drug Administration. Division of Standards and Conformity Assessment. [Internet] USA. 2024 [cited 2025 February 14]. Available from URL: https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/division-standards-and-conformity-assessment

[14] Pharmaceuticals and Medical Devices Agency. Reviews and Related Services – Assessments to Registered Certification Bodies. [Internet] Japan. 2025 [cited 2025 February 14]. Available from URL: https://www.pmda.go.jp/english/review-services/gmp-qms-gctp/0005.html

[15] Medicines and Healthcare products Regulatory Agency. Guidance: UK approved bodies for medical devices. [Internet] United Kingdom. 2025 [cited 2025 February 14]. Available from URL: https://www.gov.uk/government/publications/medical-devices-uk-approved-bodies/uk-approved-bodies-for-medical-devices

There has been a recent shift in focus of regulatory authorities and even notified bodies towards the monitoring of post-market concerns. Although regulatory authorities are responsible for enforcement through inspections and audits of the economic operators (Ball et al, 2018), the main responsibility remains that of ensuring patient safety by monitoring compliance of the devices and providing guidance for a robust PMS system. PMS could be categorised into Proactive PMS and Reactive PMS, based on the collection of data, as shown in *Figure 1.1*.

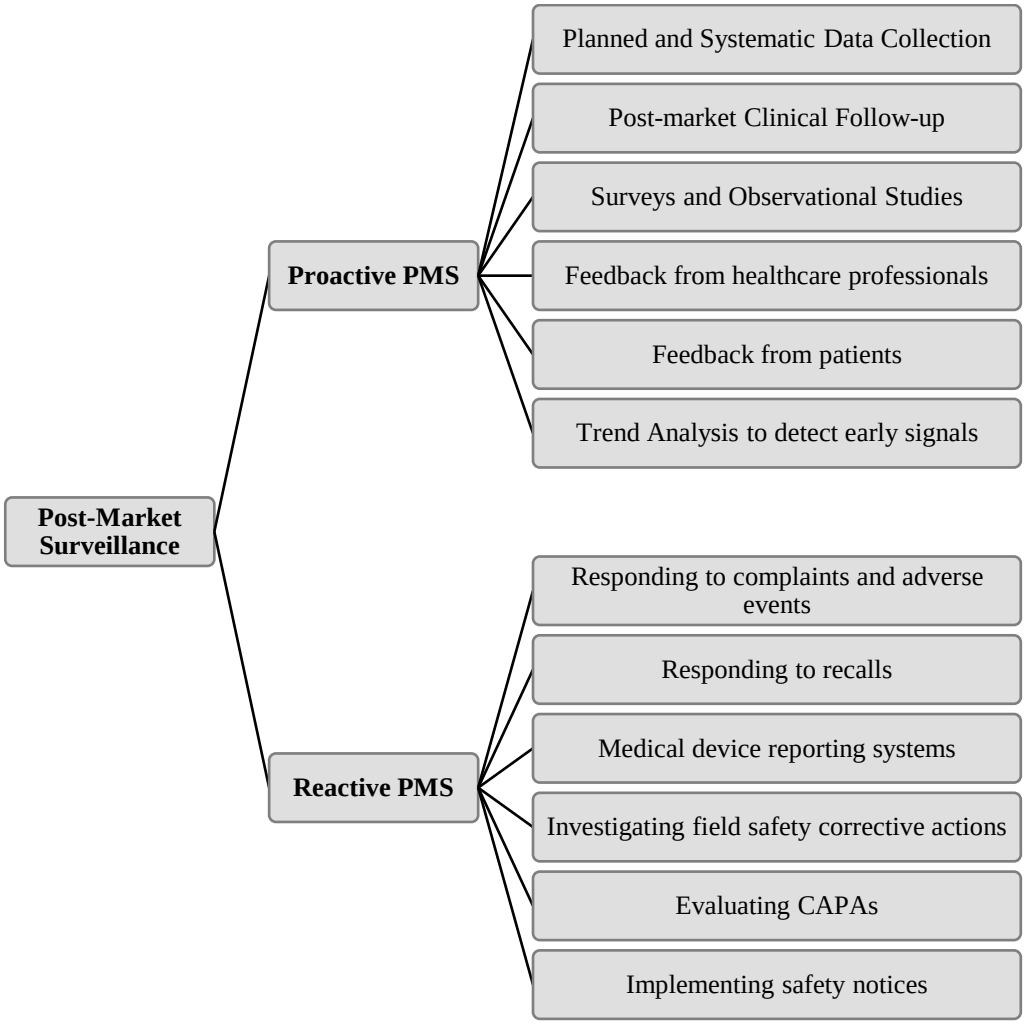

Figure 1.1. Key Characteristics of Proactive vs Reactive Post-Market Surveillance

Figure 1.1 depicts a flow diagram showing how data is collected and analysed proactively to detect potential risks before these can cause further harm, and reactively by focusing on identifying and addressing issues after these have been reported.
[CAPAs – Corrective and Preventive Actions; PMS – Post-Market Surveillance]

Despite the stringency and novelty of the new regulations, several legal exemptions have been introduced, particularly for legacy devices and custom-made devices. Legacy devices, placed on the European market or put into service after 26 May 2021, may continue to be used until 31 December 2027 or 2028, if they fulfil conditions of Article 120 of the MDR. They are devices that were either Class I devices under the older Directives with an EC Declaration of Conformity (DOC) drawn up prior to the 26 May 2021 and now requiring a notified body under the MDR, or devices that were covered by an EC certificate under the older Directives prior to the 26 May 2021.[16] These devices must still comply with relevant requirements pertaining to quality management systems, post-market surveillance and vigilance, but have a number of transitional provisions. Custom-made devices are devices specifically designed and manufactured to meet the unique needs of an individual patient, based on a medical prescription of a qualified healthcare professional, and not mass-produced or offered in standard models. Such devices include dental devices that are prescribed for an individual patient (Green, 2023) or prescribed prostheses with specific anatomical characteristics for a specific patient with a lost limb. The statement containing all relevant information pertaining to the custom-made devices now must be kept for at least ten years, instead of five years as was under the older directives (Green, 2021). If the custom-made device is implantable, this period shall be at least fifteen years from when the device has been placed on the market. Despite this increased rigour, certain legal exemptions apply, particularly regarding conformity assessments.

[16] Medical Device Coordination Group (MDCG). MDCG 2021-25 Rev.1 Regulation (EU) 2017//745 – application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC [Internet]. 2024 [cited 2025 Febraury 27]. Available from URL: https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en

The concept of vigilance directly contributes to post-market surveillance as it ensures the safety and performance of devices after they are placed on the market. It focuses on identifying, reporting and managing serious incidents and field safety corrective actions related to medical devices (Gagliardi et al, 2018). Under the EU regulations, manufacturers are obliged to report to the competent authorities any serious incidents or field safety corrective actions involving medical devices that are made available on the Union Market. Through the collection of this safety and performance data, regulatory authorities can act promptly, together with the economic operators, to prevent further harm (Pane et al, 2021).

Table 1.1 defines the differences between 'Incident' and 'Serious Incident', and relevant actions that need to be taken. Reporting deadlines are notably accelerated when public health threats are involved, underscoring the critical need for timely intervention to mitigate widespread impact. Examples of these threats include failure of *in vitro* diagnostic tests leading to the spread of infectious diseases, distribution of mislabelled devices such as non-sterile devices labelled as sterile, and cyberattacks affecting life-supporting devices.[17] The Manufacturer Incident Report (MIR) includes Field Safety Corrective Actions (FSCA), proactive measures including software updates, warnings, device modifications, and device recalls. The FSCA is communicated without delay to involved stakeholders through the Field Safety Notice (FSN) to ensure transparency.[17]

[17] Medical Device Coordination Group (MDCG). MDCG 2023-3 Rev. 2 Questions and Answers on vigilance terms and concepts as outlined in the Regulation (EU) 2017/745 and Regulation (EU) 2017/746. [Internet]. 2025 [cited 2025 January 10]. Available from: https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en

Table 1.1 The differences between 'Incident' and 'Serious Incident'

Terminology	Medical devices: (EU) 2017/745 MDR	*In vitro* diagnostic medical devices: (EU) 2017/746 IVDR	Action by Manufacturer in EU	Timelines for Reporting in EU	Timelines for Reporting in other Jurisdictions
Incident	"An 'incident' is any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect." [MDR Article 2(64)]	"An 'incident' is any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any harm as a consequence of a medical decision, action taken or not taken on the basis of information or result(s) provided by the device." [IVDR Article 2(67)]	Not reportable to competent authorities under MDR Article 87(1) and IVDR Article 82(1)	No need for reporting	No need for reporting
			Documented in QMS of manufacturer		
			Used for trend analysis as per MDR Article 88 and IVDR Article 83		
Serious Incident	"'Serious Incident' means any incident that directly or indirectly led, might have led or might lead to any of the following: (a) the death of a patient, user or other person, (b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health, (c) a serious public health threat." [MDR Article 2(65)]	"'Serious incident' means any incident that directly or indirectly led, might have led or might lead to any of the following: (a) the death of a patient, user or other person, (b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health, (c) a serious public health threat." [IVDR Article 2(68)]	Reportable to competent authorities under MDR Article 87 (1) to (5) and IVDR Article 82 (1) to (5)	When a causal relationship is established or thought possible between device and serious incident – Report within **15** calendar days	When a causal relationship is established or thought possible between device and serious incident – Report within **15** calendar days in Switzerland[18] and in UK[19] Report within **30** calendar days in Australia[20]
			Manufacturers report through the Manufacturer Incident Report (MIR), including any Field Safety Corrective Actions (FSCA)	In death or serious deterioration of a patient's health, when causal relationship is established/suspected between device and serious incident – Report within **10** calendar days	In death or serious deterioration of a patient's health, when causal relationship is established/suspected between device and serious incident – Report within **10** calendar days in Switzerland[18], UK[19] and Australia[20] Report within **30** calendar days in US[21] and Japan
				In serious public health threat – Report within **2** calendar days	In serious public health threat – Report within **2** calendar days in Switzerland[18], UK[19] and Australia[20] Report within **5** calendar days in US[21] Report within **15** calendar days in Japan (Handa et al, 2015)
				Incomplete initial report may be submitted to ensure timely reporting, to be followed up by a complete report	Incomplete initial report may be submitted to ensure timely reporting, to be followed up by a complete report

[Compiled from: public regulatory sources (see footnotes) and MDCG 2023-3 Rev. 2 Questions and Answers on vigilance terms and concepts as outlined in the Regulation (EU) 2017/745 and Regulation (EU) 2017/746. 2025 [cited 2025 January 14].
Available from URL: https://health.ec.europa.eu/document/download/af1433fd-ed64-4c53-abc7-612a7f16f976_en?filename=mdcg_2023-3_en.pdf]

[18] Swissmedic. Reporting incidents & FSCAs (vigilance): Economic operators [Internet]. 2025 [cited 2025 February 10]. Available from URL: https://www.swissmedic.ch/swissmedic/en/home/medical-devices/reporting-incidents---fscas/hersteller---inverkehrbringer.html

[19] Medicines and Healthcare products Regulatory Agency. The Medical Devices (Post-market Surveillance Requirements) [Internet]. 2025 [cited 2025 February 10]. Available from URL: https://www.gov.uk/government/publications/medical-devices-post-market-surveillance-requirements/the-medical-devices-post-market-surveillance-requirements-amendment-great-britain-regulations-2024-guidance-on-implementation

[20] Therapeutic Goods Administration. Reporting adverse events for medical devices [Internet]. 2024 [cited 2025 February 10]. Available from URL: https://www.tga.gov.au/resources/guidance/reporting-adverse-events-medical-devices

[21] Food and Drug Administration. Mandatory Reporting Requirements: Manufacturers, Importers and Device User Facilities [Internet]. 2020 [cited 2025 February 10]. Available from URL: https://www.fda.gov/medical-devices/postmarket-requirements-devices/mandatory-reporting-requirements-manufacturers-importers-and-device-user-facilities

Timely signal detection is imperative to protect patient safety. The MDR does not provide clear guidance on signal detection and there is a need for harmonisation among Member States. Currently, there is a collaborative initiative, co-funded by the European Health and Digital Executive Agency (HaDEA) through the EU4Health programme, aimed at enhancing market surveillance of devices across the EU. This project, *Joint Action on Market Surveillance 2.0* (*JAMS 2.0*), is organised into eight work packages, each led by a national competent authority. One of these distinct work packages, led by Malta's competent authority, addresses '*Signal Detection and Vigilance'*, and aims to develop harmonised European practices for vigilance and signal detection, to promptly identify and address potential safety issues, by 2026.

While the EU has yet to provide explicit guidance on signal detection, other jurisdictions have implemented signal detection mechanisms into their surveillance practices. In the US, emerging signals are evaluated by the Center for Devices and Radiological Health (CDRH). The FDA has collaborated in the development of the *National Evaluation System for health Technology* (NEST) to facilitate detection and assessment of signals from different populations and clinical settings, thus using real-world evidence.[22] The MHRA expects manufacturers to report adverse trends apart from serious incidents and FSCAs, and this reporting must be done in the Manufacturer's On-line Reporting Environment (MORE) portal.[23] Swissmedic collaborates with economic operators, healthcare professionals and other regulatory bodies to operate a materiovigilance system

[22] US Food and Drug Administration. National Evaluation System for health Technology (NEST). USA [Internet]. 2019 [cited 2025 February 22]. Available from URL: https://www.fda.gov/about-fda/cdrh-reports/national-evaluation-system-health-technology-nest

[23] Medicines and Healthcare products Regulatory Agency. The Medical Devices (Post-market Surveillance requirements). UK [Internet]. 2025 [cited 2025 February 22]. Available from URL: https://www.gov.uk/government/publications/medical-devices-post-market-surveillance-requirements

that enables the analysis of data to facilitate detection of potential signals that could affect safety.[24] The TGA manages received reports under the Incident Reporting and Investigation Scheme (IRIS), and any signals will be further assessed through data analysis.[25] In Japan, the PMDA stores reports and safety information into a database for analysis, and any findings are then reported to the MHLW for any administrative actions for patient safety.[26]

The ultimate goal of every medical device standard and regulation is to create a patient-centric system, where the patient's needs and long-term health outcomes are supported. The patients are becoming an integral part of vigilance systems, where they can directly report issues such as adverse events and device handling problems. Patient organisations could also help in collaborating with regulatory authorities (Pané, 2021), especially in disseminating safety information and notifications to the patients. In clinical settings, the responsibility of vigilance shifts to the healthcare professional who may be considered as the end user. Health care professionals should report any adverse events, device malfunctions or safety concerns to the regulatory authorities or directly to the manufacturer. Their feedback informs recalls, field safety corrective actions and other modifications such as labelling updates. Their expertise regarding adverse events plays a crucial role in the early detection and management of risks linked with device use

[24] Swissmedic. Medical devices: Reporting incidents & FSCAs (vigilance). Switzerland [Internet]. 2019 [cited 2025 February 22]. Available from URL: https://www.swissmedic.ch/swissmedic/en/home/medical-devices/reporting-incidents---fscas.html

[25] Therapeutic Goods Administration. Medical device Incident Reporting and Investigation Scheme (IRIS). Australia [Internet]. 2019 [cited 2025 February 22]. Available from URL: https://www.tga.gov.au/resources/resource/reference-material/medical-device-incident-reporting-and-investigation-scheme-iris

[26] Pharmaceuticals and Medical Devices Agency. Outline of Post-marketing Safety Measures. Japan [Internet]. 2025 [cited 2025 February 22]. Available from URL: https://www.pmda.go.jp/english/safety/outline/0001.html

(Brijesh et al, 2024). Healthcare professionals are also involved in advisory panels of regulatory authorities to review post-market surveillance and vigilance data.

Product recalls are a critical part of ensuring safety, quality and compliance in any sector. They are actions, voluntary or mandated, to safeguard the general public, but they present consequences. A report from the Organisation for Economic Co-operation and Development (OECD) suggests that there is a steady increase in the number of global recalls over the recent years, and millions of products in general are recalled every year[27]. If left unresolved, the issues triggering recalls can have effects ranging from minor disruptions to serious, life-threatening dangers (Tennant et al, 2024). A look at recalls from different sectors gives an insight as to how managing these recalls in an effective manner requires a robust and quick-thinking strategy. In certain sectors such as the space industry, product recalls are rare but significant due to the critical nature and the costs of the missions. Often, once space components are deployed, it would be either impossible or too expensive to recall. Automotive recalls are high in volume, since cars are mass-produced, and a minor defect can affect millions of units globally. In healthcare, the slightest issues can have life-threatening implications, and this makes recalls in this sector rigorous, even for the slightest deviations from quality standards.

[27] Organisation for Economic Co-operation and Development. Measuring and maximising the impact of product recalls globally – OECD Workshop Report. [Internet]. OECD Science, Technology and Industry Policy Papers. 2018 [cited 2025 January 12]. Available from URL: https://one.oecd.org/document/DSTI/CP/CPS(2018)6/FINAL/en/pdf

Table 1.2 Examples of Recalls in Different Manufacturing Sectors

Sector	Recall Description
Automotive	Around 239,000 electric Tesla vehicles were recalled in the US in January 2025, due to issues of failure of rearview cameras, increasing the risk of collisions[28].
Nautical	Sea-Doo recalled passenger seats installed on their jet skis in 2022 due to risk that the seat may unlatch from the watercraft causing the passenger to fall in the water, with the risk of injuries and death.[29]
Aviation	The Federal Aviation Administration of the US grounded 171 Boeing 737-9 MAX aircraft after 2 fatal crashes with the loss of 346 lives[30].
Space	In 2018, NASA recalled the Webb Telescope Sunshield due to issues with deployment mechanisms on ground testing. This recall resulted in a successful launch in 2021 (Menzel, 2024).
Food Industry	Tonka beans were recalled in the first quarter of 2025 in the EU due to high levels of carcinogenic aflatoxins where analytical results showed 0.53ng/kg aflatoxins when threshold is 0.04ng/kg[31].
Healthcare	FDA recalled corticosteroid injections due to fungal contamination, causing fungal meningitis and fatalities in 2012 and 2013 (Lin and Hertig, 2023; Ahmed et al, 2024).
	In 2004, Merck recalled Vioxx (rofecoxib), a drug marketed as a safer alternative to non-steroidal inflammatory drugs, but then found to increase the risk of cardiovascular events such as stroke and myocardial infarction (Ghijs et al, 2024).
	Saline Flush IV syringes were recalled by Nurse Assist in 2016 due to contamination with *Burkholderia cepacia* bacteria that caused infection outbreaks and caused 7 deaths in the US (Brooks et al, 2019).
	A global recall of millions of catheters by Cook Medical took place in 2016 due to degradation and separation of the catheter tip, which could enter the bloodstream and cause serious adverse events[32].

This table provides examples of product recalls across various sectors with a brief description of the reason for recall. The technical nature of the recall may differ, but the common theme lies in risk mitigation strategies to protect the end-user.

[28] Reuters. *Tesla recalls 239,000 US vehicles over rear-view camera issue.* [Internet]. Thomson Reuters; 2024 [cited 2025 January 12]. Available from URL: https://www.reuters.com/business/autos-transportation/tesla-recalls-about-239000-vehicles-over-rear-view-camera-issue-2025-01-10/

[29] Office for Product Safety and Standards. *Product Recall: Sea-Doo Passenger Seat (2207-0080)*. [Internet]. UK: Gov.UK; 2022 [cited 2025 January 12]. Available from URL: https://www.gov.uk/product-safety-alerts-reports-recalls/product-recall-sea-doo-passenger-seat-2207-0080

[30] Federal Aviation Administration. *Updates on Boeing 737-9 MAX Aircraft*. [Internet]. USA: United States Department of Transportation; 2024 [cited 2025 January 12]. Available from URL: https://www.faa.gov/newsroom/updates-boeing-737-9-max-aircraft

[31] European Commission. Rapid Alert System for Food and Feed (RASFF) Window – Consumers' Portal. [Internet]. 2025 [cited 2025 April 17]. Available from URL: https://webgate.ec.europa.eu/rasff-window/screen/notification/757524

[32] Cook Medical. *Cook Medical issues global voluntary recall of catheters with Beacon Tip technology*. [Internet]. USA. 2016. [cited 2025 January 12]. Available from URL: https://www.cookmedical.com/newsroom/cook-medical-issues-global-voluntary-recall-of-catheters-with-beacon-tip-technology/

FDA classifies device recalls into three classes: Class I, when there is a reasonable probability that the use of the device causes serious adverse events or death; Class II, when the device may cause temporary or reversible adverse effects; and Class III, when there is a remote possibility of serious adverse events (Mooghali et al, 2023). The most common recalls are voluntary recalls by manufacturers, done under 21 CFR 7. When the manufacturer refuses to voluntarily recall a device, the FDA has the authority to order a recall under 21 CFR 810. The FDA requests recall status reports, usually at a time interval of two to four weeks, and these reports are only to be terminated when the FDA concludes the recall.[33]

The TGA has a similar classification of device recalls to the FDA. In 2025, a new procedure for recalls, product alerts and product corrections – PRAC – is going to be implemented, aimed to simplify the existing process of executing corrective actions. The TGA is aiming for simplified terminology, enhanced communication and transparency with stakeholders, and having a more streamlined recall process.[34] The EU could draw valuable lessons from this as it continues to develop and implement EUDAMED.

The PMDA also classifies recalls in 3 classes.[35] The manufacturer is responsible to execute the recall and inform stakeholders involved. In cases where recalls have significant public health implications, the PMDA and the MHLW may issue public

[33] Food and Drug Administration. Recalls, market Withdrawals, & Safety Alerts. [Internet]. 2025 [cited 2025 February 27]. Available from URL: https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts

[34] Therapeutic Goods Administration. Procedure for recalls, product alerts and product corrections (PRAC). [Internet]. 2024 [cited 2025 February 27]. Available from URL: https://www.tga.gov.au/resources/resource/reference-material/procedure-recalls-product-alerts-and-product-corrections-prac

[35] Pharmaceuticals and Medical Devices Agency. Recall Information (Medical Devices). [Internet]. 2025 [cited 2025 February 27]. Available from URL: https://www.pmda.go.jp/safety/info-services/devices/0054.html

notifications to inform users and healthcare professionals of the potential risks associated with the device.

In case of a recall, manufacturers in the UK must inform the Defective Medicines Report Centre (DMRC), providing detailed information about the device and any initial risk assessments. The DMRC monitors the actions taken by the manufacturer during the recall and provides guidance on risk mitigation if necessary.[36] The MHRA classifies the recall in one of four categories: Class I, if there is a reasonable probability that the use of the device causes serious adverse events or death; Class II, if the device may cause temporary or reversible adverse effects; Class III, for defects that are unlikely to cause harm to the patient, such as non-compliance with specifications; and Class IV, reserved for cases where there is no threat to patients, such as minor defects in packaging. The manufacturer is obliged to provide regular updates on the progress of the recall, with a final report usually required within twelve weeks of initiating the recall. Amendments to the UK Medical Devices Regulation 2002 to include post-market surveillance requirements should be coming into force on the 16 June 2025.

Unlike these jurisdictions that have established recall processes in place, the EU differs in that the MDR and the IVDR lack specific provisions concerning the classification and standardised management of device recalls. The national competent authorities may do their own risk assessment and risk classification, but the responsibility of managing recalls relies on the manufacturers.

[36] Medicines & Healthcare products Regulatory Agency. A Guide to Defective Medicinal Products. [Internet]. 2021 [cited 2025 February 27]. Available from URL: https://assets.publishing.service.gov.uk/media/6103ba7a8fa8f5042c338d1c/DMRC_Guide-to-Defective-Medicinal_Products-Aug2021.pdf

One of the central themes that kept on recurring in discussions during the MedTech Malta 2024 conference was the role of Artificial Intelligence (AI) in driving healthcare innovations, showcasing its role in analysing complex data sets such as genetic and behavioural data, to provide deeper insights to healthcare recommendations, and also to boost the efficiency of clinical studies.[37] From the perspective of regulation, the new European Artificial Intelligence Regulation (EU) 2024/1689 [AI Act] marks a crucial turning point, introducing a new phase of AI regulation across the medical device industry (Aboy et al, 2024). The AI Act has a broad scope and impact (Busch et al, 2024) and imposes strict requirements and responsibilities on AI system providers.

A profound comprehension of the regulatory outlook overseeing medical device software is necessary (Ludvigsen et al, 2022). Examples of software as a medical device (SaMD) include electrocardiogram (ECG) analysis software, image analysis software used for breast cancer diagnosis, continuous glucose monitoring software, software for sleep apnoea management, and thermal foot scans which have just been authorised as the world's first SaMD for diabetic foot screening.[38] These devices can assist healthcare professionals to make informed decisions in treating their patients by analysing complex medical data using less resources than other devices. When the AI system is trained on high-quality, diverse and complex datasets, its performance improves, making it more accurate and reliable (Farah et al, 2023; Joshi et al, 2024). It could include mechanisms for updates and post-market surveillance, and could be used across different populations of patients.

[37] Samar W. Personalized Medicine: The Key to Longevity [Panel Discussion]. MedTech Malta 2024. Available from URL: https://med-tech.world/news/personalized-medicine-longevity-medtech-malta-2024/

[38] Samar W. Amplifai Health's AI Diabetic Foot Scanner Gets SFDA Green Light. MedTech World. [Internet] 2025. [cited February 10 2025]. Available from: https://med-tech.world/news/amplifai-health-ai-diabetic-foot-scanner-sfda-approval

Software could pose problems for the classification of devices. If it is part of a medical device, one classifies it as per the device risk category itself. If it is software as a medical device, classification may be more complicated. The MDR classifies software in 4 risk classes. This classification is comparable to what is being done globally under other legislations and by the IMDRF. Australia, Switzerland and Japan have a similar classification to the one used by EU Member States. The US, while being a member of the IMDRF, defines software in only 3 classes, aligned with the FDA medical device classification system. The UK is planning to integrate AI regulation in the new medical device regulations that should be put in force in 2025 (Maccaro A et al, 2024).

1.3 An Incomplete Infrastructure – Lacunae in the Current Regulatory Landscape

The benefits and risks of a device cannot be fully identified before the device is placed on the market (Wilkinson and van Boxtel, 2020). During the clinical investigations, in the pre-market phase, enough data may have been collected to demonstrate that the benefits of using a particular device outweigh any risks (Kaul et al, 2020; White et al, 2023). It is only when the device is put under real-world conditions, where it can be availed of by the end-user, that further information regarding its risks emerge (Xu et al, 2015; Pelayo et al, 2021). Any modifications executed on the device during its lifecycle also affect the benefit-risk ratio. Benefit-risk analysis is integral to the technical documentation that must accompany any medical device. The stricter safety requirements of the MDR and IVDR have placed several devices into a higher risk class (White et al, 2023). This heightened focus on safety directly benefits patients, but may hinder

manufacturers as it leads to increased financial burdens of clinical investigations and increased cost of devices (Maci et al, 2024).

In the EU, manufacturers bear a significant documentation and reporting burden under PMS requirements, ranging from detailed post-market surveillance plans, to clinical evaluation plans, to continuous post-market clinical follow up (PMCF) for medical devices, or post-market performance follow up (PMPF) for *in vitro* diagnostics. This demands ongoing data collection, analysis, and reporting, reinforcing the substantial nature of the manufacturer's obligations. PMCF is the highest source of proactive data for PMS to help in minimising risks of devices (Kearney et al, 2023; Hochreiter-Hufford et al, 2024), with activities including analysis of real-world performance and adverse events (Hochreiter-Hufford et al, 2024), long-term follow-up of end-users, monitoring for emerging risks, and performance of new clinical investigations if necessary. Generated clinical evaluation reports (CER) are subject to scrutiny by the notified body. The notified body's evaluation is recorded in the Clinical Evaluation Assessment Report (CEAR), adding yet another layer of regulatory oversight and reporting burden.

Periodic safety update reports (PSUR) analyse and summarise the data collected from the post-market surveillance plan by manufacturers of Class IIa, Class IIb and Class III medical devices (Lines et al, 2023) and continuously update the risk-benefit profile of the device. These obligations are also expected by Swissmedic in Switzerland.[39] The UK's proposed PMS system, that should become effective later in 2025, is introducing a

[39] Swissmedic. Vigilance regarding medical devices – Post-market surveillance vigilance and market surveillance [Internet]. 2021 [Cited 2025 January 10]. Available from URL: https://www.swissmedic.ch/swissmedic/de/home/medizinprodukte/wiederaufbereitung---instandhaltung/vigilance-mep.html

structured reporting system similar to the EU PSUR for higher-risk devices, that must be available upon request by the MHRA.[40] TGA in Australia also requires annual submission of periodic safety reports for higher-risk classes of devices, for the first three years of the device on the Australian market.[41] Other periodic post-market reviews beyond the three-year period can still be requested by TGA if a safety issue is suspected. Japan requires manufacturers to assess the benefit-risk profile of higher-risk devices, and periodic safety reports for high-risk devices may need to be submitted to the PMDA.[42] The FDA does not require comprehensive PSURs from manufacturers. In the US, there is a 'Voluntary Malfunction Summary Reporting Program' for manufacturers,[43] where summary reports about higher-risk device malfunctions may be submitted, listing any corrective actions taken. These reports are much less detailed in terms of overall safety and efficacy when compared to PSURs. This can lead to variability in post-market oversight with heavier reliance on reactive surveillance, but it provides advantages to the manufacturers such as reduced regulatory burden and lower operational costs, which may transpose to faster patient access to devices at lower costs.

The extensive administrative, reporting and documentation requirements placed on manufacturers by EU regulations, while giving the patients reassurance and confidence

[40] Medicines & Healthcare products Regulatory Agency. Implementation of the future regulations [Internet]. 2024 [Cited 2025 January 10]. Available from URL: https://www.gov.uk/government/publications/implementation-of-the-future-regulation-of-medical-devices/implementation-of-the-future-regulations

[41] Therapeutic Goods Administration. Submitting annual reports for medical devices. [Internet] Australia. 2024 [cited 2025 February 14]. Available from URL: https://www.tga.gov.au/resources/guidance/submitting-annual-reports-medical-devices

[42] Rana A, Deshwal M, Rahi S. Comparative Study of Marketing Authorization Procedure for Medical Devices in USA, EU and Japan. World Journal of Pharmacy and Pharmaceutical Sciences. 2020; 9(8):1627-1650. [Internet] [cited 2025 February 14]. Available from DOI: 10.20959/wjpps20208-16701

[43] US Food and Drug Administration. Voluntary Malfunction Summary Reporting Program [Internet]. 2024 [cited 2025 February 20]. Available from URL: https://www.fda.gov/medical-devices/medical-device-reporting-mdr-how-report-medical-device-problems/voluntary-malfunction-summary-reporting-program

in regulatory oversight, underscore the critical need for adequate resources across the board. Meeting these obligations demands not only regulatory expertise but also dedicated personnel, expensive systems for data collection and analysis (Kearney et al, 2023), and sustained organisational capacity. Without the necessary resources, manufacturers may struggle to maintain regulatory compliance (Carl et al, 2024), and this could ultimately impact both regulatory approval and patient safety.

Similar administrative and resource-related challenges are also faced by notified bodies. The issue of resource shortages has become more acute with the increased requirements of the recent regulations (Groennvold, 2017). Lack of qualified personnel may limit the ability of the notified body to give a thorough evaluation of conformity. Verifying the clinical safety of a medical device according to the manufacturer's Clinical Evaluation Report (CER) requires knowledge and experience (Kearney et al, 2023), which may be further challenged by the ever-changing requirements of guidance documents (Egbosimba, 2019). The diversity of practices of manufacturers in assigning Basic UDI-DI, which is the primary identifier of the device, and in organising technical documentation, particularly when multiple devices form part of a system device, present significant obstacles to overcome. The assessment of the manufacturers' technical documentation by the notified bodies should provide reassurance to the end users regarding the expected high level of protection. In some cases, documentation obtained from manufacturers can still be insufficient (Simunovic, 2023), placing significant demands on the resources and capacity of notified bodies. The continuous evolvement of medical devices, with complex technology and AI-based solutions, may pose difficulties to the expertise of personnel within the notified body. This may create gaps in ensuring consistent conformity assessments if there is no constant training and

adaptation. Other concerns may arise since most notified bodies in the EU are privately-owned business organisations.[44] As profit-driven entities, they may face potential conflicts of interest in balancing their own commercial needs with their regulatory role. If market conditions change, and their regulatory costs increase, notified bodies may decide to withdraw their services, and this could create delays in device access for the patients. This contrasts with jurisdictions such as the US, where regulatory assessments are carried out by public bodies that are accountable to public institutions without commercial incentive.

The IMDRF has established the Medical Device Single Audit Program (MDSAP) as a streamlined program that allows a single audit by a MDSAP-recognised Auditing Organisation to satisfy regulatory requirements of five jurisdictions: TGA in Australia, Agência Nacional de Vigilância Sanitária (ANVISA) in Brazil, Health Canada, PMDA and MHLW in Japan, and FDA in the US. Other official observers to this audit approach are the EU, the MHRA (UK), and the WHO. The audit report generated could be used as part of the evidence of assessment of the devices. If the EU were to join MDSAP, this could yield several strategic benefits such as reducing audit fatigue and streamlining global market access.[45] The EU places heavy reliance on notified bodies, who are already over-burdened, and MDSAP participation could leverage audits from other jurisdictions and ease their work while still maintaining rigorous compliance. The coordinated audit system would increase harmonisation in oversight practices.

[44] European Commission. Questions and Answers: Commission proposes an extension of the transitional periods for the application of the Medical Devices Regulation. [Internet] Brussels. 2023 [cited 2025 February 14]. Available from URL: https://ec.europa.eu/commission/presscorner/detail/en/qanda_23_24

[45] MedTech Europe. European medical technology industry calls for the EU to join the Medical Device Single Audit Program (MDSAP) as a Full Member. [Internet]. 2025. [Cited 2025 May 24]. Available from URL: https://www.medtecheurope.org/wp-content/uploads/2025/02/20250217_mte-and-cocir_reflection-paper-on-mdsap-1.pdf

Another challenge could present itself when there are legal exceptions. Transitional provisions allow legacy devices to remain on the market without disruption of the supply chain, but such legal exceptions may inadvertently compromise safety and performance and lead to gaps in the oversight of patient safety. The legal exceptions for custom-made devices may also raise safety concerns (Boyle et al, 2024) due to the lighter regulatory oversight, limited data collection, and potential variability in manufacturing standards. This risk may be on a smaller scale than that of legacy devices due to individual device use and increased likelihood of close monitoring by healthcare professionals.

In vigilance, EU regulations and relevant MDCG documents provide detailed requirements for Manufacturer Incident Reports (MIR), but these could still be inadequate and insufficient, hindering the competent authorities' evaluation (Simunovic et al, 2024). Once EUDAMED is fully operational, it should be ensuring that MIRs are comprehensive and having a standardised format to improve traceability and harmonisation. Another significant challenge faced by competent authorities is the increased volume of incident reports that they receive (Macrae, 2016; Leistikow et al, 2017) as reporting obligations continue to evolve. This influx can strain the already-limited human resources and may undermine the timely identification of safety signals. It could be difficult to determine if a finding constitutes a signal that is clinically significant and needs further assessment (Pané, 2021) without harmonised guidance. There is also insufficient focus in regulations on the importance of empowering the end users to actively participate in vigilance. The competent authorities need to raise awareness about the necessity of identifying and reporting serious incidents (Gagliardi et al, 2018), to promote patient safety.

Regulatory ambiguities in the process for recalls can result in inconsistencies in their assessment across Member States. In the absence of harmonised guidance, the recall process may be interpreted differently, leading to regulatory gaps that may pose challenges to ensuring timely and coordinated responses to safety issues. The system is relying heavily on the manufacturer's ability and willingness to identify any risks and taking rapid risk-mitigation steps. In situations where there are conflicts such as financial interests or insufficient expertise on behalf of the manufacturers, the effectiveness of recall actions for patient protection may be compromised.

Substandard and falsified (SF) medical devices refer to products that fail to meet quality and safety standards. These products can pose severe risks to patient safety and public health. They can be due to either genuine manufacturing errors, or else they can be deliberately falsified. If deliberately manufactured in a substandard or falsified manner, these issues can be very difficult to detect. The MDR has introduced critical safeguards such as traceability and supply chain accountability, but the delayed implementation of digital infrastructure and variable enforcement across Member States still pose vulnerabilities. Challenges encountered with SF medical devices include risks to the patient such as serious health concerns due to compromised quality (Ahmed et al, 2022), lack of trust in the healthcare system (Bakker-'t Hart et al, 2021), financial burden, and regulatory issues. Falsified devices may infiltrate legitimate distribution networks through complex supply chains where several importers and distributors are involved, increasing the risks of tampering of the devices (Bakker-'t Hart et al, 2021). The sudden increase in online sales platforms in these last few years may facilitate distribution of falsified devices directly to the patients (Ahmed et al, 2022). Online platforms are not strictly regulated, creating a gap where low-quality devices can enter the market (Bakker-

't Hart et al, 2021). Lack of harmonisation of international regulations complicates enforcement (Bakker-'t Hart et al, 2021).

Regulatory frameworks of different regions in the world share several similarities when it comes to approval and classification of devices, such as classification of risk with different levels of regulatory evaluation, third-party assessment, and post-market surveillance as a critical requirement for safety assurance. In contrast, regulation in the EU may be more complex than in other countries such as the US and Japan. Since it consists of different countries with separate competent authorities, the same regulations and standards may be interpreted and applied diversely (Amaral et al, 2024). The national regulatory bodies oversee the regulation of devices in a decentralised manner, and then are expected to integrate the information through EUDAMED and through other European working groups. The more complex the regulatory landscape, the higher are the demands on the competent authorities for capacity building and cross-border collaboration, exacerbating potential gaps of lack of human resources.

In the current climate of rapid technological advancement, innovation in technology tends to outpace regulation. The new regulations aim to be ahead of these innovations by being stricter on the approval processes of devices and requiring more expertise from the notified bodies that approve the devices and from the competent authorities that oversee the regulatory compliance. This promotes safety but may result in limiting sponsoring options and discouraging any higher-risk innovations that may benefit patients (Maci et al, 2022). The FDA has tried stimulating innovation by speeding up market entry through the De Novo pathway for devices without a predicate (Aboy et al, 2024), but this has raised concerns that while reducing financial burden on the manufacturers and enabling

more rapid market access for innovative devices to benefit patients, it may be compromising safety and quality (Maxwell, 2021; Everhart et al, 2023). The Sakigake Designation System in Japan also aims to promote priority review and approval of devices (Maruyama et al, 2018). In 2017, Japan also implemented the Conditional Early Approval System that allows for early approval of innovative medical devices for serious unmet medical needs by evaluating the devices' safety post-market rather than before approval.[46] For these unmet life-threatening clinical needs, Australia offers the Priority Review Pathway for expedited processing by accelerating the review time but ensuring all standard regulatory requirements are still in place.[47] The UK launched the Innovative Devices Access Pathway (IDAP) in 2023 with the aim to accelerate the market access of innovative medical devices for significant unmet medical needs[48]. The EU does not currently have a centralised early approval program. Article 59 of the MDR may only offer temporary derogation in exceptional cases such as public health emergencies, granted on a national level. Faster approval of innovative devices in other jurisdictions can disadvantage patients in the EU by delaying their access to potential beneficial technologies. While stringent safety oversight is essential to protect patients, finding the right balance between thorough evaluation and timely access remains a critical challenge.

When discussing innovation in medical device regulatory sciences, one cannot overlook the transformative role of artificial intelligence. As AI becomes more prevalent in

[46] Inoue S. Regulatory Update from MHLW/PMDA [Internet]. Pharmaceuticals and Medical Devices Agency – 5th Joint Conference of Taiwan and Japan on Medical Products Regulation. 2017 [cited 2025 February 27]. Available from URL: https://www.pmda.go.jp/files/000221880.pdf

[47] Therapeutic Goods Administration. Priority review pathway for medical devices [Internet]. 2025 [cited 2025 February 27]. Available from URL: https://www.tga.gov.au/how-we-regulate/supply-therapeutic-good/supply-medical-device/medical-device-inclusion-process/priority-review-pathway-medical-devices

[48] Medicines and Healthcare products Regulatory Agency. The Innovative Devices Access Pathway (IDAP) [Internet]. 2024 [cited 2025 February 27]. Available from URL: https://www.gov.uk/government/publications/the-innovative-devices-access-pathway-idap#full-publication-update-history

healthcare (Cacciamani et al, 2023; Balendran et al, 2024), maintaining patient safety is a critical priority. Until quite recently, regulatory bodies were more focused on the traditional frameworks governing devices. These frameworks need to be modified to integrate the requirements of national, global and European legislations on AI, for regulators to be aware of emerging innovations, and, inevitably, their emerging risks (Solaiman, 2024). Besides being an integral part of devices and *in vitro* diagnostics, AI is also transforming the way how regulatory bodies carry out their oversight activities. It enables them to process vast quantities of collected data, and prioritise serious incident reports through algorithms. There are regulatory authorities that are using AI-powered dashboards to evaluate data obtained from incident reports and to carry out trend analysis. Training for regulators on the integration of these AI tools in the oversight of device safety is a necessity. An interdisciplinary approach, where regulators work together with engineers, clinicians, data analysts and statisticians, would ultimately lead to enhanced efficiency and confidence in oversight of post-market surveillance, and provide the much-needed evidence-based modifications to the present regulatory frameworks. A setback to these frameworks could be the use of innovative medical devices that may have unorthodox regulatory obligations, due to complex AI and Machine Learning (ML) applications, where algorithms are continuously evolving and adapting (Han Y et al, 2024). A centralised EU office for AI expertise has been implemented[49], but the regulation of AI-based medical devices remains the responsibility of national competent authorities. This fragmentation may raise regulatory gaps of ensuring sufficient expertise and human resources at the national level.

[49] European Commission. Artificial Intelligence in healthcare. [Internet]. 2025. [Cited 2025 May 20]. Available from URL: https://health.ec.europa.eu/ehealth-digital-health-and-care/artificial-intelligence-healthcare_en

To address these identified challenges in the current regulatory landscape, this study turns its focus to strengthening the oversight of post-market surveillance and vigilance to ensure a reliable and sustainable approach to long-term patient safety.

1.4 Aims and Objectives

The aims of the study were to identify gaps in medical device regulatory sciences where the patient's safety may not be sustained, and to develop a regulatory framework that would provide a strategic oversight approach to post-market surveillance and vigilance activities to ensure long-term patient safety.

The objectives of the research were to:

i. identify gaps in the current post-market surveillance and vigilance scenario by reviewing the approach in EU and global market towards safeguarding patient safety in medical device use, and gain insights from regulatory experts from European competent authorities through a developed data collection tool.

ii. develop a regulatory framework that can be used as a resource by competent authorities in the oversight of post-market surveillance and vigilance.

iii. evaluate strengths, weaknesses, opportunities, and threats that may be identified or expected with the use of this framework.

CHAPTER 2

METHODOLOGY

This chapter outlines the research study setting and design aligned with the research objectives.

2.1 Research Setting

The research was carried out at the Medical Devices and Pharmaceutical Collaboration Directorate within the Malta Medicines Authority. Ethics approval for the research was obtained from the Faculty of Research Ethics Committee (FREC) of the University of Malta (*Appendix I*). The Malta Medicines Authority granted approval for the access of data used in Phase 3 of this research study.

2.2 Research Design

The design of the research study is a qualitative research approach, consisting of three phases (*Figure 2.1*).

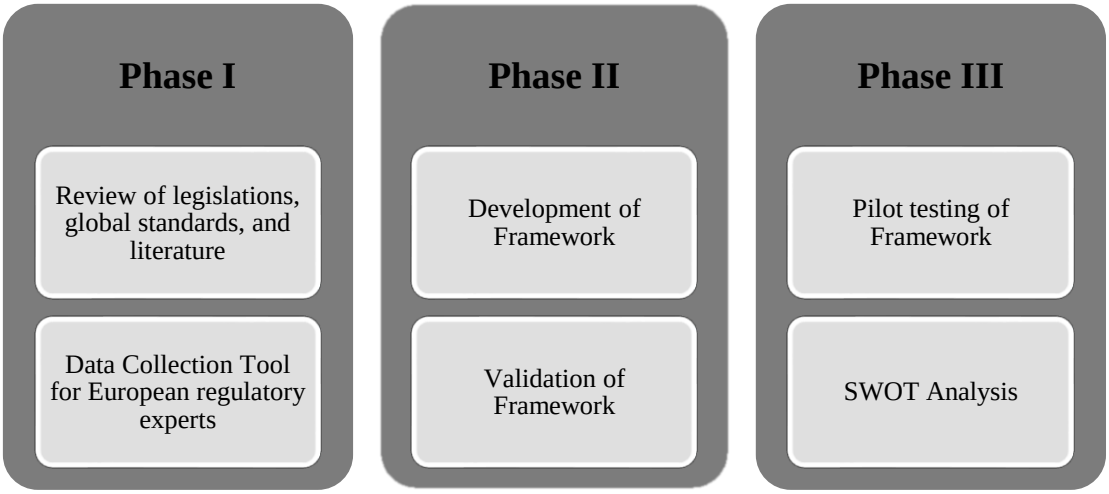

Figure 2.1 Research Design

2.3 Phase I – Gap Analysis

Phase I involved two stages:

i. ***Stage 1*** - a review of regulations, global standards, guidance documents and literature, with a particular focus on the European scenario to identify gaps related to patient safety
ii. ***Stage 2*** - the development and validation of a data collection tool to be disseminated to regulatory experts in the EU, EEA and Turkey

This phase was initiated by a comprehensive review of regulations, standards and relevant literature, to establish a foundational understanding of patient safety in the context of medical device regulatory sciences.

European regulations, Medical Devices Coordination Group (MDCG) endorsed guidance documents (*Table 2.1*), and data from fora of medical device competent authorities were reviewed to assess the European regulatory landscape that shapes compliance and safety requirements. Regulatory frameworks and processes of the United States of America (USA), the United Kingdom (UK), Switzerland, Japan, and Australia were observed, to obtain a global picture of post-market surveillance and vigilance practices. The selection of these countries was conveniently based on their well-established medical device regulatory systems and their influence on international safety standards. The review focused on the processes of their national regulatory authorities, which were obtained through the respective websites and published guidelines.

For a broader international perspective, standards from the World Health Organisation (WHO) and the International Medical Device Regulators Forum (IMDRF) were

examined. ISO standards that are directly related to conformity of medical devices, such as ISO 13485:2016 *Medical devices - Quality management systems — Requirements for regulatory purposes*, ISO 14971:2019 *Medical devices – Application of risk management to medical devices*, and ISO/IEC 17021-1:2015 *Conformity assessment — Requirements for bodies providing audit and certification of management systems - Part 1: Requirements*, were also reviewed. The relevant websites are provided in *Figure 2.2*.

Reviewed data was supplemented by information retrieved from other peer-reviewed literature. Priority was given to literature published between 2017 and 2025 to align with the most current practices, as the new EU regulations came into force in 2017. Some earlier studies were used to provide background and highlight improvements and challenges. PubMed, MEDLINE, ProQuest, Science Direct and HyDi were used as search databases. The search terms used for the literature review include: 'regulation AND patient safety', medical devices AND patient safety', 'EU AND regulation of medical devices', 'global regulation of medical devices', 'medical devices AND software regulation', 'vigilance of medical devices', 'oversight of post-market surveillance of medical devices', and 'risks of medical devices'. Only articles in the English language were considered.

This stage of phase 1 aimed to identify gaps and regulatory challenges in the evolving landscape of patient safety.

Table 2.1 MDCG Documents reviewed in Phase I

MDCG Reference	Title of Document
MDCG 2024-1	Device Specific Vigilance Guidance (DSVG) Template
MDCG 2023-3 rev.2	Questions and Answers on vigilance terms and concepts as outlined in the Regulation (EU) 2017/745 on medical devices and Regulation (EU) 2017/746
MDCG 2022-21	Guidance on Periodic Safety Update Report (PSUR) according to Regulation (EU) 2017/745
MDCG 2019-7 rev.1	Guidance on article 15 of the medical device regulation (MDR) and in vitro diagnostic device regulation (IVDR) on a 'person responsible for regulatory compliance' (PRRC)
MDCG 2019-11	Qualification and classification of software - Regulation (EU) 2017/745 and Regulation (EU) 2017/746
MDCG 2019-16 rev.1	Guidance on cybersecurity for medical devices
MDCG 2019-15 rev.1	Guidance notes for manufacturers of class I medical devices
MDCG 2020-10/1 rev.1	Guidance on safety reporting in clinical investigations
MDCG 2020-7	Guidance on PMCF plan template
MDCG 2020-8	Guidance on PMCF evaluation report template
MDCG 2020-6	Guidance on sufficient clinical evidence for legacy devices
MDCG 2020-5	Guidance on clinical evaluation – Equivalence
MDCG 2019-9 rev.1	Summary of safety and clinical performance
MDCG 2021-3	Questions and Answers on Custom-Made Devices
MDCG 2022-16	Guidance on Authorised Representatives Regulation (EU) 2017/745 and Regulation (EU) 2017/746

This table provides a list of the Medical Device Coordination Group guidance documents that were reviewed for the purpose of this study.
These documents are available from URL: https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en

Figure 2.2 Standards and Guidelines reviewed in Phase I
This figure provides websites of all relevant global data sources used in Phase I of this study.

The key areas that may present gaps in patient-centric regulatory sciences that emerged from stage 1 of this phase contributed to the development of the data collection tool in stage 2 (*Appendix II).* This tool was developed as a Google form with thirty-two close-ended questions, and its access link was disseminated via e-mail. A five-option Likert scale was used in the questions, but the respondents had the option to write comments.

The data collection tool was psychometrically validated by an expert panel consisting of two regulatory professionals with a background in vigilance and surveillance, a clinical pharmacist, a medical consultant with academic experience, and an academic professional. The experts were asked to validate tool for face validity, relevance, and clarity.

The validated tool was then disseminated to 31 competent authorities for medical devices in EU and EEA Member States, and Turkey, to gather their insights on the oversight of patient safety. A letter accompanying the e-mail with the data collection tool link provided information to the participants (*Appendix III*). Responses were received from 12 different competent authorities over a period of 14 weeks from end October 2024 to end January 2025.

2.4 Phase II – Developing the Regulatory Framework

Phase II involved two stages:

i. ***Stage 1*** - the development of a patient-centric framework
ii. ***Stage 2*** - the validation of the framework

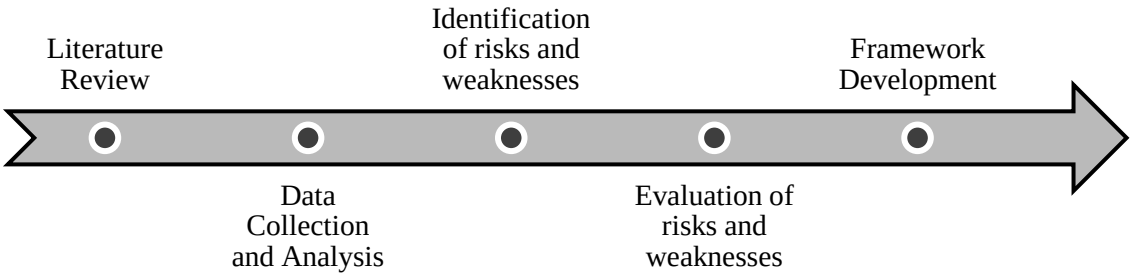

Figure 2.3 Development of the regulatory framework

The findings from Phase 1, incorporating data gathered from both Stage 1 and Stage 2, were compiled and analysed. These insights contributed to the development of a patient-centric framework - *MD-PMSV-RF01: Ensuring Patient Safety through Medical Device Regulatory Science – A Regulatory Framework for Competent Authorities* - designed to be used by regulatory bodies for the oversight of surveillance and vigilance of devices (*Addendum*).

The framework developed in Stage 1 was validated by an expert panel to verify its applicability and effectiveness in real-world regulatory settings and alignment with the current regulatory requirements. The expert panel was purposively made up of four professionals that work in the area of medical devices and pharmaceutical regulatory sciences, with particular expertise in the area of surveillance and vigilance. These experts were invited to use the evaluation form sent by e-mail to evaluate the developed framework for relevance, clarity, and adequacy of detail (*Appendix III*).

2.5 Phase III – Testing the Applicability of the Framework

Phase III involved two stages:

i. ***Stage 1*** – pilot testing of the framework on a sample of incident reports

ii. ***Stage 2*** - SWOT analysis to refine the framework

The focus of Phase 3 was on evaluating the regulatory framework *MD-PMSV-RF01* to assess its practical application in real-world scenarios. In stage 1, a sample of five incident reports was selected from the vigilance database of the Medical Devices, Pharmaceutical Collaboration and Entrepreneurship Directorate within the Malta Medicines Authority, following a convenience sampling approach. All the provided data, available documentation, and communication between stakeholders concerning the incident reports were analysed by the researcher. Details related to each incident report have been collated and documented in separate structured tables for clarity. The framework was applied to each of these five cases, to analyse its usability as a resource aid for employees in medical device regulatory sciences.

For this phase, 2 tools were developed by the researcher:

a. An *Incident Report Evaluation Template Form* (*Appendix IV*) was developed to facilitate the pilot testing of the regulatory framework by systematically assessing the incident reports. To maintain confidentiality, all identifying details including the actual names of brands and manufacturers, and internal reference codes have been replaced with 'XXX' throughout these incident reports. Any reference or batch numbers used are anonymised as well. The *Incident Report Evaluation Template* form (*Appendix IV*) was completed for each incident report to analyse all the raw data and provide a summarised version of reflections and recommendations to optimise

the framework. Reflections from the forms were further summarised and compiled in *Tables A – E (Appendix VI)*, corresponding to the 5 different incident reports. Recommendations for improving the framework were also collated in *Table 3.9.*

b. The *CASP-based Critical Appraisal Checklist for Medical Device Vigilance (Appendix V)*, which is an assessment tool for vigilance developed by the researcher as part of the regulatory framework, was used to give a risk score to each incident report. This tool was adapted from the Critical Appraisal Skills Programme (CASP) checklists[50] for case control studies and modified to incorporate a structured scoring system to enable systematic evaluation of vigilance-related concerns.

In the *CASP-based Critical Appraisal Checklist for Medical Device Vigilance*, a series of questions related to regulatory concerns and risks are given a score of 1, 2 or 3 points corresponding to *Yes*, *Can't Tell*, or *No* answers respectively. Two of the questions required different answers: one question relating to the severity impact of the incident required a score of 3 points for a *Public Health Threat*, 2 points for *Death*, and 1 point for *Deterioration of Health*; and the other question required the assessor to give a score to the probability of direct or indirect harm to the patient, with 1 point given to *Negligible* or *Low*, 2 points given to *Moderate*, and 3 points given to *Likely* or *Highly Likely*. Summing up the points at the end of the assessment provides a total score which corresponds to 1 of 3 confidence levels. A score of 57 to 72 points indicates a high confidence level with strong evidence of significant risks, and recommendation for effective regulatory action is to be taken regarding the incident report. A score of 41 to

[50] Critical Appraisal Skills Programme. CASP Checklist: For case control studies. [Internet]. 2024 [Cited 2025 May 25]. Available from URL: https://casp-uk.net/casp-tools-checklists/case-control-study-checklist/

56 points indicates a moderate confidence level with moderate evidence of some risks, and recommendation for additional monitoring is to be taken regarding the incident report. A score of 24 to 40 points indicates a low confidence level with insufficient evidence of significant risks, and recommendation for provision of additional data is to be taken regarding the incident report. This score was then inputted in the *Incident Report Evaluation Template Form (Appendix IV)* for each incident report and is also provided in *Tables A – E (Appendix VI).*

Several of the recommendations identified in this pilot-testing stage were reflected in the final version of the regulatory framework to align it better with real-world scenarios. Other recommendations will be addressed in subsequent revisions of the framework.

Following the pilot testing of the framework, a SWOT (Strengths, Weaknesses, Opportunities and Threats) analysis was conducted to assess the framework's effectiveness and identify areas for improvement.

The key internal factors that are strengths and weaknesses, and the external factors that are opportunities and threats[51], that may arise from using the developed framework in the daily activities carried out by surveillance and vigilance personnel in a competent authority were identified. This was done by initially identifying four main questions that correspond to each of the categories making up the SWOT analysis, to help the researcher scrutinise the framework and establish areas for improvement. These four questions are depicted in *Figure 2.4.*

[51] Capacity4dev. Evaluation methodological approach. Official website of the European Union [Internet]. [cited on 2025 March 25]. Available from URL: https://capacity4dev.europa.eu/groups/evaluation_guidelines/info/detailed-presentation-8_en

Relevant information that answers each question categorically was determined systematically and compiled in each respective area.

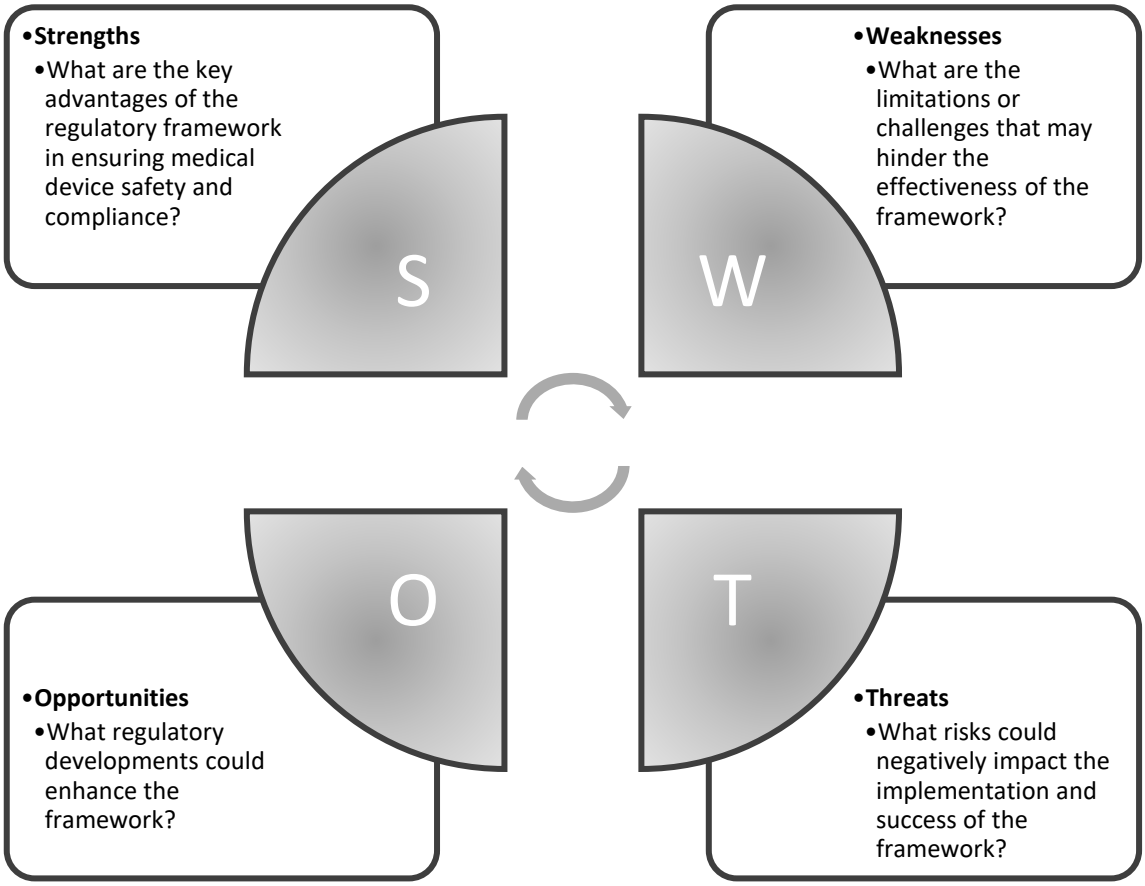

Figure 2.4 The 4 key questions leading to the SWOT analysis
These questions were used to critically assess the framework and identify areas for improvement.

CHAPTER 3

RESULTS

3.1 Phase I – Data Collection

*Table 3.*1 illustrates the 5 key domains relevant to patient-centric medical device regulatory sciences where weaknesses and challenges were identified.

Table 3.1 Five key domains emerging from the gap analysis

i.	Human resources in regulatory authorities that engage in post-market surveillance oversight and vigilance activities
ii.	Information on incident reporting
iii.	Legal requirements on legacy and custom-made devices
iv.	The recall process
v.	The integration of artificial intelligence in surveillance and vigilance regulation

These 5 key areas are addressed and systematically assessed in each of the 5 sections of the data collection tool developed in Stage 2 of Phase I.

Table 3.2 presents an overview of human resources making up the post-market surveillance and vigilance sector, as reflected in the data collection tool. It details the number of employees allocated to this regulatory area, the expertise that is considered essential for these employees, and any training needs. It distinguishes between different modes and durations of training, as offered by the competent authorities answering the data collection tool.

Table 3.2. Human resources in PMS and vigilance activities (N = 12)

Number of employees allocated for market surveillance and vigilance activities	Number of Competent Authorities
1 – 5 employees	3
6 – 10 employees	2
11 – 15 employees	2
More than 15 employees	5

Areas of Expertise considered for employees in market surveillance and vigilance	Number of Competent Authorities
Clinical Knowledge	9
Safety Surveillance	10
Risk Management	11
Product Quality Management	9
Statistical Analysis	5
Technical Knowledge	9
Engineering Knowledge	6
Legal Background / Knowledge	10

2 competent authorities listed also 'Distribution and Medical Device Use in Hospitals' and 'Pharmacological Knowledge' as additional considered areas of expertise respectively.

Investment in training of employees in market surveillance and vigilance	Number of Competent Authorities
No	4
Yes	8

Mode and Duration of Training	Number of Competent Authorities [n = 8]
In-house training only [Duration ≤8hours]	1
In-house training only [Duration >8hours]	0
External training only [Duration ≤8hours]	2
External training only [Duration >8hours]	1
In-house training + external training [Duration ≤8hours]	3
In-house training + external training [Duration >8hours]	3

- 2 of the competent authorities that provide both in-house and external training use both training timeframes.
- The competent authority that provides external training only and with a duration of more than 8 hours, stated that personnel with healthcare and industry experience and knowledge are preferably employed, but they do provide external training on subjects such as ISO 13485 and ISO 14971 standards regularly.

This table summarises collated data related to human resources capacity and expertise in the post-market surveillance and vigilance sector of competent authorities.

Table 3.3 gathers details on incident reporting obtained from the data collection tool.

Table 3.3 Vigilance data

Number of incident reports received by competent authorities monthly	Number of Competent Authorities
<100 reports	4
100 – 200 reports	3
201 – 300 reports	0
>300 reports	5

Classifying all initial incident reports received by the competent authority	Number of Competent Authorities
No	4
Yes	8

Classification types	Number of Competent Authorities [n = 8]
Categorising reports in 3 risk levels: low, medium and high	6
Categorising reports in 4 risk levels: low, medium, high and trend	1
Categorising reports in 2 risk levels: low and high	1

- 1 competent authority not classifying initial incident reports stated that according to their national legislation, a serious incident must first be notified to the manufacturer or the authorised representative, and then a copy of the notification would be forwarded to the competent authority.
- 1 competent authority not classifying initial incident reports stated that they focus on the final reports and pick up any important early signals from the reports of the healthcare professionals.

Actions taken by competent authorities for non-serious incident reports	Number of Competent Authorities
Close and archive reports	1
Categorise and document reports	2
Categorise reports and analyse for trends	2
Close and archive reports + Categorise reports and analyse for trends	1
Categorise and document reports + Categorise reports and analyse for trends	2

Other actions considered by the remaining 4 competent authorities:
- Referring all suspected serious adverse events to the manufacturers
- Forwarding to the manufacturers requesting the MIR or an explanatory statement in due time
- Contacting the manufacturers and requesting an analysis of reportability
- Non-serious incident reports are only documented, but not categorised

This table summarises collated vigilance data related to incident reports received by the competent authorities.

The most common reasons that could be listed in incident reports, adapted from the literature and guidance documents reviewed in Stage 1 of Phase I, were provided to the competent authorities. The respondents were asked to reflect on the frequency of occurrence of each given reason in the incident reports received and rate their response on a 5-Likert scale [Very uncommon, Uncommon, Neutral, Common, and Very Common] (*Figure 3.1).*

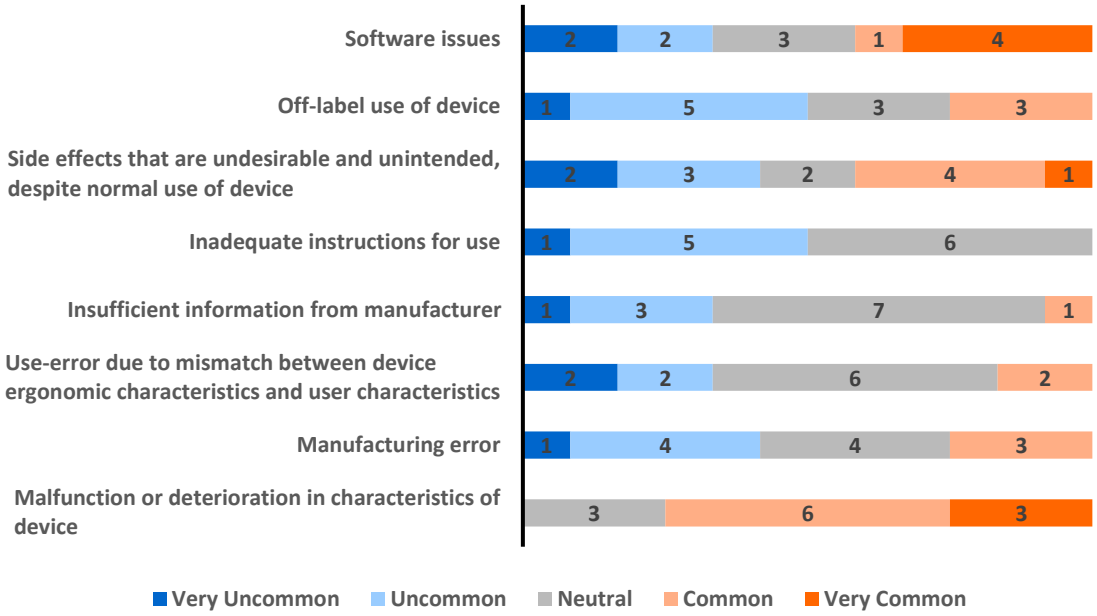

Figure 3.1 Common reasons listed in incident reports

This chart illustrates the frequency of occurrence of the most common reasons listed in incident reports received by the competent authorities. The number of respondents is provided numerically within the bar segments.

The most common reasons in incident reports were software issues [Very common = 4, Common = 1], malfunction or deterioration in the characteristics of the device [Very common = 3, Common = 6], and any undesirable and unintended side effects that may still occur despite the normal use of the device [Very common = 1, Common = 4].

Table 3.4 examines the legal requirements of legacy devices and custom-made devices.

Table 3.4 Legal exceptions for legacy and custom-made devices

Legal provisions of Legacy Devices		Expert Position	Number of Competent Authorities
No requirement for full revision of technical documentation in accordance with Annex II and Annex III of the MDR / no requirement for a performance evaluation report as requested by the IVDR for legacy devices could impact patient safety and increase incidence occurrence.		Strongly Disagree	0
		Disagree	1
		Neutral	7
		Agree	4
		Strongly Agree	0
A Person Responsible for Regulatory Compliance (PRRC) should become a requirement for the oversight of post-market surveillance of legacy devices, as for other medical devices.		Strongly Disagree	0
		Disagree	1
		Neutral	4
		Agree	7
		Strongly Agree	0
Notified bodies need to be stricter in their enforcement of post-market surveillance processes for legacy devices to comply with the requirements of the MDR and IVDR.		Strongly Disagree	0
		Disagree	0
		Neutral	6
		Agree	3
		Strongly Agree	3
Legal provisions of Custom-made Devices		**Expert Position**	**Number of Competent Authorities**
Applying post-market surveillance plans to each individual custom-made device rather than to a group of similar devices could impact patient safety:			
	It would be an unnecessary burden	Strongly Disagree	0
		Disagree	0
		Neutral	4
		Agree	8
		Strongly Agree	0
	It would have no increased influence on patient safety	Strongly Disagree	0
		Disagree	5
		Neutral	3
		Agree	4
		Strongly Agree	0
	It would increase the safety of the device	Strongly Disagree	0
		Disagree	4
		Neutral	4
		Agree	3
		Strongly Agree	1
The PSUR of Class IIa/IIb Implantable and Class III custom-made devices should be uploaded to EUDAMED as a tool in the evaluation of changes to the benefit-risk profile of the custom-made device, as for other devices.		Strongly Disagree	0
		Disagree	1
		Neutral	3
		Agree	7
		Strongly Agree	1

This table illustrates the experts' position regarding legal exceptions with legacy and custom-made devices.

Table 3.5 presents the experts' position on key activities undertaken by competent authorities in assessing compliance of manufacturers with PMS requirements and captures experts' opinion on the need for further training for economic operators.

Table 3.5 Expert position on legal requirements

Activities carried out by competent authorities to assess compliance of manufacturers to post-market surveillance requirements:		Expert Position	Number of Competent Authorities
	Comparing device with state of the art	Never	2
		Rarely	4
		Sometimes	4
		Often	2
		Always	0
	Performing clinical evaluation at sub-contracted laboratories	Never	6
		Rarely	6
		Sometimes	0
		Often	0
		Always	0
	Performing clinical evaluation at in-house laboratories	Never	7
		Rarely	5
		Sometimes	0
		Often	0
		Always	0
	Evaluating published literature applicable to the class of device	Never	0
		Rarely	8
		Sometimes	4
		Often	0
		Always	0
	Assessing technical documentation of the device	Never	0
		Rarely	3
		Sometimes	7
		Often	2
		Always	0
Medical devices have a relatively short life cycle, and can be modified from one production to another, making literature review for post-market surveillance purposes unreliable.		Strongly Disagree	0
		Disagree	1
		Neutral	6
		Agree	4
		Strongly Agree	1
Importers and Distributors need more education and training on post-market surveillance activities and on their expanded responsibilities following implementation of the new EU Regulations.		Strongly Disagree	0
		Disagree	0
		Neutral	0
		Agree	6
		Strongly Agree	6

This table shows the experts' position regarding issues on post-market surveillance requirements in the MDR and the IVDR.

The data collection tool explored issues that may be encountered if one of the Field Safety Corrective Actions (FSCA) to be taken by the manufacturer is a recall of the device.

Eight of the competent authorities stated that they have encountered situations where a manufacturer or authorised representative failed or refused to voluntarily recall a medical device that may have posed a risk to patient health. The researcher asked the competent authorities about their next plan of action should this refusal occur *(Figure 3.2).*

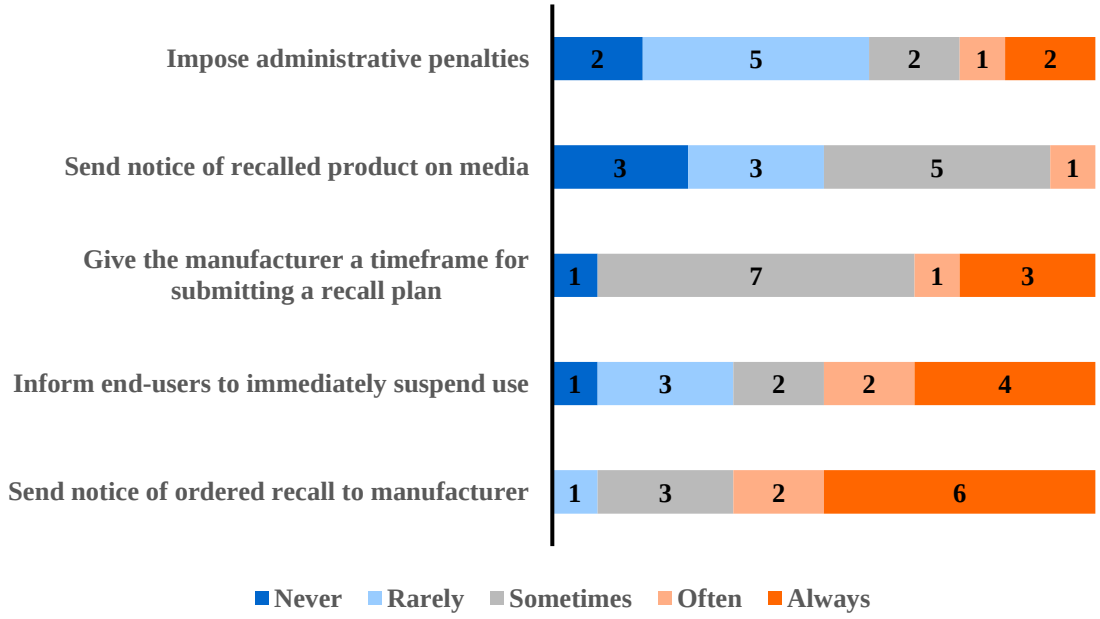

Figure 3.2 Action plans following refusal of a voluntary recall

This figure depicts the actions implemented by competent authorities following the refusal of a recall by a manufacturer. The most consistently-applied actions were sending a notice of mandatory recall to the manufacturer [Often = 2; Always = 6], and informing the end-users to suspend use of the device [Often = 2; Always = 4].

Eleven of the competent authorities agree that the manufacturer should have the right to appeal against the authority's mandatory decision on a device recall, with 2 of these respondents strongly agreeing to the right to appeal. Only 1 competent authority indicated a neutral stance. The respondents were then given a set of statements about the appeals'

procedure with a 5-point Likert scale *(Figure 3.3)*. All the competent authorities agree that an appeals' procedure should be submitted to the authority [Agree = 10, Strongly Agree = 2], and that the end-user should always be informed of any risk [Agree = 6, Strongly Agree = 6].

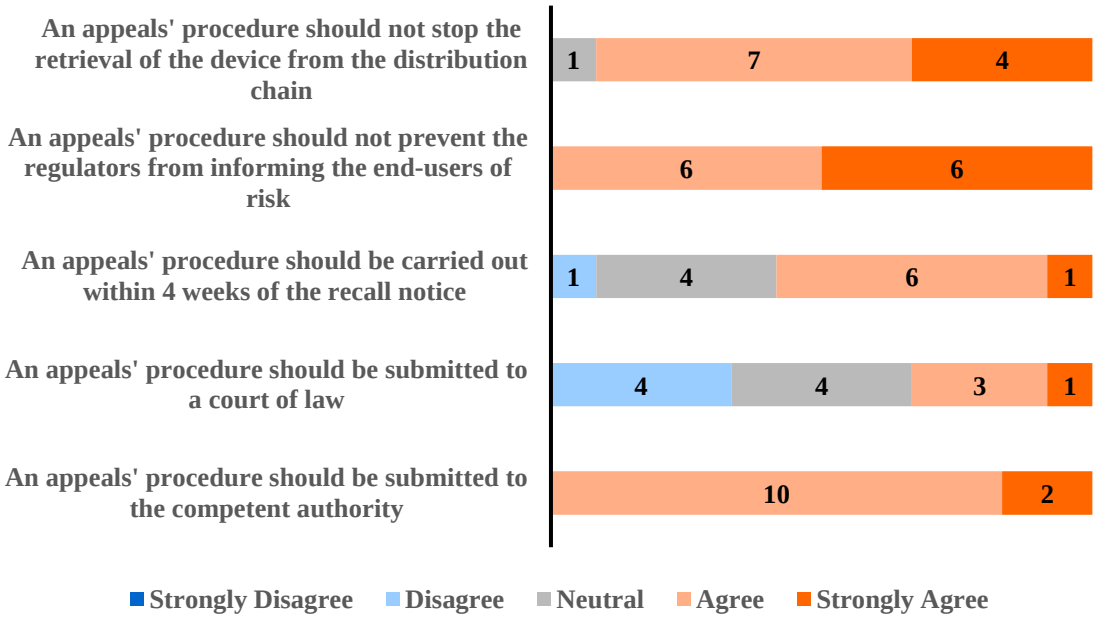

Figure 3.3 Appeals' procedure

The figure illustrates possible procedural actions within an appeals' procedure. Eleven respondents agreed that an appeal against a mandatory recall from the manufacturer should not stop the recall of the device from the distribution chain. There is an even split among the competent authorities, with 4 agreeing and 4 disagreeing to the manufacturer submitting an appeals' procedure to a court of law. Seven competent authorities agreed that an appeal should be carried out within 4 weeks of the recall notice.

Disadvantages of product recalls that were identified from literature review and global guidance documents in Stage 1 of Phase I, were provided to the competent authorities, for them to give a score on the 5-point Likert scale from 'Strongly Disagree' to 'Strongly Agree' *(Figure 3.4)*.

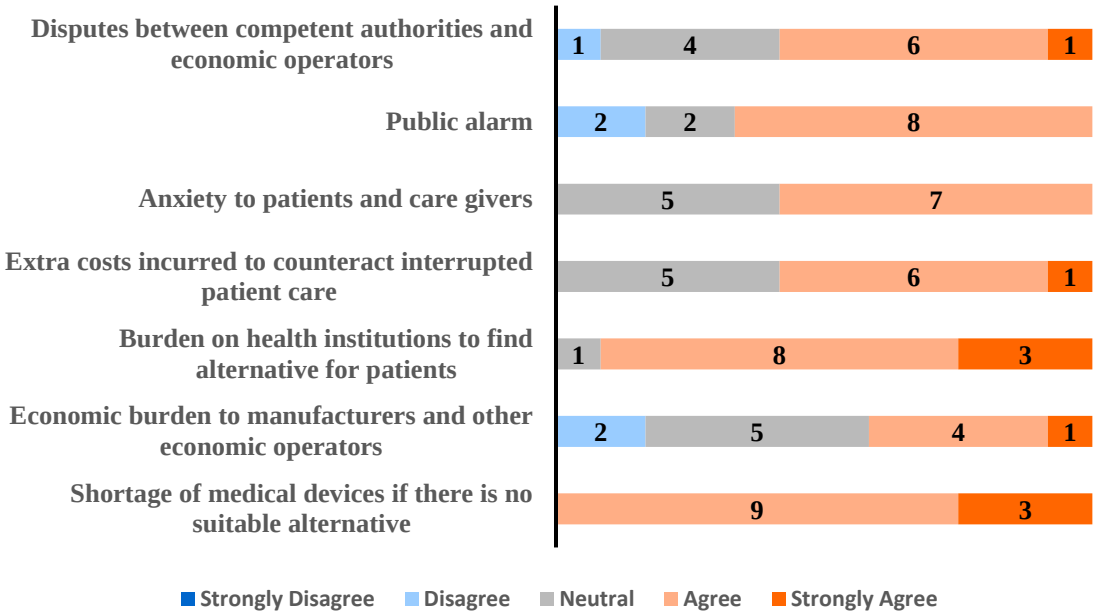

Figure 3.4 Disadvantages of device recalls

The disadvantage that was chosen unanimously by all the respondents (N = 12) was related to shortage of medical devices [Agree = 9; Strongly Agree = 3], followed with 11 responses favouring the burden on health institutions to come up with alternative solutions [Agree = 8; Strongly Agree = 3]. The response least considered as a disadvantage by the competent authorities was the fact that recalls could cause an economic burden to economic operators [Agree = 5; Strongly Agree = 1].

Table 3.6 illustrates the information provided by the respondents regarding procedures for recalls that may lead to procurement issues, and the timeframes for keeping Field Safety Notices publicly available for patient safety.

Table 3.6 Data on recall procedures and FSN timelines

Statement provided by researcher	Expert Position	Number of Competent Authorities
Access to suitable alternatives should be first identified before considering a recall that might affect procurement for health institutions, especially those supplied through the National Health System.	Strongly Disagree	0
	Disagree	3
	Neutral	2
	Agree	7
	Strongly Agree	0

Timeframe for keeping Field Safety Notices (FSN) publicly available on the website of the competent authority		Number of Competent Authorities		
	Up to 6 months	0		
	6 months – 1 year	0		
	1 year – 5 years	3		
	More than 5 years	5		
	Other opinions	4	Details of other opinions	Number of Competent Authorities [n = 4]
			FSN available indefinitely	2
			Timeframe not determined	1
			Currently FSNs are not uploaded on the authority's website	1

This table provides the expert position on the need to identify suitable alternatives prior to a recall, with 7 competent authorities in agreement. It also provides the timeframes for keeping FSNs publicly available, with 4 of the competent authorities giving different positions than those provided by the researcher.

When asked on how often the manufacturer is expected to send status reports to the competent authority for assessing the progress of a recall process, 3 of the respondents stated that they expect a report at least every 1 to 2 weeks. The other 9 respondents did not choose a timeframe set by the researcher, but provided their own comments:

a. The timeframe depends on the type of problem with the medical device.
b. A report is expected monthly.
c. The manufacturer should submit status reports at intervals agreed and accepted by the competent authority.

   This depends on the severity of the case.
d. The timeframe depends on the risk determined by the competent authority involved.
e. There is no fixed interval, and the timeframe depends on a case-by-case basis.
f. The timeframe is not determined.
g. The timeframe is decided from case to case depending on the severity of the FSCA.
h. Status reports are not asked for routinely.
i. The frequency of follow-up reports is decided by the manufacturer.

Table 3.7 investigates the opinion of competent authorities on the implementation of Artificial Intelligence (AI) in surveillance and vigilance oversight activities.

Table 3.7 Implementation of AI in surveillance and vigilance

Statement provided by researcher	Expert Position	Number of Competent Authorities
Implementing AI can complete time-consuming surveillance tasks much more rapidly and without the risk of human error.	Strongly Disagree	0
	Disagree	4
	Neutral	3
	Agree	5
	Strongly Agree	0
In the foreseeable future, AI software could provide more opportunities than challenges in medical device regulatory science.	Strongly Disagree	0
	Disagree	1
	Neutral	7
	Agree	4
	Strongly Agree	0
AI can be used for trend analysis, to detect any signal occurrence that exceeds set thresholds and to generate reports from real-world data without having to rely solely on manufacturers' reports.	Strongly Disagree	0
	Disagree	2
	Neutral	2
	Agree	8
	Strongly Agree	0
The competent authority is integrating AI tools in processes of signal detection and evaluation of post-market surveillance data.	Yes	2
	No	6
	Other	4
	The 4 competent authorities that chose 'Other' as option, provided further comments: - Not yet, but we would like to integrate AI tools - In the development of our new internal vigilance system, we are exploring the implementation of AI options - It is planned in the long-term - We are currently working on a new system that would integrate AI tools	
The competent authority is receiving, or planning to receive, government funding to aid in the implementation of AI in the oversight of patient safety.	Yes	1
	No	8
	Other	3
	The 3 competent authorities that chose 'Other' as option, provided further comments: - Not yet, but we would like to receive government funding - Not yet, but we are planning to receive government funding - We are thinking of how to implement AI in vigilance and medical device surveillance, but government funding for it is still unknown	

This table provides the experts' opinion on a set of statements provided by the researcher on the implementation of AI in post-market surveillance and vigilance processes.

3.2 Phase II – The Regulatory Framework

Phase II consisted of 2 sequential stages: the development of a regulatory framework and the subsequent pilot testing of the framework to evaluate its feasibility and applicability in a real-world regulatory context.

The different sections of the framework *Ensuring Patient Safety through Medical Device Regulatory Science - A Regulatory Framework for Competent Authorities [MD-PMSV-RF01]* are defined in *Table 3.8. MD-PMSV-RF01* outlines a comprehensive structure to support competent authorities in the oversight of post-market surveillance and vigilance activities for medical devices. It includes detailed guidance on the roles and responsibilities of key stakeholders, namely manufacturers, authorised representatives, importers, distributors and notified bodies. The framework also addresses the oversight of post-market surveillance of specific device categories. With regard to vigilance, *MD-PMSV-RF01* covers processes related to incident reporting, recalls, trend analysis and risk management. The developed *CASP-based Critical Appraisal Checklist for Medical Device Vigilance* tool (*Appendix V*) is introduced. Additionally, the framework integrates AI regulatory requirements in post-market surveillance and vigilance. Training modules on post-market surveillance and vigilance for regulatory personnel, end-users of medical devices, and local economic operators are proposed. *MD-PMSV-RF01* is supported by references to applicable EU and global regulations and guidelines, intended to support regulatory personnel in efficiently locating and applying relevant requirements.

Table 3.8. The Regulatory Framework

Ensuring Patient Safety through Medical Device Regulatory Science A Regulatory Framework for Competent Authorities MD-PMSV-RF01		
Aims		
Scope		
Definitions		
Abbreviations		
Roles and Responsibilities of Stakeholders for Post-Market Surveillance and Vigilance Activities	Manufacturers	
	Authorised Representatives	
	Importers	
	Distributors	
	Notified Bodies	
Oversight of PMS Activities by the Competent Authority	Substandard and Falsified Medical Devices	
	Custom-Made Devices	
	Legacy Devices	
Vigilance	Incident Reporting	Receiving a Medical Devices Incident Form
		Receiving a Manufacturer Incident Report
	The Recall Process	Voluntary Recall by the Manufacturer
		Mandatory Recall by the Competent Authority
	Monitoring Trends	Trend Analysis Strategy for Competent Authorities
	Risk Analysis and Risk Management	The Risk Matrix
	CASP Tool for Vigilance Skills	
Integrating AI into Medical Device Regulatory Sciences	The AI Act and Post-Market Monitoring	
	Implementing AI in PMS Oversight and Vigilance	
Training Modules on PMS and Vigilance	Training for the Regulatory Personnel	
	Training for the Healthcare Professionals and other End-users	
	Training for the Local Economic Operators	
References	EU Regulations on devices	
	EU Regulation on AI	
	IMDRF Guidelines	
	WHO Guidelines for PMS	
	WHO Guidelines for AI	
	MDCG Guidance Documents	
	ISO Standards	
Appendix A	IMDRF Adverse Event Terminology	

3.3 Phase III – Testing the Developed Framework *MD-PMSV-RF01*

Phase III comprised 2 stages: the pilot testing of the developed framework using 5 incident reports to assess its practical applicability, followed by a SWOT analysis to evaluate its strengths, weaknesses, opportunities, and threats in the context of regulatory implementation.

The risk scores emerging from the *CASP-based Critical Appraisal Checklist for Medical Device Vigilance* tool (*Appendix V*) for incident reports 1, 3, 4, and 5 (*Tables A, C, D, and E* in *Appendix VI*) were in the range of 57 – 72 points, indicating strong evidence that effective regulatory action is needed. Incident report 2 (*Table B*) obtained a score in the range of 41 – 56 points, indicating with moderate evidence the need of additional monitoring.

Reflections (*Tables A-E in Appendix VI*) from the pilot testing of the developed framework *MD-PMSV-RF01* outlined gaps in stakeholder compliance with the regulatory obligations, and lack of communication from the notified body. Deficiencies in reporting were observed, including lack of detail in the incident reports received by the healthcare professionals and by the manufacturers. Oversight by the competent authority was proactive, involving documentation requests, stakeholder engagement, consultations with the advisory committee and verification of corrective actions. Differences in risk assessment were observed between the competent authorities and the economic operators. The integration of AI was identified as a promising avenue to enhance incident tracking,

stakeholder communication, and patient engagement. Training needs were emphasised, especially for adequate incident reporting.

Recommendations for improvement of the developed framework *MD-PMSV-RF01* were suggested in every *Incident Report Evaluation Template* form. These are indicated in *Table 3.9.* The recommendations relate to three key areas: risk assessment, training and feedback mechanisms, and data validation in reporting. The recommendations related to risk classification have already been incorporated in version 01 of *MD-PMSV-RF01*. Recommendations for feedback during training were suggested in version 01 of *MD-PMSV-RF01,* to be adopted in upcoming training sessions. Recommendations related to the integration of validation steps in online reporting were not implemented with the current version of the framework, as they require additional digital infrastructure.

Table 3.9 Recommendations for improving the developed framework

Training module for healthcare professionals and end-users could have a qualitative feedback tool such as a 'training satisfaction survey'.	Suggested in Incident Reports 1 and 3
	It is suggested in version 01 of MD-PMSV-RF01
	Qualitative feedback tool to be developed for future training sessions
The framework could incorporate a training module for economic operators on regulatory responsibilities.	Suggested In Incident Report 4
	This is integrated in version 01 of MD-PMSV-RF01
The framework could incorporate a structured format such as a standard operating procedure for risk assessment with diagram for justifying risk classification and conflict resolution when there is disagreement or misalignment between the manufacturer and the competent authority.	Suggested in Incident Reports 2, 3, 4 and 5
	Incorporated in the risk management responsibilities of the competent authority in MD-PMSV-RF01
A validation step could be integrated in the online incident report form at the stage of data submission to check for completeness and flag any incomplete sections.	Suggested in Incident Reports 3 and 5
	Not yet integrated in version 01 of MD-PMSV-RF01 To be suggested for digital implementation

Pilot-testing the developed regulatory framework MD-PMSV-RF01 on the 5 incident reports resulted in recommendations to enhance the framework's applicability.

The pilot testing of the developed framework *MD-PMSV-RF01* was followed by the SWOT analysis. The 4 key questions of the SWOT analysis generated relevant insights corresponding to the 4 different categories.

The key findings of the SWOT analysis are summarised in *Figure 3.5*, presenting the main strengths, weaknesses, opportunities and threats. A more detailed analysis, including supporting observations for each category, is provided in *Appendix VII.*

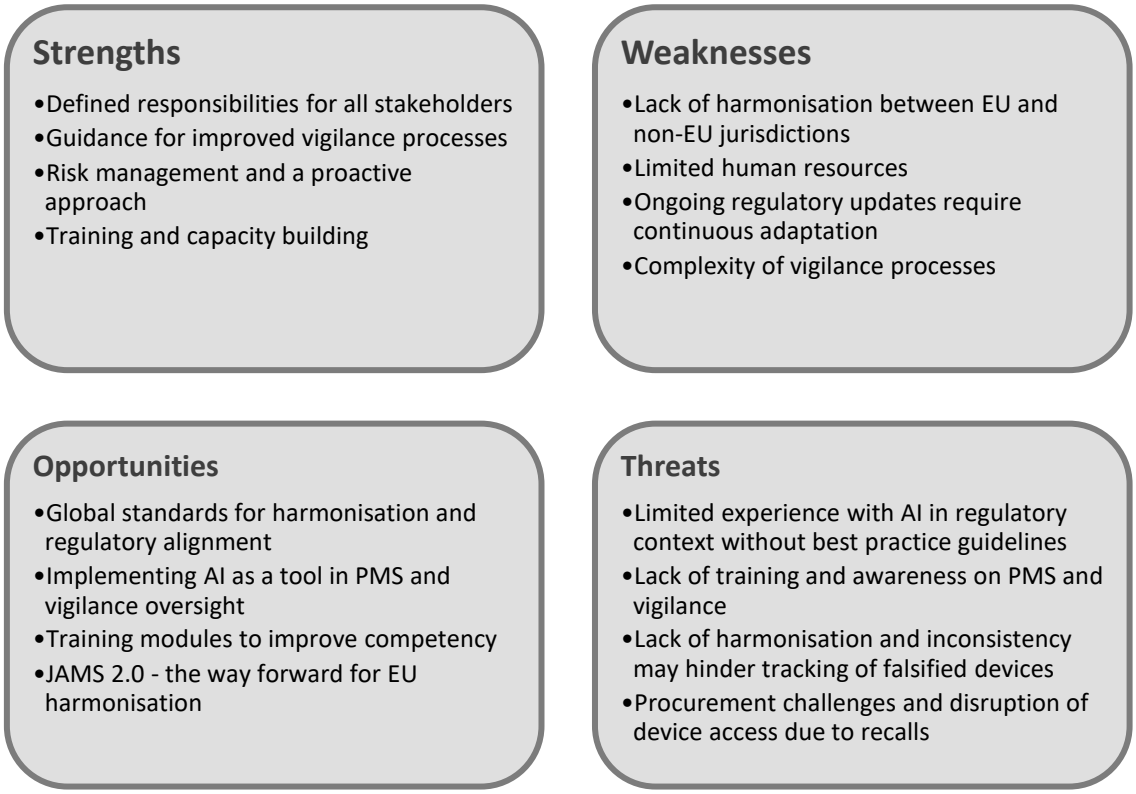

Figure 3.5 The key findings of the SWOT analysis

CHAPTER 4

DISCUSSION

The research attempted to identify weaknesses in the field of medical device regulatory science, with particular emphasis on the evolving EU regulatory landscape under the MDR and the IVDR. The research focused on key implementation challenges surrounding post-market surveillance (PMS) and vigilance, whilst exploring how other jurisdictions, mainly the USA, UK, Japan, Australia and Switzerland, structure their post-market regulatory systems in order to adopt best practices. In response to these gaps, the research developed a strategic framework aimed at enhancing regulatory evaluation and addressing real-world challenges such as legacy devices oversight, regulatory resource responsibilities, and under-reporting of adverse events.

4.1 Moving Towards a Stronger Post-Market Surveillance

Medical devices industry stakeholders and EU experts on medical devices working groups often reflect on the challenge that the older directives 93/42/EEC (MDD), 90/385/EEC (AIMDD) and 98/79/EC (IVDD) focused more on the pre-market conformity assessments rather than post-market surveillance requirements, in relation to the current EU regulations. Manufacturers had wide discretion over how post-market data was collected and analysed, with no mention of PMS plans or periodic updates or systematic data collection. A post-market clinical follow-up was only done if the manufacturer decided that it was necessary. When stricter regulations were being proposed in the EU, the European Commission Staff Working Document[52] in 2012 had

[52] European Commission. Commission Staff Working Document: Impact Assessment on the Revision of the Regulatory Framework for Medical Devices. [Internet]. Brussels. 2012 [cited 2025 April 13]. Available from URL: https://eur-lex.europa.eu/resource.html?uri=cellar:487acc33-213b-4fdf-bdbb-8840209a8807.0001.04/DOC_1&format=PDF

suggested that the PMS system was not proactive and it was not strong enough to ensure that medical devices were being investigated for non-compliances after they were placed on the market. The manufacturers' obligations for vigilance were also not clearly stated. Harmonisation between different competent authorities from different Member States seemed to be lacking, because a device that was recalled or withdrawn in one Member State did not necessarily indicate that the device was not still on the market in others, due to Member States reacting differently to the same incident reports. In an attempt towards stricter harmonised legal requirements, the new regulations (EU)2017/745 MDR and (EU) 2017/746 IVDR provide a strong focus on the pre-market assessment and a more robust framework for post-market surveillance and vigilance, shifting from concentrating mainly on market entry to continuous oversight throughout the lifecycle of the device. PMS has become increasingly critical because pre-market clinical investigations and performance studies cannot capture long-term diverse patient outcomes. There is a global trend towards strengthening PMS, contributing to a broader harmonisation effort. The FDA has a robust PMS system, and the PMDA of Japan is currently giving more importance to PMS and vigilance activities by expanding requirements. Australia and Switzerland have similar PMS requirements compared to the current EU requirements, while the UK is expecting an intensified reform in PMS later on this year. This global perspective enables a greater definition of harmonisation and attempts at providing a basis for common regulatory structures rather than silo systems. The WHO also highlights the importance of having a robust PMS system to ensure the ongoing compliance of medical devices with safety, quality and performance requirements after they are placed on the market[53]. The International Organization for Standardization published ISO/Technical

[53] World Health Organization. Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics. 2020. [Cited 2025 April 13]. Available from URL: https://www.who.int/publications/i/item/9789240015319

Report (TR) 20416:2020 in 2020 to serve as a guide for manufacturers to strengthen their PMS systems.

4.2 Addressing challenges in Regulatory Implementation

Determining the importance of post-market surveillance is not enough. Competent authorities and other stakeholders are often struggling with the allocation of more human resources to address implementation challenges, a factor often reflected upon during networking discussions at EU medical devices working group meetings. Competent authorities are realising the importance of PMS and vigilance in ongoing device safety, and this has led to the allocation of human resources to address these areas in medical device regulation. From the data collection tool of Phase I, it was determined that these personnel are expected to have a wide spectrum of expertise, ranging from risk management knowledge to technical and clinical knowledge with a legal background. To further reinforce this expertise, the majority of competent authorities invest in training their employees. It is of note to reflect that one of the work packages pertaining to the Joint Action on Market Surveillance (JAMS 2.0), of which Malta is a co-task leader, focuses on building and reinforcing expertise within competent authorities within the EU, assisting these experts to keep abreast with innovations within the medical device industry whilst learning to discuss and enhance communication. Building on this initiative and extending its scope, the developed framework of this research proposes training strategies for regulatory employees to strengthen PMS and vigilance practices under the MDR and IVDR, taking into consideration global standards such as ISO 13485 and ISO 14971. Ongoing training is crucial for competent authorities to remain updated on best practices

and new requirements in a constantly evolving regulatory landscape. Training addresses any potential skill gaps to help in more efficient implementation of PMS oversight systems. Although the competent authority may opt for training to be delivered by an external organisation for certain programs such as those including ISO standards, external training for all regulatory processes may be an expensive and time-consuming option. To avoid overwhelming already-busy workloads, some training modules that could be delivered in-house may be carried out in regular but short sessions that may be incorporated into the daily schedules without too much disruption.

Human resource challenges emerged for economic operators as well, under the more demanding requirements of the new regulations. This is a persistent issue often put forward through discussions with local and international stakeholders. Training is required to cover regulatory affairs, quality assurance, clinical evaluation and data analysis. As per Article 15 of the MDR and the IVDR, manufacturers need at least one Person Responsible for Regulatory Compliance (PRRC) with expertise in the field of devices. Global standards such as ISO 13485 need to be implemented in the QMS. Personnel with expertise for clinical post-market follow-up are not easy to find. Distributors are no longer passive players but have significantly expanded roles and explicit regulatory obligations for PMS that are detailed in framework *MD-PMSV-RF01*. One possible root cause for Incident Report No.5 (*AppendixVI*) used in the pilot testing of the framework could be sub-optimal transport and storage conditions of the device on behalf of the local distributor – an example of how distribution practices can impact device safety and contribute to post-market issues. The competent authorities answering the data collection tool of Phase I unanimously agreed that importers and distributors need more education and training on PMS activities and responsibilities under the new

regulations. On the local scene, the majority of stakeholders are importers and distributors, with very few manufacturers. Consequently, key learning points for the training of local economic operators in *MD-PMSV-RF01* concentrate more on the responsibilities of distributors and importers. Considering that most economic operators for devices are small and medium size enterprises (Bretthauer et al, 2023), the complexity of the MDR and IVDR requirements may be discouraging and too costly for these smaller organisations. Since EUDAMED is not yet fully operational, economic operators have to report PMS and vigilance data to different competent authorities, who themselves use different interfaces and different national procedures. This is a time-consuming process that increases the burden of documentation for all stakeholders. Providing short training sessions for economic operators can be beneficial in mitigating these challenges.

Vigilance is an area that poses challenges to any competent authority. Large amounts of incident reports are received on a regular basis, many of which result incomplete or of variable quality, creating logistical and analytical issues. Incident reports require initial triage, risk assessment, and follow-up, increasing the work burden on regulatory resources. Having a centralised competent authority such as the FDA in the US, the PMDA in Japan, and the TGA in Australia, may enable faster aggregation and analysis of incident reports with standardised prioritisation criteria, and support of coordinated field safety corrective actions from the manufacturer. Post-Brexit, the UK is also working on strengthening a fully centralised body for signal detection, integration of PMS and recall processes. In the absence of a centralised authority for medical devices in the EU, vigilance is fragmented, and there is usually duplication of work and efforts between national competent authorities, leading to slower trend detection. The EU initiative Joint Action on Market Surveillance (JAMS 2.0) is serving as a temporary bridge to address

these fragmentation gaps and prepare the competent authorities for full integration with EUDAMED's vigilance module once this is fully functional. The program, within Work Package 5 led by Malta, is the collaborative solution of EU Member States to harmonise timely vigilance and improve transparency. As JAMS 2.0 progresses, any conclusive outcomes and recommendations are expected to be published in 2026, which may further inform vigilance practices across Member States. Malta is a proactive advocate in current undergoing discussions to take signal detection within medical devices vigilance as a continued project beyond 2026. Having a centralised vigilance system increases the chances of a quicker response to a detected signal (Sorenson et al, 2014). Similar to the European Medicines Agency (EMA) for medicines, a centralised authority for devices would streamline vigilance and regulatory oversight. To still involve some degree of national autonomy, Member States could be involved in evaluation processes to give their opinion in expert committees, as they do for medicines in the Committee for Medicinal Products for Human Use (CHMP) within EMA. Medical devices are more diverse than medicines, usually involving complex technologies, and this diversity would require a tailored complicated approach to harmonisation which would necessitate significant investment. Since national competent authorities have been working with their own established vigilance systems, implementing a centralised vigilance framework at this point could be challenging because there may be reluctance from some Member States to disrupt their current working processes and integrate them into one process. Collaborative efforts between all Member States could be instrumental in implementing a centralised medical device vigilance system by leveraging EMA's experience rather than reinventing the wheel.

The regulatory framework *MD-PMSV-RF01* aims to include risk prioritisation and trend analysis strategies. It provides structured details on the regulatory processes to be undertaken when an incident report is received from an economic operator or from the end-user. It also focuses on the possible scenarios of voluntary and mandatory recalls, and provides a step-wise approach in each circumstance. Its priorities are aligned with the priorities of JAMS 2.0 and EUDAMED for harmonisation. The *CASP-Based Critical Appraisal Checklist for Medical Device Vigilance*, which was adapted by the researcher from a CASP tool for research evidence appraisal, aims to ensure consistency in review of different incident reports and reduce interpretation subjectivity. The CASP tool converts qualitative information obtained from incident reports to quantitative scores that reflect the risk involved and the required depth of regulatory concern. The relevant personnel need to critically assess the provided data. This could be viewed as a limitation to the usage of the tool because users require initial training to ensure familiarity. Training on use of the CASP tool was one of the key learning points in the training module for regulatory personnel proposed in *MD-PMSV-RF01*. Correct usage of this tool depends on the quality of the incident reports received, because if there are several "Can't tell" responses, this could cause bias in the final score. The SWOT analysis in Phase III of the study provided a mitigation solution to this limitation, where reports that have many "Can't tell" responses can be flagged for further data collection before being assessed and assigned a CASP score.

While competent authorities face the daunting challenge of processing vast quantities of vigilance data, a seemingly contradictory issue persists – the under-reporting of adverse events by healthcare professionals, especially with Class I medical devices (Guarnieri et al, 2024). This could be due to several factors such as lack of awareness, time constraints,

uncertainty about the causality relationship between the adverse event and the device, or perception that the incident may not be severe enough to warrant a report (Craig et al, 2019; Kavanagh et al, 2019). Under-reporting from healthcare professionals could lead to a paradoxical situation where the competent authorities are overloaded with data from incident reports, and yet could be missing critical safety signals from adverse events that are not reported. To address this issue, *MD-PMSV-RF01* proposes a training module for healthcare professionals and other end-users, targeting vigilance training and increasing awareness on the necessity of incident reporting to increase patient safety.

Another challenge remains the issue of extending the transition period for legacy devices. This provides some benefits for economic operators and notified bodies, but comes at a risk of having stakeholders who delay the regularisation process. This period provides time for manufacturers to continue selling their devices while upgrading technical documentation, conducting clinical evaluations, and working with notified bodies to meet the new MDR and IVDR requirements. This is beneficial to patients and end-users because it prevents disruptions in the supply of devices, especially critical ones, while the transition is underway. It also eases the bottleneck for notified bodies, allowing more time for conformity assessments under the new regulations. The transition period can create oversight confusion for stakeholders across the board. This can happen because legacy devices are exempt from some MDR/IVDR requirements, but must still comply with some other requirements such as those for post-market surveillance and vigilance. SMEs may still find it challenging to carry out MDR recertification by the end of the transition period. Being small enterprises, they may have limited access to already-overwhelmed notified bodies when compared to large manufacturers with established relationships. If in-house regulatory personnel are not available, outsourcing might be

too costly. Upgrading the technical documentation comes also with high costs. The cost-benefit ratio of low-profit legacy devices would be unfavourable, and this might lead them to abandon the market (Maresova et al, 2021). The biggest challenge to end-users will be market shortages, especially for certain niche devices that are in low demand thus lacking commercial appeal, but are vital for specific patient populations. This is further exacerbated because the MDR and the IVDR apply a uniform level of scrutiny for all devices from large manufacturers to SMEs. Legacy devices do not need a full revision of the technical documentation like MDR-conforming devices. Only four of the respondents in the data collection tool agreed that such legal exceptions for legacy devices throughout the transition period could impact patient safety and increase incidence occurrence. This could suggest that legacy devices may be viewed as sufficiently proven and low-risk as long as they continue to meet MDD/AIMDD/IVDD requirements until the transition period is over. Legacy devices without updated clinical and technical data could lead to theoretical gaps in ensuring patient safety, but these gaps could be compensated for by subjecting these devices to the MDR/IVDR's stricter vigilance and PMS requirements. Half of the respondents participating in Phase I data collection agreed that notified bodies should follow stricter strategies in enforcing post-marketing surveillance processes for legacy devices, with the other half of the respondents taking a neutral stance. Only one of the respondents considers that performing literature review of similar devices for post-market surveillance purposes may be unreliable due to the short life cycle of medical devices and the possibility of modification from one production to another. This indicates that competent authorities recognise the complexity of balancing safety with regulatory burden in an already strained system. Access continuity is a priority especially for legacy devices that have demonstrated a history of safe use. Comparing this to the upward trend in incident reporting and number of recalls, this may

prompt a concern that some notified bodies may not be yet equipped to meet the demands of the evolving regulations. Seven of the twelve respondents of the data collection tool think that a Person Responsible for Regulatory Compliance (PRRC) should oversee PMS activities of legacy devices, consistent with the approach for other devices. Reasons for this could include ensuring compliance with vigilance and PMS obligations, and improving vigilance quality through consistent incident reporting, trend analysis and FSCA evaluations. All requirements for legacy devices during the transition period are listed in *MD-PMSV-RF01* to facilitate rapid verification by regulatory personnel.

On another front, custom-made devices open up new possibilities to treat complex medical conditions that were previously difficult to manage with conventional devices. These devices are usually unique and innovative, but the new EU regulations, though necessary to sustain patient safety and to ensure risks are not overlooked (Boyle et al, 2024), may be too inhibitive and time-consuming, thus limiting care options (Willemsen et al, 2019). Navigating through the gap of the interface between what new technologies could achieve in terms of personalised patient care through the use of innovative techniques and what the regulatory systems determine as safe, can be confusing and expensive (de Jong et al, 2023). This could lead to choices falling on conventional treatment rather than custom-made devices. The majority of competent authorities answering the data collection tool agreed that for custom-made devices, post-market surveillance plans can be applied to groups of similar devices without affecting patient safety. This would decrease the burden for the manufacturer of having to apply PMS plans to each individual device. However, most of the competent authorities think that the Periodic Safety Update Report for Class IIa and Class IIb implantable and Class III custom-made devices should be uploaded to EUDAMED to evaluate their benefit-risk

profile. This would promote a transparent and proactive PMS system, and facilitate engagement with the competent authority. There are less legal requirements for custom-made devices when compared to other devices. These are identified in the framework *MD-PMSV-RF01* to make it easier for the regulatory personnel to assist stakeholders who design and manufacture custom-made devices in any queries. The template, '*Statement for Custom-Made Devices as per Section 1 of Annex XIII of the MDR (EU) 2017/745',* was developed for manufacturers of custom-made devices to notify the competent authority of a custom-made device that they have produced for a particular patient. This statement of information will increase traceability of custom-made devices, ensuring patient safety throughout the lifecycle of the device. Australia, Switzerland and the UK are relatively aligned with the EU regarding restrictive regulation of custom-made devices. However, the new reforms in the UK are expected to be more flexible regarding approval of innovative technologies. In Japan, custom-made devices do not have any exemption from premarket review, and are generally approved slower than in the US, where they do not need a pre-market approval. The FDA also has an exemption for the use of custom-made devices in patients with rare unmet medical conditions (Willemsen et al, 2019). There are still limitations in the regulation of custom-made devices. Innovative technologies such as 3D printing has the potential to transform and reshape healthcare through personalised treatment options (Reis et al, 2022), but the current EU regulations do not specifically address this emerging technology. The proactive approach proposed by the European Medicines Agency (EMA) for technological development of pharmaceuticals focuses on regulatory adaptation, training and early interaction. This could be mirrored in the medical device sector to support innovation while ensuring safety, traceability, and alignment with green, resource-efficient manufacturing

practices[54]. The rise of point-of-care manufacturing in the clinical setting challenges the traditional supply chain model of having a manufacturing plant manufacturing the device to put on the market to finally reach the end-user. The MDR is very specific in its definition of a custom-made device, and its requirements do not cover patient-matched devices such as those produced with 3D printing,[55]unless the prerequisites of a custom-made device are met. This puts these devices in the same category of other devices that must undergo full conformity assessments even though produced individually, creating significant burdens for the manufacturer.

When considering device recalls, they emerge as a critical mechanism for protecting public health, presenting both benefits and drawbacks. What seems, presumably, to be a small number of recalls yearly, may impact the safety and quality of life of millions of patients worldwide (Morgenthaler et al, 2022). This may be attributed to the fact that several issues with the devices are discovered during the post-market surveillance phase, after the device is already in widespread use. When a device needs to be suddenly withdrawn from the market, this puts a strain on the demand and supply cycle, because substitute devices may not always be readily available and in sufficient quantities to make up for the demand (Nizam et al, 2024). When supply does not meet demand, this would lead to delays in treatment for patients, and also delays in medical procedures. If less innovative or less effective devices are used as an alternative, this may also compromise state-of-the-art patient care. Health care professionals may require training on the

[54] European Medicines Agency. EMA Regulatory Science to 2025: Strategic Reflection. [Internet] 2020. [cited 2025 April 16]. Available from URL: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf

[55] Medical Device Coordination Group. MDCG 2021-3 Questions and Answers on Custom-Made Devices & Considerations on Adaptable medical devices and Patient-matched medical devices. [Internet]. 2021 [cited 2025 April 16]. Available from URL: https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en

alternative devices used. Manufacturers may also halt production processes until the whole manufacturing system and production lines are reassessed, causing further delays in supply. The suppliers of possible alternatives may not always be fully prepared to expedite production and distribution in wake of a sudden surge in demand of their devices. Healthcare facilities may face higher costs of procurement of alternative devices. This can be further pronounced when there are spikes in prices as the demand surges worldwide. Vulnerability to shortages of devices is additionally notable due to a limited manufacturer pool, since many devices have only one or very few approved manufacturers. Seven of the competent authorities participating in Phase I data collection noted that the availability of alternative devices is a key consideration when evaluating a recall of a device supplied through the National Health System, due to the potential implications for procurement and continuity of care. Beyond shortages and the burden of healthcare institutions to rapidly source alternatives, other disadvantages chosen by the respondents included the additional costs incurred to maintain continuity of care, emotional toll on patients and caregivers, and heightened public alarm. Additional impacts of recalls on economic operators, such as the financial burden and any disputes that may arise between economic operators and regulatory authorities, were acknowledged by fewer respondents. This could reflect the regulatory mandate of competent authorities to prioritise patient safety and public health over industry-level concerns. The MDR and the IVDR offer a framework for manufacturers to have a more proactive post-market surveillance, but there is still room for strengthening mechanisms that account for the operational and financial impact of recalls on the economic operators. These could be integrated in future updates of *MD-PMSV-RF01*. The development of an MDCG guidance document specifically addressing the practical implementation of

recalls, with all the necessary communication, coordination and shared responsibilities that they entail, could help bridge this gap and promote a more balanced recall procedure.

When competent authorities participating in Phase I were asked if they ever encountered situations where a manufacturer failed or refused to recall a device when this was necessary, eight answered in the affirmative. The chosen plans of action of these competent authorities reflect differing thresholds for escalation and public communication strategies. Only three reported often or always imposing penalties on the manufacturer, and just one authority would often notify the media of the recalled product. There was strong consensus that the manufacturers can appeal against a mandatory recall, and that this appeal should always be submitted to the competent authority. Respondents agreed that the appeal process should not delay urgent risk communication to end users. Similarly, most authorities agreed that the appeal mechanism should not obstruct the retrieval of the affected devices from the supply chain. This reflects a shared understanding that precautionary action must take precedence over procedural disputes when there is potential risk of harm to patients. A few of the respondents concurred that appeals should also be open to judicial review in a court of law, though this was not widely endorsed. These variations in responses underline the fragmented nature of recall enforcement across Member States, in the absence of centralised EU-level guidance.

A recall could be seen as a weakness in the overall maintenance of safety, or a sign of rigorous oversight and strict regulations (Hwang et al, 2016; Jarman et al, 2021; Astvansh et al, 2024). From a regulatory perspective, competent authorities often view recalls as a necessary and responsible action that reflects vigilance and accountability. Findings from the pilot testing of the framework in Phase III indicated that the regulatory experts

consistently recommended a recall or a temporary market withdrawal following incident reports, pending further investigations on the device. This may suggest a precautionary approach in vigilance, reflecting the regulators' prioritisation of patient safety in uncertain situations where information is still incomplete. From a commercial standpoint, this proactive stance may encounter resistance from manufacturers and their local economic operators due to the financial repercussions of a recall, as was demonstrated in *Incident report No.1* and *Incident Report No.5 (Table A and Table E [Appendix VI]).* From a public perspective, recalls may trigger concern or mistrust in the device and in the healthcare system in general, that could be overcome only through transparent communication. The most effective way to address the growing issue of unexpected safety-related recalls lies in fostering coordinated global efforts and open communication between patients, stakeholders and regulators (Świeczkowski et al, 2022).

Despite growing interest in the role of artificial intelligence in regulatory systems, the responses obtained from the data collection tool suggest a cautious and fragmented landscape when it comes to its integration into post-market surveillance and vigilance processes. While there is some recognition of the potential of AI, particularly in areas like trend analysis, there is still considerable hesitation around its broader application, especially in terms of improving efficiency or reshaping medical device regulatory science. This cautious outlook is reflected in the limited adoption of AI tools, low levels of government funding, and divided views on whether AI presents more opportunities than challenges. These responses point to a regulatory environment that is still in the early stages of digital transformation, where practical implementation and structural support, such as national funding or harmonised guidance, remains limited. They reflect a regulatory gap where AI technologies may be evolving faster than the adaptation of

existing regulatory frameworks. The developed framework *MD-PMSV-RF01* aims to provide strategies to bridge this gap by identifying the key requirements of the new European Artificial Intelligence Regulation (EU) 2024/1689 (AI Act) regarding post-market surveillance and vigilance of medical devices, and incorporating them into a hybrid guidance which implements both the requirements of the AI Act and those of the MDR/IVDR. Besides regulatory oversight, the relevant personnel in competent authorities must also be knowledgeable to evaluate AI-enabled medical devices, particularly as AI technologies become increasingly complex and dynamic. If they are not adequately trained and prepared before the AI Act comes fully into application, there is a risk of oversight gaps, delayed response to safety issues, and insufficient scrutiny of high-risk AI systems. Without targeted capacity building, the competent authorities may struggle to fulfil their obligations under the AI Act, and this may compromise compliance to the MDR and the IVDR as well. Ultimately, patient safety needs to be safeguarded.

Challenges to compliance for AI include regulatory complications. A conflict for regulatory oversight would be when there is a device with continually evolving AI. This device would be granted market approval under a certain risk class, but stakeholders across the board might find it challenging to trust the device once it continues to self-learn and alter itself (Hay et al, 2024). The current regulatory frameworks need to be continuously adapted to be equipped to handle the complexities of AI systems. Vigilance processes need to be improved to include devices with AI (Kale et al, 2024). This may lead to concerns about safety, efficacy, and proper oversight by regulatory bodies. Unregulated or under-regulated AI systems in healthcare can pose risks to patient safety. The intersection between technology, patient safety, and societal impact may raise ethical challenges (Templin et al, 2024). These challenges revolve around ensuring fairness,

transparency, accountability, and patient safety. Algorithms used may be biased because the device model may not be representative of the entire population. This can lead to discrimination in small groups such as patients with rare diseases. The AI-based device may perform well in the population studied in clinical investigations or performance studies but could then lead to incorrect diagnoses or treatments in demographics that were not represented. Complex AI and Machine Learning (ML) models may prove difficult for clinicians to understand and trust. This is problematic when a device needs to be used to establish a diagnosis on a patient. A strong post-market surveillance system can play a key role in regulatory oversight through identifying and addressing these biases in ML algorithms.[56] Determining accountability for an AI-driven medical device is also a critical ethical issue (Fraser et al, 2023). In the case of a misdiagnosis by a device based on an AI recommendation, it could be challenging to assign responsibility to the manufacturer, as there are multiple parties involved, such as software developers and the healthcare providers themselves. AI systems often rely on large amounts of data, including sensitive patient information. With General Data Protection Regulation (GDPR) practices in place in the EU, and other similar data protection legal frameworks such as the Health Insurance Portability and Accountability Act (HIPAA) in the US, and Japan's Act on Protection of Personal Information, there should be greater control and protection of the patients' personal data. However, patients might still feel concerns about their privacy and autonomy when it comes to AI systems (Templin et al, 2024). Breaching of sensitive patient information can lead to significant problems such as identity theft, discrimination, and stigmatisation. One needs to make sure that patients are aware of the involvement of AI with all its risks and benefits. In a fast-paced world,

[56] World Health Organisation. Ethics and Governance of Artificial Intelligence for Health- WHO Guidance. [Internet]. 2021. [Cited 2025 April 19]. Available from URL: https://iris.who.int/bitstream/handle/10665/341996/9789240029200-eng.pdf?sequence=1

one needs to find a balance between the integration of AI with the preservation of clinical expertise and human judgement (Joshi et al, 2024). One must keep in mind that technology should complement, rather than replace, human healthcare providers. The challenge of equity in access to healthcare can also escalate with the use of advanced AI and ML technologies. The gap between different demographics could widen, with advanced technologies being accessible only to wealthier or well-funded populations.

Replicability is essential for ensuring reliable diagnostics, treatments and patient care in a medical context. In AI-driven medical devices, this could be disputable, due to factors such as data variability, algorithm sensitivity, lack of standardisation, and insufficient regulatory oversight. Variability in data could range from diversity across different patient populations in real-world settings, to diversity in inputted data such as low-quality radiology images when compared to high-quality images that the AI medical device was trained upon. Algorithm sensitivity makes reproducibility a challenge, especially in critical clinical situations (Templin et al, 2024). If the AI model is highly sensitive to slight changes in input data, any minor differences would yield a different output. An example of this could be a highly-sensitive device that diagnoses a disease based on imaging, that would yield different results if the image quality, angles, or contrast settings vary even minimally. This could be seen from the other side of the fence, where a device could be overfitted and trained on a certain amount of data, and would lack reliability when faced with a smaller or different set of data. When one is working with dynamic model updates, the continuous learning and updates would improve model performance, but on the other hand, it may lead to situations where different results are generated at different times with the same set of input data. This would complicate diagnoses and clinical oversight (Templin et al, 2024). One way to tackle this would be with clear

documentation control. Developers of AI devices in healthcare need to be provided with clear and standardised protocols for training, validating, and testing of their AI models, to avoid inconsistencies in implementation, and enhance reproducibility (Kolbinger et al, 2024). The current still-evolving regulations for AI may not adequately address the issue of reproducibility, particularly across diverse patient populations and environments, before approval. This might lead to AI medical devices that perform well in limited trials, but fail to replicate those successful results in real-world applications. When AI medical devices need to integrate with electronic health records, imaging systems, hospital software systems, and other digital medical devices, the differences in data formats can lead to inconsistencies in AI performance, leading to inconsistent results that could not be replicated (Kolbinger et al, 2024). Lack of reproducibility with these medical devices leads to a challenge in the oversight of post-market surveillance.

Cybersecurity poses another significant challenge for compliance. Both the MDR and the IVDR include pre-market and post-market cybersecurity requirements to be considered throughout the lifecycle of the device. It is imperative to include security issues when assessing risks of software (Puder et al, 2023). The MDCG guidance document 2019-16 rev.1 *Guidance on Cybersecurity for Medical Devices* explains clearly that challenges in risk assessment can arise either when security is too weak, for example, an implanted high-risk device protected by a weak password, or when security is too stringent, for example, the same implanted high-risk device being highly protected against malicious tampering but then being inaccessible by medical personnel during an emergency. Cyberattacks on wearable or implanted devices pose significant risk to patient safety, as unauthorised individuals are able to alter the functionality, disrupt normal operations or extract sensitive medical data (Sethuraman et al, 2019). A recall of

Medtronic MiniMed insulin pumps was carried out by the FDA in 2019 due to security flaws allowing unauthorised wireless access, enabling hackers to manipulate the insulin dosage (Klonoff and Han, 2019; Tsantikidou et al, 2024). Such compromises underscore the critical need for robust cybersecurity measures in the design of medical device software to protect patients from harm. Manufacturers should be responsible to issue encrypted software updates whenever there is a sign of emerging vulnerability. They should also collaborate with regulatory bodies to keep all stakeholders updated on any newly identified threats to safety. Patients and healthcare providers should be provided training to safely manage their device against cybersecurity risks, such as by password management and avoiding unauthorised software installations. Since cybersecurity risks change over time, pre-market surveillance on its own is insufficient to adequately control threats. The necessity of adopting a robust post-market approach is highlighted in IMDRF document IMDRF/CYBER WG/N60Final:2020 *Principles and Practices for Medical Device Cybersecurity* and MDCG 2019-16 rev.1 *Guidance on Cybersecurity for Medical Devices*. Data from devices that are in use, such as error reports, unauthorised access attempts and attack logs, should be collected regularly and analysed for new cybersecurity risk trends. The same obligations for a PMS system and a vigilance system as for other devices are required for cybersecurity monitoring. When using data sources for the post-market clinical follow-up (PMCF) study plan, proactive sources such as literature searches or surveys need to have a timespan that is adequate to the device in question. An acceptable time period of data for a surgical instrument such as a scalpel is not identical to that of software devices, because software adapts and changes continuously.

MD-PMSV-RF01 suggests the use of patient health data as real-world evidence and the integration of medical device information into national patient health portals. This is aligned with the objectives of the European Health Data Space (EHDS) Regulation[57], which is a new EU initiative, entered into force on the 26 March 2025, to create a common framework for the secure sharing and access of patient health data across Member States. One of the EHDS's main goals is to empower individuals by giving them digital access and control over their health data, including data related to diagnoses, treatments and medical technologies. By proposing the extension of national health portals to include medical device information, such as batch numbers, manufacturer details, maintenance schedules, and any field safety notices, the framework mirrors the EHDS's emphasis on patient-centric data access and the AI Act's principles of transparency. Linking national portals to competent authorities' websites to provide real-time safety updates and regulatory notices reflects the EHDS's drive towards interoperable infrastructures that support uses of health data. The concept of an electronic health record for devices, particularly for patients with implanted devices, complements the EHDS's planned structured electronic health records by ensuring that device-specific data becomes part of a patient's health history. Integrating device data into systems that were traditionally focused on medicines, the framework promotes holistic healthcare data management that supports clinical care and strengthens surveillance.

[57] European Commission. European Health Data Space Regulation (EHDS). [Internet] 2025. [Cited 2025 April 20]. Available from URL: https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space-regulation-ehds_en

4.3 Stricter regulations: a challenge to innovation?

The regulatory intent of stricter regulation of post-market surveillance and vigilance is patient safety, and not to stifle innovation. Despite this principle, manufacturers, particularly SMEs and start-ups, are reporting an increase in costs and market withdrawals (Bretthauer et al, 2023). Some manufacturers opted not to transition devices compliant under the previous directives to MDR or IVDR certification. There seems to be a fine line between regulation to safeguard patient safety and over-regulation that may possibly deter making the device available on the market. This is proving to be a current challenge on the EU playing field. An efficient PMS system needs to be robust and risk-based, but also proportionate and supportive of innovation, with competent authorities and economic operators coordinating efforts and aligning effective strategies (Chettri et al, 2024). On the 4 December 2024, MedTech Europe issued a statement regarding a call for reform of the MDR and the IVDR on behalf of the European medical technology industry, to ensure that while maintaining patient safety, access to innovative medical technologies is supported. This position followed a discussion at the EU Employment, Social Policy, Health and Consumer Affairs Council (EPSCO), where Member States stated that Europe is facing challenges to innovation, safety and healthcare access[58]. Considerable strain on the regulatory and healthcare systems is particularly felt in terms of delay in patient access to essential devices. This is largely due to the requirement of re-certification of most medical devices, with additional clinical investigations, which are costly and time-consuming. As a result, many clinically valuable devices may be withdrawn or delayed because of the burden of compliance. Focus on legacy devices

[58] MedTech Europe. The Future of Europe's Medical Technology Regulations: Position Paper. [Internet]. 2024 [cited 2025 April 17]. Available from URL: https://www.medtecheurope.org/news-and-events/news/medtech-europes-post-epsco-statement-on-the-necessary-reforms-of-mdr-ivdr/

could also divert the already-limited resources away from assessment of innovative devices, and this could compromise timely access of new technologies for patients (Nüssler, 2023). Another financial repercussion could result from the significant narrowing of the concept of equivalence under the MDR/IVDR when compared to previous directives or to other non-EU processes such as the FDA's 510(k) pathway (Sündermann J et al, 2024). Equivalence requires access to detailed technical documentation and justification of clinical, biological and technical similarities, which could present difficulties if data belongs to other manufacturers and is not made public (Bretthauer et al, 2023; Sündermann et al, 2024). This challenge should be easier to overcome once EUDAMED is fully functional, and the necessary device data is made available (Bretthauer et al, 2023). The 510(k) pathway in the US permits market clearance based on substantial equivalence to a predicate device already on the market, making the process less resource-intensive, and providing an incentive for manufacturers to prioritise the US as a launch market over the EU (Peñarrubia-Ortiz et al, 2025).

In March 2025, MedTech Europe released a comprehensive report as a contribution towards the European Commission's evaluation of the MDR and the IVDR for a potential update. One of the key elements of this report states that post-market surveillance costs have increased up to 49% on the transition from the directives to the new regulations. Reasons for the increased costs include administrative burden, unpredictable timelines for assessment and review practices by the notified body, forms with complex format to fill in, MIR forms submitted for each device implicated in the same incident, incident reporting time frames for low-risk incidents, and the possibility of duplication of reports between trend reporting and serious incident reporting (Melvin et al, 2023). The report calls for reducing administrative burden while maintaining the regulatory objectives of

ensuring patient safety, transparency, and innovation support. Simplifying PMS requirements is seen as essential to achieving a more efficient and sustainable regulatory environment[59]. Even prior to the end of the transitional deadlines, MedTech Europe is reporting a noticeable decline in the EU being viewed as the preferred region for first market entry, with a 33% decrease for large manufacturers and 19% decrease for SMEs under the MDR, and 40% decrease for large manufacturers and 12% decrease for SMEs under the IVDR. Manufacturers are opting to launch their devices in other markets, mainly the US, UK, Japan and Canada for *in vitro* medical devices, and the US, UK, Australia, New Zealand, China and Canada for medical devices. This decline is largely significant for large manufacturers rather than SMEs[60], mainly due to a higher financial possibility of global reach with more flexibility of shifting launching strategies.

A balanced solution for navigating an increasingly complex and still-maturing regulatory environment seems to be a holistic approach of getting together experts from the engineering and regulatory fields, designers, clinical researchers, industry analysts and business strategists (Rêgo et al, 2023). This need for strong collaboration among all key stakeholders involved in the implementation of the new regulations was emphasised also by the EU Competent Authorities for Medical Devices (CAMD) at its 55th meeting in Hungary in November 2024[61].

[59] MedTech Europe. Report on Administrative Burden under IVDR and MDR: MedTech Europe's Proposal for IVDR/MDR Targeted Evaluation. [Internet]. 2025 [cited 2025 April 17]. Available from URL: https://www.medtecheurope.org/wp-content/uploads/2025/03/250318_mte-report-on-admin-burden-ivdr_mdr_final.pdf

[60] MedTech Europe. MedTech Europe 2024 Regulatory Survey: Key Findings and Insights. [Internet]. 2024 [cited 2025 April 17]. Available from URL: https://www.medtecheurope.org/resource-library/medtech-europe-2024-regulatory-survey-key-findings-and-insights/

[61] Mina Blaess. Competent Authorities for Medical Devices - 55th CAMD Meeting Statement. [Internet]. 2025. [Cited 2025 April 18]. Available from URL: https://www.camd-europe.eu/news/

Viewing the financial burden of post-market surveillance from a risk perspective, manufacturers should still be encouraged to aim for structured approaches for an enhanced safety profile of their devices. If they leverage the data gathered from post-market surveillance reports proactively, they would be able to monitor the quality of their devices and detect any potential issues early by taking the necessary corrective actions to address any shortcomings and avoid costly future mistakes. This data would also help in controlling the quality of their suppliers, by providing insights into any deficiencies that would ultimately contribute to bigger risks. Comparing these direct post-market surveillance costs to expensive consequences of malfunctioning devices, such as global recalls, legal liability and reputational risks, demonstrates that proactive investment in surveillance is economically and ethically justified. The European Commission could facilitate this burden of compliance by implementing EUDAMED where economic operators can have access to shared tools and information. The competent authorities can offer clear guidance on the expectations of post-market surveillance and vigilance processes. *MD-PMSV-RF01* aims to serve as a practical tool in assisting competent authorities in this task by outlining the PMS and vigilance processes in a stepwise approach. Harmonised templates for PMS and vigilance between all Member States, reflecting other global standards such as the IMDRF terminology, can help mitigate administrative burden.

4.4 Study Limitations

A key limitation of this study is the limited geographical spread and response rate. The data collection tool was disseminated to all EU and EEA countries and Turkey, and twelve

respondents completed the questions. The incident reports used for pilot testing the regulatory framework in Phase III were chosen through purposive sampling for convenience. The SWOT analysis in Phase III is also subject to personal interpretation as it was carried out only by the researcher. A limitation of the current framework is that it does not explicitly address strategies to mitigate the operational and financial burdens faced by economic operators during the recall process. While the focus remains on regulatory evaluation and public health protection, future adaptations of the framework could incorporate more balanced approaches that also consider industry sustainability.

4.5 Recommendations for further research

Further studies could be carried out to explore the preparedness of competent authorities in the oversight of surveillance of rapidly evolving technologies such as digital health tools, wearables and personalised medical devices, in light of the new Electronic Health Data Space Regulation. Future studies could investigate in depth the unique challenges associated with custom-made devices that were highlighted in this study, and propose policy developments that could help overcome these gaps. Other studies could evaluate the decline in the number of new medical devices being launched in the EU compared to non-EU markets. Orphan devices could also be a significant area for future regulatory studies, especially given the challenges in their post-market surveillance due to limited patient populations, and considering that the current medical device regulations do not address regulation of these devices.

4.6 Conclusion

In conclusion, this research has examined the current challenges of post-market surveillance and vigilance within the EU regulatory landscape under Regulation (EU) 2017/745 (MDR) and (EU) 2017/746 (IVDR). The MDR and the IVDR represent a significant advancement towards a more proactive lifecycle approach in regulation of devices, but challenges persist, such as fragmented oversight among Member States and limited interoperability due to the delayed rollout of EUDAMED.

The significance of the research lies within the proposed regulatory framework that was designed to support strategic oversight of post-market surveillance and vigilance activities. This framework, *MD-PMSV-RF01*, aims to be at the interface between the MDR/IVDR and the AI Act, anticipating the increasing integration of AI into medical devices and the corresponding need for coordinated regulatory oversight to bridge two still-evolving regulatory domains. It reinforces principles belonging to the MDR such as transparency and accountability and risk management, but also supports the development of harmonisation through global standards such as the IMDRF terminology, WHO guidelines on medical devices and software, and ISO Standards for devices, software and risk management. The framework aims to contribute to a more resilient regulatory system that prioritises patient safety, while also recognising that increasingly complex medical technologies are essential to advancing healthcare and driving innovation.

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List of Publications

Cachia A, Attard Pizzuto M, Azzopardi LM. Regulatory Oversight of Patient Safety in Medical Devices. MedInPharma, 2024; Valletta, Malta.

Cachia A, Attard Pizzuto M, Azzopardi LM. Regulatory Oversight of Patient Safety in Medical Devices. University of Malta Research Expo, 2025; Valletta, Malta.

Cachia A, Attard Pizzuto M, Azzopardi LM. Regulatory Oversight of Patient Safety in Medical Devices. 83rd International Pharmaceutical Federation (FIP) World Congress of Pharmacy and Pharmaceutical Sciences, 2025; Copenhagen Denmark.

APPENDICES

Appendix I

Faculty of Research Ethics Committee Approval

Researcher / Student Area

Applicant Details

Name:

Audrey

Surname:

Cachia

Email:

audrey.cachia.00@um.edu.mt

Submit New REDP Form

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Application ID	Application Date	Project Title	Faculty	Status
MED-2024-00365	02/09/2024	Regulatory oversight of patient safety in medical devices	Faculty of Medicine & Surgery	Approved

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Appendix II

Data Collection Tool (Phase 1)

Questionnaire:

Regulatory Oversight of Patient Safety in Medical Devices

This Doctorate research tool is investigating possible gaps in the medical device regulatory science of post-market surveillance to potentially enhance patient safety. The information provided by you in this questionnaire will be used solely for research purposes.

SECTION A – GENERAL INFORMATION

This section aims to gather background information to aid in the compiling of resources.

1. In which country is your regulatory authority located?

2. How many human resources are allocated for market surveillance and vigilance in your authority?

☐ 1 – 5

☐ 6 – 10

☐11 – 15

☐More than 15

3. What expertise would you consider for regulatory personnel who oversee surveillance and vigilance at your regulatory agency?

Please tick the box that you think best describes your answer. You may tick more than one answer.

☐Clinical knowledge

☐Legal background/knowledge

☐Safety surveillance

☐Risk management

☐Product quality management

☐Statistical analysis

☐Technical knowledge

☐Engineering knowledge

☐Other. Please specify:

4. Does your regulatory agency invest in training regulatory personnel on surveillance and vigilance?

☐Yes

☐No

☐Other comments:

5. If yes, training is:

	Yes	No
Delivered in-house	☐	☐
Delivered by an external organization	☐	☐
Attained over a timeframe of 8 hours or less	☐	☐
Attained over a timeframe of more than 8 hours	☐	☐

Other comments:

SECTION B

6. How many incident reports in general are received monthly at your regulatory agency?

☐ Less than 100

☐ 100 - 200

☐ 201 - 300

☐More than 300

☐Other. Please comment:

7. Do you classify all initial incident reports, pertaining to all device classes, received by your authority?

☐Yes

☐No

☐Other comments:

8.1 Do you classify initial incident reports by criticality, using the categories: low, medium, and high risk?

☐Yes

☐No

8.2. If the answer to Question 8.1 is '*No*', please specify other risk categories used.

9. When non-serious incident reports are received from health institutions or end-users, these are:

Please tick the box that you think best describes your answer.

☐Closed and archived

☐Categorised and documented

☐Categorised and analysed for trends

☐Other. Please comment:

10. Reflect on the frequency of occurrence of the most common reasons listed in incident reports received by your authority.

For each statement, please tick the box that you think best describes your answer.

	Very Uncommon	**Uncommon**	**Neutral**	**Common**	**Very Common**
Malfunction or Deterioration in characteristics of device	☐	☐	☐	☐	☐
Manufacturing error	☐	☐	☐	☐	☐
Use-error due to mismatch between device ergonomic characteristics and user characteristics	☐	☐	☐	☐	☐
Insufficient information from manufacturer	☐	☐	☐	☐	☐
Inadequate instructions for use	☐	☐	☐	☐	☐
Off-label use of device	☐	☐	☐	☐	☐
Side effects that are undesirable and unintended, despite normal use of device	☐	☐	☐	☐	☐

Software issues	☐	☐	☐	☐	☐

Any other reasons or comments:

11. Importers and distributors need more education and training on post-market surveillance activities and responsibilities with the new Regulations in place.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

SECTION C

12. Do you receive incident reports for legacy devices?

[As per MDCG 2021-25, legacy devices are devices, which, in accordance with Article 120(3) of the MDR, are placed on the market after the MDR's date of application (DoA) and until 26 May 2024 if certain conditions are fulfilled. Those devices can be:
• devices which are class I devices under Directive 93/42/EEC (MDD), for which an EC declaration of conformity was drawn up prior to 26 May 2021 and for which the conformity assessment procedure under the MDR requires the involvement of a notified body; or
• devices covered by a valid EC certificate issued in accordance with Directive 90/385/EEC (AIMDD) or the MDD prior to 26 May 2021]

☐Yes

☐No

13. Exceptions put in place for legacy devices such as, no requirement for a full revision of the technical documentation in accordance with Annex II and Annex III of the MDR, or no requirement for a performance evaluation report as requested by the IVDR, could impact patient safety, and increase incidence occurrence.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

14. Article 15 of the MDR and IVDR require manufacturers/authorised representatives to appoint a *Person Responsible for Regulatory Compliance* (PRRC), but this does not apply to legacy devices. A PRRC should also be required for the oversight of post-market surveillance activities of legacy devices.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

15. Notified bodies should be stricter in enforcing post-market surveillance processes for legacy devices to comply with the Regulation (EU) 2017/745 and (EU) 2017/746.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

16. Applying post-market surveillance plans to each individual custom-made device, rather than to a group of similar devices:

For each statement, please tick the box that you think best describes your answer.

	Strongly disagree	**Disagree**	**Neutral**	**Agree**	**Strongly agree**
would increase the safety of the device	☐	☐	☐	☐	☐
would have no increased influence on patient safety	☐	☐	☐	☐	☐
Would be an unnecessary burden	☐	☐	☐	☐	☐

17. Periodic Safety Update Reports (PSUR) for Class IIa/IIb Implantable or Class III **custom-made devices** are required to be part of the documentation available, upon request, for notified bodies and competent national authorities, as per MDR Article 86 and MDCG 2021-3. Uploading the PSUR to EUDAMED for these custom-made devices, as is done for other Class IIa/IIb Implantable and Class III medical devices,

would be a necessary tool in the evaluation of changes to the benefit-risk profile of the device.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

18. What are the main activities done by your authority to assess the manufacturer's compliance to post-market surveillance regulations?

For each statement, please tick the box that you think best describes your answer.

	Never	**Rarely**	**Sometimes**	**Often**	**Always**
Assessing technical documentation of the device	☐	☐	☐	☐	☐
Evaluating published literature applicable to the class of device	☐	☐	☐	☐	☐
Performing clinical evaluation at in-house laboratories	☐	☐	☐	☐	☐
Performing clinical evaluation at sub-contracted laboratories	☐	☐	☐	☐	☐
Comparing device with state of the art *[The state of the art embodies what is currently and generally accepted as good practice in technology and medicine. The state of the art does not necessarily imply the most technologically advanced solution. (as per ISO 14971-2019)]*	☐	☐	☐	☐	☐

Other comments:

19. Considering that most medical devices have a relatively short life cycle and can be modified from one production to another, performing literature review of similar devices for post-market surveillance purposes may be unreliable.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

SECTION D

20. Did you ever encounter a situation where a manufacturer or authorised representative failed or refused to voluntarily recall a medical device that may pose a risk to patient health?

Please tick the box that you think best describes your answer.

☐Yes

☐No

21. What should the next plan of action of the regulatory authority be, if a manufacturer or authorised representative refuses a voluntary recall?

For each statement, please tick the box that you think best describes your answer.

	Never	**Rarely**	**Sometimes**	**Often**	**Always**
Send notice of ordered recall to manufacturer	☐	☐	☐	☐	☐
Inform end-users to immediately suspend use	☐	☐	☐	☐	☐

Give the manufacturer a timeframe for submitting a recall plan	☐	☐	☐	☐	☐
Send notice of recalled product on media	☐	☐	☐	☐	☐
Impose administrative penalties	☐	☐	☐	☐	☐

Other comments:

_____

_____

_____

22. The manufacturer should have the right to appeal against the regulatory authority's decision on a product recall.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

23. An appeals' procedure:

For each statement, please tick the box that you think best describes your answer.

	Strongly Disagree	**Disagree**	**Neutral**	**Agree**	**Strongly Agree**
Should be submitted to the regulatory authority	☐	☐	☐	☐	☐
Should be submitted to a court of law	☐	☐	☐	☐	☐
Should be carried out within 4 weeks of the recall notice	☐	☐	☐	☐	☐

Should not prevent the regulators from informing the end-users of risk	☐	☐	☐	☐	☐
Should not stop the retrieval of the device from the distribution chain	☐	☐	☐	☐	☐

24. In assessing the progress of a recall process, the manufacturer is expected to send status reports to your regulatory authority:

Please tick the box that you think best describes your answer.

☐Daily

☐Every 2 – 5 days

☐Every 5 – 7 days

☐At least every 1 – 2 weeks

☐Other. Please comment.

25. A product recall might affect procurement for health institutions that are supplied through the National Health System. When considering such a recall, access to suitable alternatives is first identified.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

26. Disadvantages of product recalls include:

For each statement, please tick the box that you think best describes your answer.

	Strongly Disagree	**Disagree**	**Neutral**	**Agree**	**Strongly Agree**

Shortage of medical devices if there is no suitable alternative	☐	☐	☐	☐	☐
Economic burden to manufacturers and other economic operators	☐	☐	☐	☐	☐
Burden on health institutions to find alternative for patients	☐	☐	☐	☐	☐
Extra costs incurred to counteract interrupted patient care	☐	☐	☐	☐	☐
Anxiety to patients and care givers	☐	☐	☐	☐	☐
Public alarm	☐	☐	☐	☐	☐
Disputes between regulatory authorities and economic operators	☐	☐	☐	☐	☐

27. For how long do you keep Field Safety Notices (FSN) publicly available on your authority's website?

Please tick the box that you think best describes your answer.

☐Up to 6 months

☐6 months – 1 year

☐1 year – 5 years

☐More than 5 years

☐Other. Please comment.

SECTION E

28. Implementing artificial intelligence (AI) can complete time-consuming surveillance tasks much more rapidly and without the risk of human error.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

29. In the foreseeable future, AI software could provide more opportunities than challenges in medical device regulatory science.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

30. AI can be used for trend analysis because it can easily detect any signal occurrence that exceeds set thresholds, and it can generate reports from this real-world data without having to rely solely on manufacturers.

Please tick the box that you think best describes your answer.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
☐	☐	☐	☐	☐

31. Are you integrating AI tools in your systems for signal detection and evaluation of post-market surveillance data?

Please tick the box that you think best describes your answer.

☐Yes

☐No

☐Other comments

32. Do you receive, or plan to receive, any government funding to implement AI in the oversight of patient safety?

Please tick the box that you think best describes your answer.

☐Yes

☐No

☐Other comments: _____

_____

_____

Appendix III

Invitations for Participation in Study

i. Invitation for Participation in Phase 1 Data Collection

Dear Sir/Madam,

My name is Audrey Cachia, and I am a student at the University of Malta, presently reading for a Doctorate in Pharmacy, at the Department of Pharmacy, Faculty of Medicine and Surgery, in collaboration with the College of Pharmacy, University of Illinois, Chicago, USA. I am presently conducting a research study for my dissertation titled *Regulatory Oversight of Patient Safety in Medical Devices*; this is being supervised by Prof. Lilian M. Azzopardi, professor of pharmacy and head of the Department of Pharmacy at the University of Malta, and co-supervised by Dr. Maresca Attard Pizzuto, senior lecturer at the University of Malta. This letter is an invitation to participate in this study. Below you will find information about the study and about what your involvement would entail, should you decide to take part.

The aim of my study is to identify gaps in medical device regulatory sciences where the patient's safety may not be sustained. A regulatory framework will be developed, aiming to overcome these challenges by providing a strategic oversight approach for post-market surveillance to ensure long-term patient safety. Your participation in this study would help contribute to a better understanding of the contribution regulators can give to oversee post-market surveillance activities carried out by the manufacturers of medical devices. Any data collected from this research will be used solely for purposes of this study. All anonymised data will be held up to one year from submission of this dissertation.

Participation in this study is entirely voluntary; in other words, you are free to accept or refuse to participate, without needing to give a reason. You are also free to withdraw from the study at any time, without needing to provide any explanation and without any negative repercussions for you. Should you choose to withdraw, any data collected from your feedback will be erased as long as this is technically possible, unless erasure of data would render impossible or seriously impair achievement of the research objectives, in which case it shall be retained in an anonymised form.

Should you choose to participate, kindly access the questionnaire through the following link:
https://docs.google.com/forms/d/e/1FAIpQLSdJt7yBu6fa5DQ26grAMisXsCiNT88QnIW57crhkWcz76Y6HQ/viewform?usp=sf_link

If you choose to participate, please note that there are no direct benefits to you and your participation does not entail any known or anticipated risks.

Please note also that, as a participant, you have the right under the General Data Protection Regulation (GDPR) and national legislation to access, rectify and where applicable ask

for the data concerning you to be erased. All data collected will be stored in an anonymised form for up to one year from completion of this study.

A copy of this information letter is being provided for you to keep and for future reference.

Thank you for your time and consideration. Should you have any questions or concerns, please do not hesitate to contact me by e-mail on audrey.cachia.00@um.edu.mt.

Sincerely,

Audrey Cachia
✉audrey.cachia.00@um.edu.mt

Prof. Lilian M. Azzopardi
✉lilian.m.azzopardi@um.edu.mt

ii. Invitation for Participation in Phase II Expert Panel for Validation of Framework

Dear participant,

Thank you for participating in the expert panel evaluation of the regulatory framework with the title ‘Ensuring Patient Safety through Medical Device Regulatory Science ~ A Regulatory Framework for Competent Authorities’.

For this process, you are kindly asked to review the framework and provide feedback on its relevance, clarity and adequacy of included detail in the table attached with this letter.

Thank you for your time and expertise. I look forward to your valuable input.

Best regards,

Audrey Cachia

Evaluation Form

Validation Criteria	Expert Reply	
Relevance Does the framework align with the existing regulatory requirements and effectively address current challenges in the regulatory landscape?	☐ Yes	☐ No
Comments:		
Clarity Is the framework clearly structured and presented in a way that is easy to understand?	☐ Yes	☐ No
Comments:		
Adequacy of detail Does the framework provide sufficient detail to support its implementation and practical application?	☐ Yes	☐ No
Comments:		

Appendix IV

Incident Report Evaluation Template Form

Incident Report Evaluation Template using the Regulatory Framework	
1. General Information	
Incident Report Reference Code	☐Yes ☐No
Device Details [Name, Model, Batch/Lot No]	☐Yes ☐No
Manufacturer Details	☐Yes ☐No
Healthcare Institution [if report is generated from HCPs]	☐Yes ☐No
Regulatory Status of device [CE-mark, custom-made device, legacy device]	☐Yes ☐No
Comments:	

2. Roles and Responsibilities of Stakeholders			
Manufacturer	☐	Authorised Representative	☐
Importer	☐	Distributor	☐
Notified Body	☐	End-User	☐

Were regulatory obligations of stakeholders fulfilled?

☐Yes ☐No

Comments:

Were there deficiencies in reporting?

☐Yes ☐No

Comments:

Were the responses of stakeholders in line with the Regulations?

☐Yes ☐No

Comments:

3. Oversight by the Competent Authority

Has the incident report been acted upon by the CA?

☐Yes ☐No

Comments:

Regulatory Actions taken:

☐ None

☐ Request for additional information from economic operators

☐ Request for additional information from notified body

☐ Request for additional information from reporting health institution / end-user

☐ Request for advice from advisory committee

☐ Follow-up on quarantine or recall recommendation

☐ Uploading FSN on the website

4. Vigilance System Evaluation

Was the incident report as per provided template form?

☐Yes ☐No

Reporting Gaps:

Monitoring Trends:

Was this incident a recurring issue?

☐Yes ☐No

Is trend analysis being conducted?

☐Yes ☐No

5. Risk Analysis and Risk Management

Was a risk assessment conducted by the manufacturer?

☐Yes ☐No

Comments:

Was a risk assessment conducted by the CA?

☐Yes ☐No

Comments:

Was the risk classification adequate?

☐Yes ☐No

Comments:

Were CAPA implemented by the manufacturer?

☐Yes ☐No

Comments:

6. Integration of AI in post-market surveillance

Could AI tools enhance vigilance in this particular case?

☐Yes ☐No

Comments:

7. Training and Awareness

Were any training needs identified?

☐Yes ☐No

Comments:

CASP-Based Critical Appraisal Checklist Score given by the researcher:

Recommendations for improvement of the framework:

Appendix V

CASP-Based Critical Appraisal Checklist for Medical Device Vigilance

CASP-Based Critical Appraisal Checklist for Medical Device Vigilance	
Assessor Name	
Incident Report Reference No.	
Appraisal Date	
Section 1: Validity of Incident Report and Data Received by the Competent Authority	
1.1 Source Reliability	
Is the MIR complete and accurate?	Yes ☐ No ☐ Can't tell ☐
Is data sourced from a verified system? [e.g. IMDRF, EUDAMED…]	Yes ☐ No ☐ Can't tell ☐
Was the MIR sent within the regulatory timelines?	Yes ☐ No ☐ Can't tell ☐
1.2 Causality Assessment	
Is there uncertainty about the link between the device and the reported adverse event?	Yes ☐ No ☐ Can't tell ☐
Are there no other factors, such as patient comorbidities, that could contribute to the adverse event?	Yes ☐ No ☐ Can't tell ☐
1.3 Consistency of Data	
Is there only one incident reported for this device or device group?	Yes ☐ No ☐ Can't tell ☐
Is it an expected adverse event?	Yes ☐ No ☐ Can't tell ☐
Section 2: Risk Assessment and Impact Analysis	
2.1 Severity of the Incident	
What is the impact of the incident?	☐ Public health threat – 3 points ☐ Death – 2 points ☐ Deterioration in health – 1 point

What is the probability of direct or indirect harm to the patient being caused by the device?	☐ Negligible – 1 point ☐ Low – 1 point ☐ Moderate – 2 points ☐ Likely – 3 points ☐ Highly Likely – 3 points
2.2 Risk-Benefit Analysis	
Have appropriate risk mitigation measures been initiated by the manufacturer?	Yes ☐ No ☐ Can't tell ☐
2.3 Signal Detection and Trend Analysis	
Is there an emerging pattern of non-serious incidents?	Yes ☐ No ☐ Can't tell ☐
Do signals and trends indicate that an FSCA is not necessary?	Yes ☐ No ☐ Can't tell ☐
Section 3: CAPA Evaluation	
3.1 Root Cause Analysis	
Has the manufacturer conducted a comprehensive root cause analysis?	Yes ☐ No ☐ Can't tell ☐
Are the identified root causes plausible and evidence-based?	Yes ☐ No ☐ Can't tell ☐
3.2 Effectiveness of CAPA	
Are the corrective actions appropriate?	Yes ☐ No ☐ Can't tell ☐
Are preventive measures in place to avoid recurrence?	Yes ☐ No ☐ Can't tell ☐
3.3 Stakeholder Communication	
Has the manufacturer issued a FSN?	Yes ☐ No ☐ Can't tell ☐
Were healthcare professionals and other end-users adequately informed?	Yes ☐ No ☐ Can't tell ☐
Section 4: Decision Making	
4.1 Regulatory Compliance	

Is the manufacturer compliant with MDR (EU 2017/745) and IVDR (EU 2017/746)?	Yes ☐ No ☐ Can't tell ☐
Have all reporting and documentation requirements been met?	Yes ☐ No ☐ Can't tell ☐
4.2 Regulatory Action Plan	
Was further investigation or on-site inspection initiated?	Yes ☐ No ☐ Can't tell ☐
Were the economic operator's decisions consistent with the competent authority's assessment?	Yes ☐ No ☐ Can't tell ☐
4.3 Continuous Monitoring and Improvement	
Are post-market follow-up (PMCF) activities in place?	Yes ☐ No ☐ Can't tell ☐
Are periodic safety update reports (PSUR) being submitted?	Yes ☐ No ☐ Can't tell ☐

Evaluation Rating System		
Yes	1 point	
Can't Tell	2 points	
No	3 points	
57 - 72 points	High Confidence Level (67 – 100%)	Strong evidence; Effective regulatory action is recommended
41 - 56 points	Moderate Confidence Level (34 – 66%)	Moderate evidence; Additional monitoring is required
24 – 40 points	Low Confidence Level (Below 34%)	Insufficient evidence; Request for additional data is required

[Adopted and modified from a Critical Appraisal Skills Programme tool used for the critical appraisal of research evidence in cohort studies and case-control studies; available from URL: https://casp-uk.net/casp-tools-checklists/]

Appendix VI

Reflections from Incident Reports for Pilot Testing of Framework

Tables A – E Reflections from pilot testing the developed framework

Table A - Incident Report 1	
Regulatory obligations of economic operators: Not fulfilled	The local distributor forwarded the incident reports and the requests of the competent authority to the manufacturer.
	The manufacturer sent a MIR to the competent authority.
	There was initial resistance to proceed with recall on behalf of the economic operators.
Regulatory obligations of notified body: Not fulfilled	The notified body did not communicate with the competent authority.
Deficiencies in reporting:	The reports from the end-users were not very detailed. The competent authority had to communicate with the health institution on several occasions to obtain more details on the incidents. The reports were not as template form, leading to reporting gaps.
	The MIR was detailed. However, it only contained 1 IMDRF code for the Medical Device Problem (A).
The responses of economic operators were in line with the regulation (EU) 2017/745	The manufacturer provided the MIR within the timeframe requested by the competent authority.
	The distributor followed the recommendations of the advisory committee to carry out a recall and provide an alternative for the patients.
Oversight by the Competent Authority	The competent authority initiated communication with all stakeholders immediately, requested all required documentation, and started risk assessment.
	Upon receiving the MIR, the competent authority requested recommendations from the advisory committee due to the risk to patient safety.
	The recall process was followed thoroughly and verified before the case was closed.
	Regulatory actions taken: - Request for additional information from economic operators - Request for additional information from notified body - Request for additional information from reporting health institution / end-user - Request for advice from advisory committee - Follow-up on quarantine or recall recommendation - Uploading FSN on the website
Trend Analysis	No Trend analysis is being conducted.
Risk Analysis and Management	Risk assessment was reviewed and found to be adequate by the manufacturer. The patient's discomfort was considered an expected side effect of the process.
	Result of risk assessment by CA differed to that of the manufacturer and the case was brought up to the advisory committee for discussion.
	Risk classification was not adequate considering the young age of the patients, and the risk of deterioration of health.
CAPA	The manufacturer changed the Instructions For Use (IFU) by adding an additional instruction for this type of hydrophilic catheter.
	Root cause – possibly a new raw material that is being used is making the catheters less flexible and more rigid upon sterilisation.
Integration of AI	AI could help regulators be more efficient in searching data on potential similar incidents from other global regulatory sources.
	The incident reports could be documented in a database where they are analysed for emerging trends, to be proactive if other similar cases emerge.
	Having communication platforms such as chatbots on the vigilance database could make communication between all stakeholders more efficient.
	Having the possibility of patient-reporting on the patient's digital health portal would increase vigilance efficiency.
Training Needs	Training needs for adequate incident reporting by healthcare professionals
CASP-Based Critical Appraisal Checklist Score	58 points
	High Confidence Level – Strong Evidence
	Effective regulatory action is required

Table B - Incident Report 2	
Regulatory obligations of economic operators: Fulfilled	The local distributor forwarded the incident reports and the requests of the competent authority to the manufacturer.
	The manufacturer sent a MIR to the competent authority.
	There was open communication between the economic operators, the competent authority and the health institution involved.
Regulatory obligations of notified body: Not applicable	No notified body involved
Deficiencies in reporting:	The reports from the end-users were not very detailed. The competent authority had to communicate with the health institution on several occasions to obtain more details on the incidents. The reports were not as template form, leading to reporting gaps.
	The MIR was detailed. It contained all relevant IMDRF codes.
The responses of economic operators were in line with the regulation (EU) 2017/745	The manufacturer provided the MIR within the timeframe requested by the competent authority.
	The distributor followed the recommendations of the advisory committee to collect sample for manufacturer and provide an alternative for the patients.
Oversight by the Competent Authority	The competent authority initiated communication with all stakeholders immediately, requested all required documentation, and started risk assessment.
	Upon receiving the MIR, the competent authority requested recommendations from the advisory committee due to the risk to vulnerable patients' safety.
	The competent authority is still waiting for final MIR.
	Regulatory actions taken: - Request for additional information from economic operators - Request for additional information from reporting health institution / end-user - Request for advice from advisory committee
Trend Analysis	No Trend analysis is being conducted.
Risk Analysis and Management	Risk assessment was reviewed and found to be adequate by the manufacturer. Incidents were classified as 'All other reportable incidents', with 2 possible root causes – batch-related problem or issues with user technique.
	Result of risk assessment by CA differed to that of the manufacturer and the case was brought up to the advisory committee for discussion.
	Risk classification was not adequate considering the vulnerability of the patients, and the risk of deterioration of health due to increased risk of infection.
CAPA	The manufacturer changed the IFU by adding video instructions for training.
	Training will be provided by a representative of the manufacturer to all the hospital staff working with the device.
Integration of AI	The incident reports could be documented in a database where they are analysed for emerging trends, to be proactive if other similar cases emerge.
	Having communication platforms such as chatbots on the vigilance database could make communication between all stakeholders more efficient.
	Having the possibility of utilising automated transcriptions generated from video calls with the manufacturer's representative as future reference for new staff.
Training Needs	Training needs for adequate incident reporting by healthcare professionals
	Training for the healthcare personnel on best practice guidelines for particular devices by a representative of the economic operator
CASP-Based Critical Appraisal Checklist Score	47 points
	Moderate Confidence Level – Moderate Evidence
	Additional monitoring is required

Table C - Incident Report 3	
Regulatory obligations of economic operators: Fulfilled	The local distributor forwarded the incident reports and the requests of the competent authority to the manufacturer.
	The manufacturer sent a MIR to the competent authority.
	There was open communication between the economic operators, the competent authority and the health institution involved.
Regulatory obligations of notified body: Not fulfilled	The notified body did not communicate with the competent authority.
Deficiencies in reporting:	The reports from the end-users were not very detailed. The competent authority had to communicate with the health institution on several occasions to obtain more details on the incidents. The reports were not as template form, leading to reporting gaps.
	The MIR was detailed. It contained all IMDRF codes.
The responses of economic operators were in line with the regulation (EU) 2017/745	The manufacturer provided the MIR within the timeframe requested by the competent authority.
	The distributor followed the recommendations of the advisory committee to carry out a recall and provide an alternative for the patients.
Oversight by the Competent Authority	The competent authority initiated communication with all stakeholders immediately, requested all required documentation, and started risk assessment.
	Upon receiving the MIR, the competent authority requested recommendations from the advisory committee due to the risk to vulnerable patients' safety.
	The competent authority is still waiting for the final MIR.
	Regulatory actions taken: - Request for additional information from economic operators - Request for additional information from notified body - Request for additional information from reporting health institution / end-user - Request for advice from advisory committee
Trend Analysis	Incident was a recurring issue. Trend analysis is being conducted.
Risk Analysis and Management	Risk assessment was reviewed and found to be adequate by the manufacturer. Incidents were classified as 'All other reportable incidents'.
	Result of risk assessment by CA differed to that of the manufacturer and the case was brought up to the advisory committee for discussion.
	Risk classification was not adequate considering the vulnerability of the patients, and the risk of deterioration of health.
CAPA	Not implemented yet – waiting for return of defective device to start further investigations on the new incident reports.
Integration of AI	AI could help regulators be more efficient in searching data on potential similar incidents from other global regulatory sources.
	The incident reports could be documented in a database where they are analysed for emerging trends, to be proactive if other similar cases emerge.
	Having communication platforms such as chatbots on the vigilance database could make communication between all stakeholders more efficient.
	Having the possibility of patient-reporting on the patient's digital health portal would increase vigilance efficiency.
Training Needs	Training needs for adequate incident reporting by healthcare professionals
CASP-Based Critical Appraisal Checklist Score	64 points
	High Confidence Level – Strong Evidence
	Effective regulatory action is required

Table D - Incident Report 4	
Regulatory obligations of economic operators: Not fulfilled	The local distributor forwarded the incident reports and the requests of the competent authority to the manufacturer.
	The manufacturer did not send a MIR to the competent authority.
	The manufacturer did not provide an IFU with the devices.
Regulatory obligations of notified body: Not fulfilled	The notified body did not communicate with the competent authority.
Deficiencies in reporting:	The reports from the end-users were not very detailed. The competent authority had to communicate with the health institution on several occasions to obtain more details on the incidents. The reports were not as template form, leading to reporting gaps. One of the reports lacked the x-ray requested as evidence.
	No MIR was provided by manufacturer.
The responses of economic operators were not in line with the regulation (EU) 2017/745	The manufacturer did not provide the MIR within the timeframe requested by the competent authority.
Oversight by the Competent Authority	The competent authority initiated communication with all stakeholders immediately, requested all required documentation, and started risk assessment.
	The competent authority requested recommendations from the advisory committee due to the risk to patients' safety and the lack of comprehension on the manufacturer's part.
	The competent authority is still waiting for the MIR.
	Regulatory actions taken: - Request for additional information from economic operators - Request for additional information from notified body - Request for additional information from reporting health institution / end-user - Request for advice from advisory committee
Trend Analysis	Incident was a recurring issue. No Trend analysis is being conducted.
Risk Analysis and Management	Risk assessment was conducted and found to be adequate by the manufacturer. Manufacturer stated that quality control will be strengthened.
	Result of risk assessment by CA differed to that of the manufacturer and the case was brought up to the advisory committee for discussion.
	Risk classification was not adequate considering the vulnerability of the patients, and the risk of deterioration of health.
CAPA	Not implemented
Integration of AI	AI could help regulators be more efficient in searching data on potential similar incidents from other global regulatory sources.
	The incident reports could be documented in a database where they are analysed for emerging trends, to be proactive if other similar cases emerge.
	Having communication platforms such as chatbots on the vigilance database could make communication between all stakeholders more efficient.
Training Needs	Training needs for adequate incident reporting by healthcare professionals
	Training needs for distributors regarding the regulatory responsibilities when making a device available on the local market. The device was put on the market without an IFU.
CASP-Based Critical Appraisal Checklist Score	68 points
	High Confidence Level – Strong Evidence
	Effective regulatory action is required

Table E - Incident Report 5	
Regulatory obligations of economic operators: Not fulfilled	The local distributor forwarded the incident reports and the requests of the competent authority to the manufacturer.
	The manufacturer sent an incomplete MIR to the competent authority.
Regulatory obligations of notified body: Fulfilled	The notified body communicated with the competent authority.
Deficiencies in reporting:	The reports from the end-users were not very detailed. The competent authority had to communicate with the health institution on several occasions to obtain more details on the incidents. The reports were not as template form, leading to reporting gaps.
	Manufacturer provided incomplete MIR without risk assessment.
The responses of economic operators were not in line with the regulation (EU) 2017/745	The manufacturer provided MIR without risk assessment, stating that incidents are non-reportable.
Oversight by the Competent Authority	The competent authority initiated communication with all stakeholders immediately, requested all required documentation, and started risk assessment.
	The competent authority requested recommendations from the advisory committee due to the risk to patients' safety.
	Regulatory actions taken: - Request for additional information from economic operators - Request for additional information from notified body - Request for additional information from reporting health institution / end-user - Request for advice from advisory committee
Trend Analysis	No Trend analysis is being conducted.
Risk Analysis and Management	Risk assessment was not conducted by the manufacturer.
	Result of risk assessment by CA stated that there was risk of deterioration of health and the case was brought up to the advisory committee for discussion.
CAPA	Manufacturer determined that the incidents were non-reportable through destructive tests conducted.
Integration of AI	AI could help regulators be more efficient in searching data on potential similar incidents from other global regulatory sources.
	The incident reports could be documented in a database where they are analysed for emerging trends, to be proactive if other similar cases emerge.
	Having communication platforms such as chatbots on the vigilance database could make communication between all stakeholders more efficient.
Training Needs	Training needs for adequate incident reporting by healthcare professionals
	Training needs for distributors regarding the regulatory responsibilities for storage and delivery conditions of medical devices.
CASP-Based Critical Appraisal Checklist Score	63 points
	High Confidence Level – Strong Evidence
	Effective regulatory action is required

Appendix VII

SWOT Analysis

Strengths	
Defined responsibilities for all stakeholders	Defined responsibilities for economic operators in post-market surveillance and vigilance, under the (EU) 2017/745 MDR and (EU) 2017/746 IVDR
	Defined responsibilities for notified bodies in post-market surveillance and vigilance, under the (EU) 2017/745 MDR and (EU) 2017/746 IVDR
Guidance for improved vigilance processes	Ensuring a comprehensive incident reporting system for healthcare professionals, patients, and manufacturers
	Regulatory personnel in competent authorities can align their work procedures not only to EU Regulations, but also to global standards such as the WHO guidelines, the IMDRF terminology guidelines, and ISO Standards such as ISO 13485 and ISO 14971
	AI-driven signal detection can improve efficiency of systems for oversight of post-market surveillance and vigilance
	Integrating the European Artificial Intelligence Regulation (EU) 2024/1689 [AI Act] with MDR and IVDR for a legal framework for vigilance before the AI Act's formal application date, as a proactive approach to ensure regulatory readiness of the personnel in competent authorities
Risk management and a proactive approach	Integrating trend analysis helps identify emerging risks
	Using risk analysis techniques such as those proposed in ISO 14971 increases harmonisation in risk management in post-market surveillance and vigilance
	Proactive approach to reduce risk of having substandard and falsified devices on the market
Training and capacity building	Training modules for healthcare professionals can improve reporting accuracy
	Training modules for regulatory employees in post-market surveillance and vigilance aim to increase efficiency and minimise risks. Using the adapted CASP tool aims to enhance vigilance skills.

Weaknesses	
Lack of harmonisation between EU and non-EU jurisdictions	There could be lack of harmonisation in requirements of the EU compared with those of other jurisdictions such as the USA or Japan, and also compared to global standards such as those of the WHO.
Limited human resources	There are limited resources to guide regulatory personnel in the detection of substandard and falsified devices. A strong global collaboration between all stakeholders from end-users to the competent authorities is a necessary tool in the fight against falsified devices (Świeczkowski et al, 2002).
	Resource allocation for oversight of post-market surveillance and vigilance can be a challenge for competent authorities.
	Training of regulatory personnel is expensive and time-consuming, and can place additional strain on already stretched resources in competent authorities.
Ongoing regulatory updates require continuous adaptation	Legacy devices may still lack robust PMS data. Continuous changes in MDR transitional provisions as per Article 120 of the MDR may create inconsistencies in compliance to PMS requirements.
	There is still uncertainty regarding AI-based post-market surveillance and vigilance, and how this is going to affect the working procedures of competent authorities.
	There are still no standardised AI post-market surveillance and vigilance protocols in the EU.
Complexity of vigilance processes	A complex reporting system can discourage healthcare professionals and patients from incident reporting with devices, mostly due to lack of time and knowledge respectively.
	Lack of public awareness campaigns on device vigilance leads to under-reporting from the patients and their carers.
	The '*CASP-Based Critical Appraisal Checklist for Medical Device Vigilance*' relies on report quality for optimal results. If the reports are not thoroughly completed by the reporter, there is a risk of having several "Can't Tell" responses, that may cause bias in the final score.

Opportunities	
Global standards for harmonisation and regulatory alignment	Global regulatory standards such as those of the WHO and ISO that are referenced in the framework may be used as an additional source of knowledge to help regulation of patient safety. Their integration into the work processes of competent authorities leads to more consistency and harmonisation.
	The integration of IMDRF terminology in reporting and in trend analysis leads to international alignment and harmonisation.
	Guidance on incident reporting for economic operators through digital platforms such as EUDAMED, WHO GSMS, and other national databases should be encouraged.
Implementing AI as a tool in PMS and vigilance oversight	AI-based real-world evidence can be used proactively in vigilance to avoid or decrease risk of serious incidents.
	Using AI in trend analysis and signal detection to manage to capture and analyse large sets of data increases efficiency.
	Competent authorities should look at AI as a necessary tool in PMS and vigilance activities.
Training modules to improve competency	Training modules for regulatory personnel are a means of ensuring and enhancing competency and expertise.
	Training modules specifically tailored for healthcare professionals improve awareness on the benefits of reporting and may promote a positive reporting culture.
JAMS 2.0 - the way forward for EU harmonisation	The *Joint Action on Reinforced Market Surveillance of Medical Devices and In Vitro Medical Devices* [JAMS 2.0] project aims to provide standardised protocols for surveillance and vigilance to enhance harmonisation.

Threats	
Limited experience with AI in regulatory context without best practice guidelines	The uncertainty in the intersection of the AI Act with the MDR and IVDR can hinder AI PMS and vigilance adoption, until further guidelines are established.
	Using AI tools in vigilance and trend analysis could cause bias and lead to misinterpretation of signals.
	Cybersecurity can be a complex process for regulatory systems.
	Having to comply with the General Data Protection Regulation [GDPR] may be complex and may conflict with the monitoring of real-time data for vigilance.
Lack of training and awareness on PMS and vigilance	Not all distributors and importers may invest in efficient PMS and vigilance systems, due to financial pressures and lack of awareness of their responsibilities as per the MDR/IVDR.
	Regulatory personnel need to be adequately trained on AI integration, to be able to provide the required training to other stakeholders involved in PMS and vigilance.
Lack of harmonisation and inconsistency may hinder tracking of falsified devices	Competent authorities may lack harmonised databases with traceable and transparent information on all devices placed on the market in their territory, making tracking of falsified devices difficult.
Procurement challenges and disruption of device access due to recalls	Recalls of devices as FSCAs can cause big problems to patients and healthcare institutions as an alternative device needs to be procured for the benefit of the patient.

Regulatory Oversight of Patient Safety in Medical Devices

Addendum

Ensuring Patient Safety Through Medical Device Regulatory Science
A Regulatory Framework for Competent Authorities
MD-PMSV-RF01

Submitted in partial fulfilment of the requirements of
the Degree of Doctorate in Pharmacy

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2025

Ensuring Patient Safety

through

Medical Device Regulatory Science

A Regulatory Framework for Competent Authorities

MD-PMSV-RF01

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Purpose

The purpose of this regulatory framework is to establish a robust and comprehensive system for competent authorities to monitor and oversee the safety, quality and performance of medical devices and *in vitro* diagnostic devices after they are placed on the market.

Aims

Aims		**This framework aims to:**
i.	**Ensuring Patient Safety**	protect patients by identifying, assessing, and mitigating risks associated with medical device use.
ii.	**Continuous Monitoring**	serve as a tool for regulators to continuously evaluate the safety and effectiveness of devices in real-world settings.
iii.	**Promotion of public trust**	increase the patient's trust in competent authorities by ensuring effective post-market oversight and by keeping an open communication regarding any risks.
iv.	**Encouraging innovation**	encourage the introduction of innovative devices and foster technological advancement while ensuring regulatory compliance.
v.	**Harmonisation of practices**	align oversight practices with EU and global regulatory standards.
vi.	**Verification of effectiveness**	be reviewed on a regular basis to verify its effectiveness and to have any modifications implemented, for the benefit of the patients.

Scope

This framework applies to all aspects of post-market surveillance and vigilance for medical devices and *in vitro* diagnostic devices.

It covers:

- all classes of medical devices – Class I, Class IIa, Class IIb, and Class III
- all classes of *in vitro* diagnostic devices – Class A, Class B, Class C, and Class D

Geographical scope – European Union

Definitions

EUDAMED
The European databank for medical devices. It is a secure, web-based portal which enables the exchange of information between National Competent Authorities and the European Commission. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Unique Device Identifier (UDI)
A series of numeric or alphanumeric characters that is created through internationally accepted device identification and coding standards and that allows unambiguous identification of specific devices on the market. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

CE Marking of Conformity
A marking by which a manufacturer indicates that a device is in conformity with the applicable requirements set out in this Regulation and other applicable Union harmonisation legislation providing for its affixing. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

User
Any healthcare professional or lay person who uses a device. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Economic Operator
A manufacturer, an authorised representative, an importer, a distributor, or the person referred to in Article 22(1) and 22(3) of the MDR. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Making available on the market
Any supply of a device, other than an investigational device, for distribution, consumption or use on the Union market in the course of a commercial activity, whether in return for payment or free of charge. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Post-Market Surveillance
All activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Incident
Any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Serious Incident
Any incident that directly or indirectly led, might have led or might lead to any of the following: (a) the death of a patient, user or other person, (b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health, (c) a serious public health threat. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Serious public health threat
An event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Risk
The combination of the probability of occurrence of harm and the severity of that harm. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Benefit-risk determination
The analysis of all assessments of benefit and risk of possible relevance for the use of the device for the intended purpose, when used in accordance with the intended purpose given by the manufacturer. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Risk-based classification system for IVDs & MDs
This is based on four risk classes: ▪ Class A: Low individual risk and low public health risk ▪ Class B: Moderate individual risk and low public health risk ▪ Class C: High individual risk and/ or moderate public health risk ▪ Class D: High individual risk and high public health risk

Field safety corrective action
A corrective action taken by a manufacturer for technical or medical reasons to prevent or reduce the risk of a serious incident in relation to a device made available on the market. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Field safety notice
A communication sent by a manufacturer to users or customers in relation to a field safety corrective action. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Recall
Any measure aimed at achieving the return of a device that has already been made available to the end user. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Total recall
The action of withdrawing all batches from the distribution chain and users.

Defect classification
Recalls are classified with regards to the relative health hazard associated with the use of or exposure to the recalled product; Class I: defects are potentially life threatening. Class II: defects could cause illnesses or mistreatment but are not Class I. Class III: defects may not pose a significant hazard to health, but withdrawal may be initiated for other reasons. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Depth of recall
The level within the distribution channel from which a product is recalled, i.e.: wholesale, retail, user/consumer. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Rapid alert
An urgent notification from one supervisory authority to other authorities that a batch recall has been instituted in the country originating the rapid alert. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Withdrawal
Any measure aimed at preventing a device in the supply chain from being further available from the market. [Regulation (EU) 2017/745 & Regulation (EU) 2017/746]

Abbreviations

AI	Artificial Intelligence
AIMDD	Active Implantable Medical Device Directive
CAPA	Corrective and Preventive Action
CASP	Critical Appraisal Skills Programme
CE	Conformité Européene (CE marking of conformity)
CEF	Compliance Exchange Form
DoC	Declaration of Conformity
DSVG	Device Specific Vigilance Guidance
EMDN	European Medical Device Nomenclature
FSCA	Field Safety Corrective Action
FSN	Field Safety Notice
GHTF	Global Harmonization Task Force (now replaced by the IMDRF)
IEC	International Electrotechnical Commission
IFU	Instructions for Use
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IVDR	*In Vitro* Diagnostic Medical Device Regulation
IVDs	*In Vitro* Diagnostic Devices
JAMS 2.0	Joint Action on Reinforced Market Surveillance of Medical Devices and *in Vitro* Medical Devices

MDCG	Medical Device Coordination Group
MDD	Medical Device Directive
MDPCD	Medical Devices and Pharmaceutical Collaboration Directorate (Malta)
MDR	Medical Device Regulation
MDs	Medical Devices
MIR	Manufacturer Incident Report
ML	Machine Learning
PMCF	Post-Market Clinical Follow-Up
PMS	Post-Market Surveillance
PRRC	Person Responsible for Regulatory Compliance
PSUR	Periodic Safety Update Report
QMS	Quality Management System
SaMD	Software as Medical Device
SOPs	Standard Operating Procedures
SPH	Superintendent of Public Health (Malta)
SSCP	Summary of Safety and Clinical Performance
UDI	Unique Device Identifier
UDI-DI	Unique Device Identifier-Device Identifier
WHO	World Health Organization

Roles and Responsibilities of Stakeholders for Post-Market Surveillance and Vigilance Activities

6.1 Manufacturers

i.	A manufacturer means "a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trade mark" [(EU) 2017/745 Article 2 (30)]
ii.	Manufacturers are responsible for the implementation and maintenance of a post-market surveillance system [(EU) 2017/745 Article 83]
iii.	If a device placed on the market or put into service does not conform with the Regulations, the manufacturers are responsible to carry out corrective and preventive actions (CAPA), withdraw or recall the device as necessary.
iv.	Manufacturers are responsible to inform other economic operators involved of the non-conformity of the device and of the consequential action.
v.	In serious incidents, the manufacturers are responsible to immediately inform the competent authorities of the Member States where their device is marketed.
vi.	In serious incidents with devices of Class Is, Im, Ir, IIa, IIb and III, the manufacturers are also responsible to immediately inform the notified body that issued the certificate for that particular device.
vii.	Manufacturers are responsible for maintaining a system to record and report incidents and field safety corrective actions (FSCA).
viii.	Manufacturers are responsible for cooperation with the competent authority if asked for any documentation, or if asked to carry out any corrective action deemed necessary by the competent authority to mitigate any risk.

ix.	Manufacturers need to have one or more persons responsible for regulatory compliance (PRRC), with expertise in regulatory affairs or in quality management systems in the area of medical devices. The PRRC will be responsible for all post-market surveillance obligations, and vigilance reporting obligations of the manufacturer.
x.	Manufacturers are responsible for having a post-market surveillance report for class Is, Im and Ir devices, and this must be available to the competent authority upon request.
xi.	Manufacturers are responsible for preparing and maintain a periodic safety update report (PSUR) for class IIa, IIb and III devices. This PSUR should be updated every two years for class IIa devices, and annually for class IIb and III devices.
xii.	The manufacturer is responsible for drawing up a summary of safety and clinical performance (SSCP) for Class III and implantable devices. It includes information on the device, a summary of clinical evaluation, post-market clinical follow-up (PMCF) information and any warnings. This SSCP is submitted to the notified body for validation, and then is made available to the public via EUDAMED by the notified body.
xiii.	Manufacturers are responsible for a post-market surveillance system that is proportionate to the risk class of the device and that monitors the safety and performance of the device throughout its lifetime, as per Article 83 of (EU) 2017/745.

6.2 Authorised Representatives

i.	An authorised representative means “any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer, located outside the Union, to act on the manufacturer's behalf in relation to specified tasks with regard to the latter's obligations under this Regulation” [(EU) 2017/745 Article 2 (32)]
ii.	Authorised representatives are responsible for cooperation with the competent authority if asked for any documentation, or if asked to carry out any corrective action deemed necessary by the competent authority to mitigate any risk, as per mandated designation by the manufacturer.
iii.	Authorised representatives must inform the manufacturer immediately about any complaints and reports from healthcare professionals, patients and other end-users of devices that they are designated for.

6.3 Importers

i.	An importer means “any natural or legal person established within the Union that places a device from a third country on the Union market” [(EU) 2017/745 Article 2 (33)]
ii.	Importers are responsible to inform the competent authority of the Member State in which they are established of any serious risks caused by the device.
iii.	Importers are responsible for maintaining a register of complaints, recalls and withdrawals of non-conforming devices and inform the manufacturers, authorised representatives, and distributors of the non-conformity, providing any information necessary for investigation from their end.
iv.	In serious incidents, importers are responsible to immediately inform the competent authorities of the Member States where their device is made available.
v.	In serious incidents with devices of Class Is, Im, Ir, IIa, IIb and III, importers are also responsible for immediately informing the notified body that issued the certificate for that particular device.
vi.	Importers must inform the manufacturers and authorised representatives immediately about any complaints and reports from healthcare professionals, patients and other end-users of devices that they have placed on the market.
vii.	If importers change intended purpose of device, modify device, or register device under their name or trade mark, they shall assume the obligations of manufacturers, as per Article 16 of (EU) 2017/745.

6.4 Distributors

i.	A distributor means “any natural or legal person in the supply chain, other than the manufacturer or the importer, that makes a device available on the market, up until the point of putting into service” [(EU) 2017/745 Article 2 (34)]
ii.	In cases of non-conformity of the device, distributors are responsible of informing manufacturers, authorised representatives and importers of the non-conformity, and refrain from making the device available on the market until brought to conformity.
iii.	In serious incidents, distributors are responsible to immediately inform the competent authority of the Member State where it is established. This has to be done also in cases where the distributor is initiating the FSCA.
iv.	Distributors are responsible for cooperating with manufacturers, authorised representatives, importers, and competent authorities to ensure that CAPAs, withdrawals or recalls are undertaken as necessary for non-conforming devices.
v.	If the distributor has made the device available in other Member States than that in which it is established, the distributor is responsible to immediately inform the competent authorities of these Member States in cases of serious incidents.
vi.	Distributors must inform the manufacturers, authorised representatives, and importers, immediately about any complaints and reports from healthcare professionals, patients, and other end-users of the device that they have made available on the market.
vii.	Although the manufacturer is responsible for issuing of FSNs, distributors should still have procedures as part of their QMS to handle FSCAs that are notified by the manufacturers of the devices they distribute.

viii.	Distributors are responsible for maintaining a register of complaints, recalls and withdrawals of non-conforming devices and inform the manufacturers, authorised representatives, and importers of the non-conformity, providing any information necessary for investigation from their end.
ix.	A recall procedure should also be part of the QMS of the distributor, to ensure traceability and effectiveness. This procedure needs to take into consideration the reconciliation of the devices placed on the market by the distributor and the quantities that are collected from the end-user.
x.	Distributors are responsible for cooperation with the competent authority if asked for any documentation, or if asked to carry out any corrective action deemed necessary by the competent authority to mitigate any risk.
xi.	If distributors change intended purpose of device, modify device, or register device under their name or trade mark, they shall assume the obligations of manufacturers, as per Article 16 of (EU) 2017/745.
xii.	Distributors are responsible for maintaining traceability of the devices that they are making available on the market. This is done by keeping records of: ▪ all the suppliers that devices are obtained from ▪ all the customers supplied with a device, e.g. clinical institutions, pharmacies, healthcare professionals ▪ invoices related to devices ▪ receipts of tenders awarded for the National Health System ▪ details of all devices, including name, codes, batch/lot numbers, quantities supplied ▪ contact details of all the economic operators who supply them with the devices

	▪ internal audits Any of these records can be requested by the competent authority. These records must be kept by the distributor for 10 years after the last device has been placed on the market. If the device is implantable, the records must be kept for 15 years after the last device has been placed on the market.
xiii.	Distributors are not obliged to register themselves as actors in the 'Actor Registration' module on EUDAMED. In the local scenario, since the majority of economic operators are distributors, it is necessary that all distributors notify the competent authority regarding their business and also the devices that they are placing on the market.

6.5 Notified Bodies

i.	A notified body means “a conformity assessment body” designated as per (EU) 2017/745 MDR and/or (EU) 2017/746 IVDR.
ii.	As per Article 56 of (EU) 2017/745, if the notified body should find that the manufacturer is not compliant with the Regulations, it can suspend or withdraw the certificate or impose restrictions on it until the manufacturer takes the necessary corrective actions.
iii.	Until the EUDAMED post-market surveillance and vigilance module is operational and mandatory, the notified body must discuss with the manufacturer on the best procedure used to be advised on serious incidents.
iv.	The notified body is responsible for reviewing the periodic safety update report (PSUR) of the device. The PSUR for class III and implantable devices will be submitted to the notified body through EUDAMED. The notified body is responsible for adding its evaluation of the report on EUDAMED. The PSUR for other device classes is made available to the notified body. The notified body should ensure that the PSUR of class IIa devices is updated every two years, while that of class IIb and class III devices is updated annually.

Oversight of Post-Market Surveillance Activities by the Competent Authority

The oversight of post-market surveillance is a critical regulatory function that ensures that medical devices and *in vitro* diagnostic devices continue to meet safety, quality and performance standards, throughout their lifecycle, after they are placed on the market. The competent authority aims to identify, assess and mitigate any risks that emerge after these devices are placed on the market, with the main target of protecting public health and promoting continuous improvement in the quality and safety of these devices.

i.	▪ The role of the competent authority is to oversee that economic operators comply with EU and national post-market surveillance requirements. ▪ Malta's local scenario is different to other EU Member States, mainly due to its smaller size. There are few local manufacturers and importers, but a large number of distributors. ▪ The competent authority should keep an updated database containing details of all manufacturers, importers, distributors and authorised representatives operating on its territory.
ii.	The key legal requirements under MDR (EU) 2017/745 and IVDR (EU) 2017/746 are: ▪ PMS System Requirements [Article 83 (MDR) / Article 78 (IVDR)] ▪ PMS Plan [Article 84 (MDR) / Article 79 (IVDR)] ▪ PMS Report [Article 85 (MDR) / Article 80 (IVDR)] ▪ Periodic Safety Update Report [Article 86 (MDR) /Article 81 (IVDR)] ▪ Post-Market Clinical Follow-Up [Annex XIV (MDR)] Post-Market Performance Follow-Up [Annex XIII (IVDR)]

iii.	A PMS system that is proportionate to the risk class and type of the device must be integrated into the manufacturer's QMS, complying with the MDR / IVDR and ISO 13485 requirements. This PMS system: ▪ Confirms device safety and performance throughout its lifecycle ▪ Identifies any need for CAPAs ▪ Detects issues as early as possible ▪ Contributes to continuous risk management as required by Annex I of the MDR ▪ Aids in updating product information such as instructions for use and labelling of device ▪ Aids in improving device design
iv.	A PMS Plan, as mentioned in Article 84 of the MDR / Article 79 of the IVDR, should be drawn up for all devices, as per requirements listed down in Annex III of the MDR / IVDR. These include: ▪ Systematic, proactive monitoring of device performance ▪ Comparison with similar products on the market ▪ Risk-benefit assessment updates with defined indicators and thresholds ▪ Investigation of complaints ▪ Trend reporting ▪ Clear communication protocols with competent authorities and other stakeholders ▪ CAPAs ▪ Post-Market Clinical Follow-Up where necessary This PMS Plan shall be a part of the technical documentation of every device.

v.	The PMS Report must be prepared for all Class I devices, giving a summary of the analyses of PMS data and any CAPAs taken if needed. The competent authority can request this report when necessary.
vi.	For Class IIa, IIb, and III devices, a PSUR is needed to give a summary of the analyses of PMS data and any CAPAs taken if needed. The PSUR includes: ▪ Conclusion of benefit-risk determination ▪ Summary of findings of the Post Market Clinical Follow Up ▪ Volume of sales, usage frequency, and details of population using device The PSUR should be part of the technical documentation of the device. The PSUR is updated annually for Class IIb and class III devices. The PSUR is updated every two years for Class IIa devices. For Class III and implantable devices, the PSUR should be submitted by the manufacturer to the notified body through EUDAMED. The notified body adds its own evaluation. The competent authority can access this PSUR through EUDAMED. For Class IIa and IIb non-implantable devices, the PSUR is made available to the notified body. If requested, the PSUR is made available to the competent authority.
vii.	▪ Annex XIV of the MDR set down the requirements for a Post-Market Clinical Follow-Up (PMCF) process, where real-world clinical data is collected and evaluated after the device is placed on the market. This is done through a PMCF Plan, which must be integrated into the overall clinical evaluation strategy, ensuring that any new clinical data is used to update the evaluation continuously. A PMCF Plan is a requirement for devices of all classes, including legacy devices. A template of the PMCF

	Plan is provided in MDCG 2020-7 *Post-market clinical follow-up (PMCF) Plan Template - A guide for manufacturers and notified bodies* to increase harmonisation between the manufacturer, the notified body and the competent authorities. The findings are documented in a PMCF evaluation report, and this is included in the clinical evaluation report and the technical documentation of the device for review by the notified bodies. A template of the PMCF Evaluation Report is provided in MDCG 2020-8 *Post-market clinical follow-up (PMCF) Evaluation Report Template - A guide for manufacturers and notified bodies* to increase harmonisation between the manufacturer, the notified body and the competent authorities. The PMCF Evaluation Report must be updated annually for Class III and implantable devices and uploaded on EUDAMED. ▪ In the IVDR, Annex XIII provides the requirements for a Post-Market Performance Follow-Up (PMPF) which give an ongoing evaluation of the device's performance and risk in real-world conditions. The findings from the PMPF must be integrated into risk management processes [ISO 14971 compliance]. The findings are documented in a PMPF evaluation report, and this updates the performance evaluation report and the technical documentation of the device. In re-assessment of notified bodies, the competent authority can review PMCF/PMPF evaluation reports to verify that there is proper assessment of long-term safety and performance with adequate clinical data collection methods.

7.1 Substandard and Falsified Medical Devices

Substandard and falsified (SF) medical devices are products that fail to meet quality and safety standards.

As per (EU) 2017/745 Article 2 (9):

A falsified device means “any device with a false presentation of its identity and/or of its source and/or its CE marking certificates or documents relating to CE marking procedures. This definition does not include unintentional non-compliance and is without prejudice to infringements of intellectual property rights”.

The critical role of the competent authority in minimising the risks associated with substandard and falsified medical devices to safeguard public health includes several strategies:

i.	All devices made available on the national market should be notified to the Authority and these are kept on a database which is regularly updated.
ii.	All the notified devices have the UDI number for easy traceability throughout their lifecycle. For legacy devices without a UDI number, the Authority could issue an identification number to be used until the transition period to conformity with the MDR/IVDR is over, or until EUDAMED is fully functional to link the legacy device to the Regulation-compliant device.
iii.	Assessing notified bodies and ensuring that they do a thorough assessment of the technical documentation of the devices within their scope.
iv.	Conducting inspections of the economic operators routinely.

v.	Conducting inspections of any facilities that may sell medical devices, keeping in mind that some devices are even sold in facilities such as supermarkets, and not just in a healthcare environment.
vi.	Having quality control laboratories manned by personnel with expertise to ensure the quality of devices. If there is a report from the public or healthcare professionals of any suspected falsified or substandard devices, the device could easily be analysed in the laboratories of the competent authority, and action could be taken within a shorter timeframe.
vii.	Incorporate a tool on the online medical device vigilance system that can be used by members of the public who wish to report non-compliances or suspicions of falsified devices in a confidential manner.
viii.	Investigate incident reports of device failures as potential substandard or falsified devices.
ix.	Collaborate with the media to increase awareness by spreading information about falsified medical devices. Increase awareness of the general public in identifying genuine medical devices from falsified devices.
x.	Collaborate with health institutions to increase awareness of substandard devices among healthcare professionals and to increase reporting.
xi.	Prepare a legal notice to target the distribution of falsified medical devices, together with the legal office of the competent authority, to enable the authority to take legal action against any companies that are found to be involved in the production or the distribution of these devices. Legal actions may consist of fines, product recalls and business closure.

xii.	Collaborate with the Customs Department to avoid falsified devices from reaching the patients.
xiii.	Exchange information and best practices with other competent authorities and global organisations to ensure the safety and quality of devices reaching the patients.
xiv.	Participate in meetings of the Member State Mechanism on Substandard and Falsified Medical Products organised by the WHO to benefit from global recommendations. Analyse data and reports of falsified medical products available on the WHO Global Surveillance and Monitoring System.

7.2 Custom-made Devices

Custom-made devices are devices "specifically made in accordance with a written prescription of any person authorised by national law by virtue of that person's professional qualifications which gives, under that person's responsibility, specific design characteristics, and is intended for the sole use of a particular patient exclusively to meet their individual conditions and needs." A mass-produced device is not considered a custom-made device, even if produced in accordance with a written prescription.
[(EU) 2017/745 Article 2 (3)]

Requirements for Custom-made Devices:

i.	"Manufacturers of custom-made devices shall follow the procedure set out in Annex XIII and draw up the statement set out in Section 1 of that Annex before placing such devices on the market." [(EU) 2017/745 Article 52] If the devices are class III custom-made implantable devices, they shall also be subject to the conformity assessment as specified in Chapter I of Annex IX of the MDR or Part A of Annex XI of the MDR.
ii.	This statement should contain the following information: - Details of manufacturer including all manufacturing sites - Details of authorised representative, if applicable - Details on the device - The identification of the patient or user for whom the device is exclusively intended [name, acronym or numerical code] - Details of the prescriber and health institution - Details on the specific characteristics of the device as prescribed

	- Conformity to the general safety and performance requirements of Annex I of the MDR - Justification in the case that any general safety and performance requirements of Annex I of the MDR are not met - If applicable, a statement that the device contains a medicinal substance, human blood or plasma derivative, or tissues or cells of human or animal origin This statement should be kept for a period of 10 years after the device has been placed on the market, and for 15 years if the custom-made device is implantable.
iii.	For custom-made devices, the *Person Responsible for Regulatory Compliance* (PRRC) may demonstrate the requisite expertise by having two years of relevant professional experience instead of four years. The PRRC does not need to be registered in EUDAMED.
iv.	Custom-made devices do **not** need the CE mark.
v.	Custom-made devices do **not** need the UDI-DI.
vi.	Custom-made devices do **not** need a *Summary of Safety and Clinical Performance* (SSCP).
vii.	Custom-made devices do **not** need a post-market surveillance plan as part of the technical documentation.
viii.	A post-market surveillance report for Class I custom-made devices and a Periodic Safety Update Report (PSUR) for Class IIa, IIb and III custom-made devices is required. However, for Class III implantable custom-made devices, the PSUR does not need to be sent to the notified bodies or EUDAMED as for other Class III implantable devices, but kept as part of the documentation of the device.

ix.	If Article 52 (8) of the MDR and Annex XIII of the MDR have been complied with, Member States cannot stop the custom-made device from being available on the market, as per Article 21 of the MDR.
x.	The manufacturer has to submit a list of such devices available in the territory to the competent authority.
xi.	The manufacturer should apply post-market surveillance, clinical evaluation, risk management and vigilance obligations, to groups of custom-made devices with the same intended purpose, materials used, process utilised and same design, and not to each individual design.
xii.	The manufacturer has to report any serious incidents and FSCAs immediately to the competent authority, as for other devices.
xiii.	The competent authority should keep a database with a list of all the custom-made devices available on its territory.
xiv.	Once it receives a list of custom-made devices from a manufacturer, the competent authority should inform that manufacturer of the legal obligations required, especially those for vigilance.
xv.	Prescribers of custom-made devices, such as dental surgeons, orthodontists, and orthopaedic surgeons, should be reminded, on a regular basis, about the importance of reporting any vigilance issues with the device they have prescribed. An email with a direct link to the competent authority to report such issues could be sent.
xvi.	It is of absolute importance to respect patient confidentiality, since the statement of information received from the manufacturer could contain the specific name of the patient instead of an acronym or code.

A template for the statement to be provided by manufacturers of custom-made devices has been created, taking into consideration the requirements of Section 1 of Annex XIII of the MDR and MDCG 2021-3 *Questions and Answers on Custom-Made Devices (& considerations on Adaptable medical devices and Patient-matched medical devices).* This template is to be made available on the website of the competent authority as an aid to manufacturers who want to place a custom-made device on the market.

STATEMENT FOR CUSTOM-MADE DEVICES AS PER SECTION 1 OF ANNEX XIII OF THE MDR (EU) 2017/745	
Manufacturer Details	
Name	
Address	
List all Manufacturing Sites	
Authorised Representative Details (if applicable)	
Name	
Address	
Device Details	
Name or Reference of Device	

Description of Device	
Specific Characteristics of the Device Unique to the Patient/User Anatomic-Physiological Features or Pathological Condition	
Image of Device	
Patient/User Details	
Name/Acronym/Code	
Prescriber Details	
Name	
Occupation	
Clinic Details (if applicable)	
Legal Requirements	

A. This custom-made device conforms with General Safety and Performance Requirements as defined in Annex I of the MDR (EU) 2017/745. ☐ Yes ☐ No	
If your answer is No, list Exceptions with Justifications	
B. This custom-made device incorporates a medicinal substance, including human blood or plasma derivative, or tissues of human or animal origin. ☐ Yes ☐ No	
Signature	

Figure 1. Statement Template for Custom-Made Devices.
[Applied from Annex XIII of the MDR and MDCG 2021-3 Questions and Answers on Custom-Made Devices (& considerations on Adaptable medical devices and Patient-matched medical devices.)
Available from URL: (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745) and (https://health.ec.europa.eu/document/download/385d7e20-d8b5-49d0-abd7-8daf269bf1b8_en?filename=mdcg_2021-3_en)]

7.3 Legacy Devices

As per MDCG 2021-25 Rev.1 *Application of MDR requirements to* ***"legacy devices"*** *and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC*, legacy medical devices are "devices, which, in accordance with Article 120(3) of the MDR, are placed on the market or put into service after the MDR's date of application (DoA) and until either 31 December 2027 or 31 December 2028 if the conditions set in Article 120(3c) of the MDR are fulfilled.

Those devices can be:

- devices which are class I devices under Directive 93/42/EEC (MDD), for which an EC declaration of conformity was drawn up prior to 26 May 2021 and for which the conformity assessment procedure under the MDR requires the involvement of a notified body;
- devices covered by a valid EC certificate issued in accordance with Directive 90/385/EEC (AIMDD) or the MDD prior to 26 May 2021."

As per MDCG 2022-8 *Regulation (EU) 2017/746 - application of IVDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2022 in accordance with Directive 98/79/EC*, legacy *in vitro* devices are "s IVDs, which, in accordance with the IVDR's transitional provisions, are placed on the market or put into service after the IVDR's date of application (i.e. 26 May 2022) if certain conditions are fulfilled.

Those devices can be:

- devices covered by a valid EC certificate issued by a notified body in accordance with Directive 98/79/EC on *in vitro* diagnostic medical devices (IVDD) prior to 26 May 2022;

- devices for which a declaration of conformity was drawn up prior to 26 May 2022 in accordance with the IVDD and for which the conformity assessment procedure pursuant to the IVDR (contrary to the IVDD) requires the involvement of a notified body.

Requirements for Legacy Devices:

i.	All legal requirements of the MDR relating to post-market surveillance, market surveillance and vigilance of devices apply to legacy devices (since 26 May 2021).
ii.	The risk class of the legacy device is the one in accordance with the MDD. If the legacy device will have a change of risk class under the MDR, this is used only to determine the end of the transitional period.
iii.	Consider active implantable devices and their accessories as Class III to apply the relevant MDR requirements.
iv.	All obligations of economic operators under the MDR apply to economic operators of legacy devices.
v.	The Declaration of Conformity for legacy devices refers to the MDD or AIMDD. The manufacturer may add DoC with Article 120 of the MDR, and ensure traceability of all versions of the DoC.
vi.	Manufacturers must also have in place a QMS in accordance with Article 10(9) of the MDR since 26 May 2024, or Article 10(8) of the IVDR since 26 May 2025. There are legal exceptions to the QMS of legacy devices: ▪ no need for all general safety and performance requirements as for other devices under the MDR / IVDR

	▪ no need for a risk management system that is required for other devices in Section 3 of Annex I of the MDR / IVDR ▪ no need for clinical evaluation as per Article 61 and Annex XIV of the MDR ▪ no need for performance evaluation as per Article 56 and Annex XIII of the IVDR The manufacturer has to state how compliance with these MDR / IVDR requirements will be achieved during the transitional period.
vii.	Legacy devices do **not** need UDI-DI.
viii.	Legacy devices do **not** need a Person Responsible for Regulatory Compliance (PRRC) as required by Article 15 of the MDR and Article 15 of the IVDR. [Inclusion of PRRC oversight could be suggested to economic operators even if not mandated as this would help in reinforcing regulatory continuity during the transition period, particularly for PMS and vigilance obligations under MDR/IVDR.]
ix.	Legacy devices do **not** need to abide by the requirements of Article 16(3) and (4) of the MDR, where the distributors and importers are required to: ▪ have their own QMS in place ▪ putting their details on the device or on the packaging of the device ▪ informing the manufacturer and the competent authority where they intend to make the device available, and provide a sample of device, 28 days prior to making device available on the market ▪ submit to the competent authority the notified body certificate 28 days prior to making device available on the market

x.	Implantable legacy devices do **not** need Implant cards as requested by Article 18 of the MDR.
xi.	In the case of systems and procedure packs containing legacy devices, the transitional period for the pack ends when the transitional period for the legacy device of the highest risk class ends.
xii.	Implantable legacy devices are exempt from having a Summary of Safety and Clinical Performance (SSCP) as part of the documentation that is required for implantable and class III devices under Article 32 of the MDR. Class C and D IVD legacy devices are also exempt from having a Summary of Safety and Performance as requested in Article 29 of the IVDR.
xiii.	There is no requirement for a full revision of the technical documentation as required by Annex II and Annex III of the MDR / IVDR.
xiv.	Class I legacy devices still need to have a PMS report as per Article 85 of the MDR, even though these devices might now be classified in a higher class under the MDR.
xv.	The PSUR of Class IIa, IIb and III devices should be made available to competent authorities and notified bodies outside EUDAMED. Class C and D IVD legacy devices are exempt from having a PSUR as requested in Article 81 of the IVDR.

The transition period under the MDR:

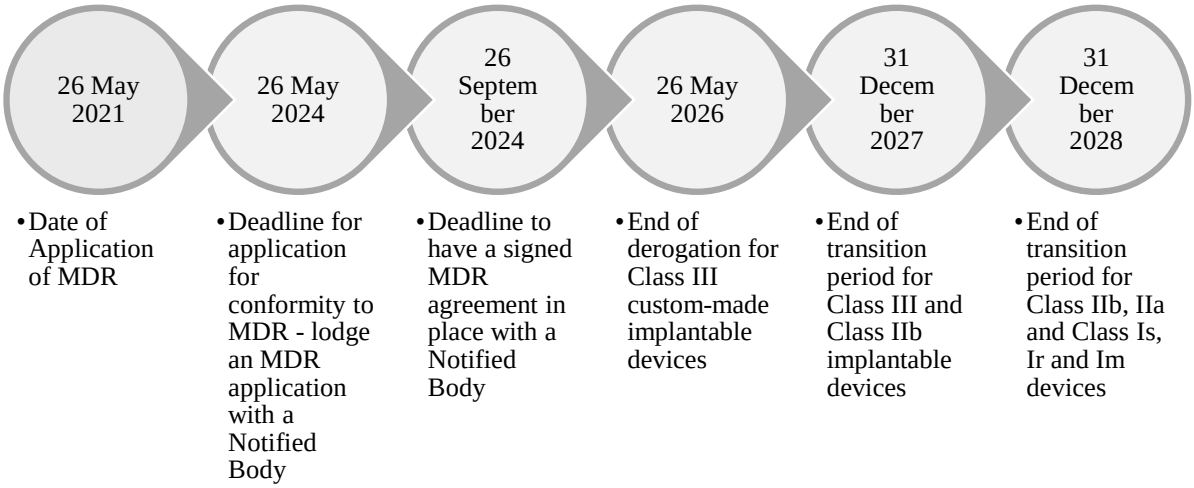

Figure 2. MDR Transition Period

The transition period under the IVDR:

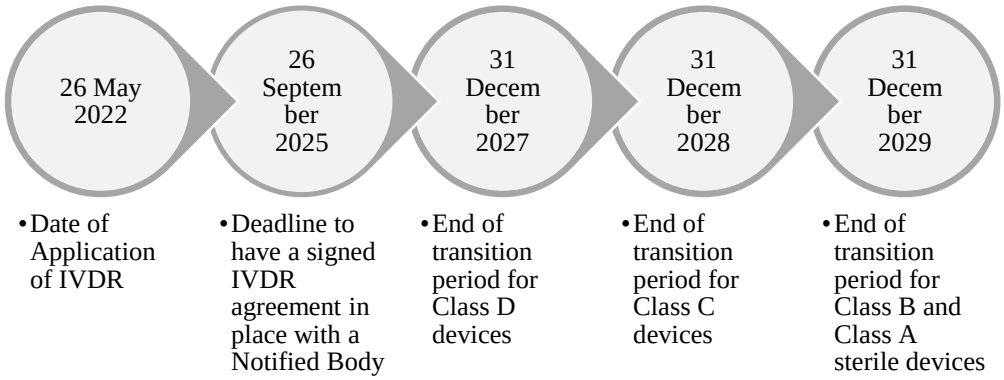

Figure 3. IVDR Transition Period

Vigilance

8.1 Incident Reporting

When an incident report related to an issue with a medical device is received by the competent authority, a systematic process must be followed to assess this report, and the appropriate actions need to be taken. An incident report can be received from a manufacturer or another economic operator, or it can be received from a healthcare professional, a patient, or another end-user. An incident is classified as serious when there is reasonable possibility of a causal relationship between the incident and the device, and when the incident leads, or might potentially lead, to significant adverse health outcomes.

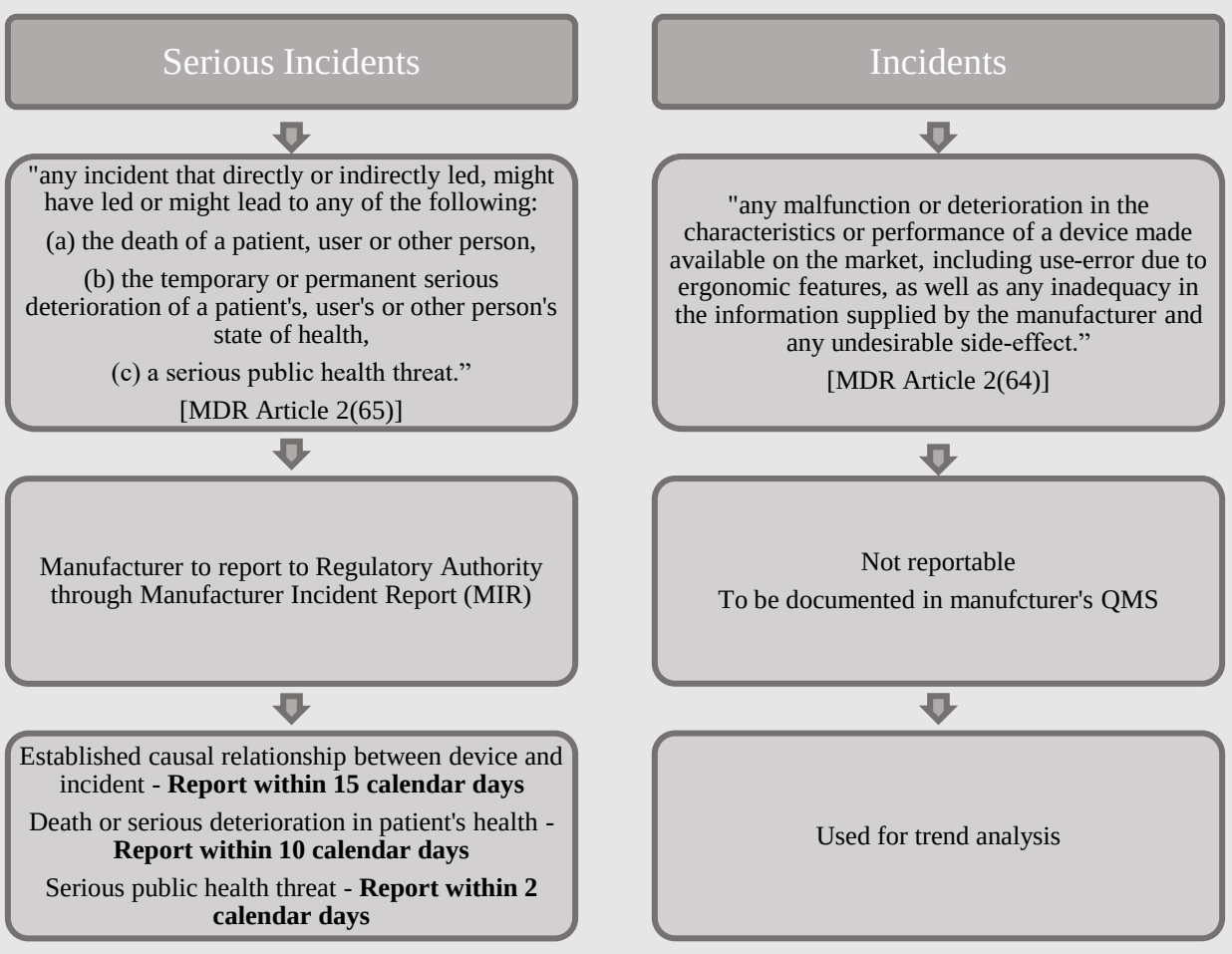

Figure 4. Serious Incidents vs Incidents [as per (EU) 2017/745 MDR]

8.1.1 Receiving a Medical Devices Incident Form

i.	▪ **Healthcare Professionals** A guidance document for healthcare professionals with comprehensive instructions on how to report a safety issue with a medical device should be made available. The competent authority should provide a '*Medical Devices Incident Report Form for Healthcare Professionals'* on their website. This form is to be filled in electronically. ▪ **Patients, Carers and other End-users** A guidance document for the general public with comprehensive instructions on how to report a safety issue with a medical device should be made available. The competent authority should provide a '*Medical Devices Incident Report Form for the General Public'* on their website. This form is to be filled in electronically. The public can send an email or call the Authority for help in filling the form.
ii.	Once the form is received by the competent authority, an acknowledgement is sent to the reporter.
iii.	The incident report is registered and assigned a reference number on the database of the competent authority. Details of the incident, the device, and the reporter are included in database.
iv.	If the report is found to be related to a medical device or an *in vitro* diagnostic device, the supplier details need to be identified.

v.	A risk analysis needs to be carried out on the incident report, leading to risk classification of the report. Intrinsic risk can be classified as: Very Low Risk, Low Risk, Medium Risk, High Risk, Very High Risk, and Extremely High Risk. This risk classification guides the timeline score, where: ▪ in low risk [Very Low Risk, Low Risk] – stakeholder is informed within 4 days ▪ in medium risk [Medium Risk] – stakeholder is informed within 3 days ▪ in high risk [High Risk, Very High Risk, Extremely High Risk] – stakeholder is informed within 2 days
vi.	The supplier, manufacturer, and if applicable, the notified body, are notified of the incident.
vii.	The manufacturer sends the initial Manufacturer Incident Report (MIR).
viii.	The initial MIR is followed up with documentation and clinical feedback.
ix.	The manufacturer sends the final MIR. [There may be cases where the initial and final MIR are provided in one report.]
x.	The final MIR is analysed by the designated assessor and documented.
xi.	The incident report, together with the collected information, is then discussed within a Vigilance Advisory Committee. The Advisory Committee should be composed of regulatory experts, clinical experts, procurement experts and representatives of economic operators involved in the incidents.
xii.	All stakeholders involved are informed with the outcome decided upon by the Vigilance Advisory Committee.

xiii.	The competent authority ensures that all the required actions are taken.
xiv.	The incident report is closed and documented in database.

8.1.2 Receiving a Manufacturer Incident Report

i.	Under the EU Regulations, manufacturers are obliged to report to the competent authorities any serious incidents or field safety corrective actions involving medical devices that are made available on the Union Market.
ii.	The competent authority should have a link easily available on its website for manufacturers or their authorised representatives to report vigilance issues.
iii.	Importers and distributors should also be able to report any vigilance issues on the same link on the Authority's website.
iv.	When an initial Manufacturer Incident Report (MIR) is received, the competent authority acknowledges its receipt and initiates the evaluation of this report.
v.	The severity of the incident report is assessed, and the incident should be classified according to risk.
vi.	Serious incidents with CE-marked devices used in clinical investigations or in performance studies should also be reported.
vii.	The competent authority must ensure that the report contains as much comprehensive detail as possible on the manufacturer, device, incident, and any Field Safety Correction Action (FSCA) to be carried out. Although the initial MIR can have missing information to allow the manufacturer to send it immediately, the final MIR should be detailed, and all required criteria should be filled in.

viii.	IMDRF adverse event terms and codes increase harmonisation and ease communication between the economic operators and the competent authority. The use of these codes should be encouraged. [See Appendix A]
ix.	European Medical Device Nomenclature (EMDN) codes are mandatory for device registration in EUDAMED. When EUDAMED is fully functional, these codes will be mandatory across all relevant modules, including vigilance. Using these codes in incident reports will facilitate categorisation of reports by competent authorities, improve trend detection, and enable easier transition into future EUDAMED workflows. To find EMDN codes, browse this link: https://health.ec.europa.eu/medical-devices-topics-interest/european-medical-devices-nomenclature-emdn_en
x.	The root cause analysis and the manufacturer's initial investigation is assessed.
xi.	The competent authority verifies if the incident is isolated or if there are more similar incidents with the same device. The competent authority sends Compliance Exchange Form (CEF) if necessary to other competent authorities in other member states to enquire about the possibility of other similar incidents with the device.
xii.	If after the initial MIR, the manufacturer establishes that the incident is not serious, the final MIR should be marked 'Final (Non-reportable incident)', and a rationale for this conclusion should be provided, as per MDCG 2023-3 Rev.2 *Questions and Answers on vigilance terms and concepts as outlined in the Regulation (EU) 2017/745 and Regulation (EU) 2017/746.*

	If the CA does not agree with this decision, this is communicated with the manufacturer and other economic operators involved, and the case is taken up to the Advisory Committee for recommendations on way forward.
xiii.	The manufacturer must carry out FSCAs to prevent or reduce the risks of a serious incident. Examples of such FSCAs are provided in Question 17 of MDCG 2023-3 Rev.2 *Questions and Answers on vigilance terms and concepts as outlined in the Regulation (EU) 2017/745 and Regulation (EU) 2017/746.* The manufacturer's FSCAs need to be evaluated for adequacy. The competent authority should coordinate with the manufacturer to see that Field Safety Notices (FSNs) are issued in the required timeframe as proposed in the MDR/IVDR. The FSNs received should be uploaded on the competent authority's website. When EUDAMED is fully functional, the FSNs need to be uploaded by the manufacturer to be accessible to the general public. The FSN should include: ▪ Identification of device using basic UDI-DI and EMDN codes for traceability ▪ Identification of manufacturer ▪ Level of risk of incident ▪ Reasons for FSCA ▪ Any actions to be taken by users [as per (EU) 2017/745 Article 89 and (EU) 2017/746 Article 84]
xiv.	If the manufacturer refuses to take the appropriate corrective action, especially in the necessity of a recall or withdrawal of the device, the competent authority should impose actions such as a mandatory recall or legal actions to stop the

	availability of the device to the general public until corrective actions are carried out to make the device safe. In the case of recalls or withdrawals, the competent authority should issue safety alerts and public warnings if it deems that the device poses significant risks to its users.
xv.	If necessary, inspections at the manufacturer's site are carried out to verify compliance of the QMS with the regulatory requirements of the MDR and ISO 13485:2016.
xvi.	The competent authority should ensure that the notified body, if relevant, is informed of the incident.
xvii.	When EUDAMED is fully functional, the competent authority should ensure that the final MIR and the CAPA status are uploaded in the vigilance module. For now, the competent authorities may have an application that allows the economic operators to check the progress of their report on the authority's database. The database has to be updated periodically.
xviii.	If the competent authority now ensures that all the CAPAs are satisfactory, the incident report is closed and documented in database.

8.2 The Recall Process

Recall means taking a medical device back from the market after it has already been distributed or sold. This is usually done due to safety concerns or regulatory non-compliance. [(EU) 2017/745 Article 2 (62)]

Withdrawal refers to stopping a medical device from being made available in the market before it reaches the end-users. It applies to devices that are still in the supply chain but have not yet been used by the end-users. [(EU) 2017/745 Article 2 (63)]

8.2.1 Voluntary Recall by the Manufacturer:

i.	On the emergence of a serious incident, the manufacturer may consider that the best FSCA is the recall or withdrawal of the device. This is notified to the competent authorities of all member states affected with the recalled batch/es of device, through a FSN or a voluntary batch recall notification. Other economic operators that are making the device available on the market could notify the competent authority of the voluntary batch recall.
ii.	The competent authority enters the data into a recall database, and immediately initiates a risk assessment of the incident to determine the severity and potential harm.
iii.	While the manufacturer initiates the corrective actions, the competent authority communicates with all stakeholders involved in the FSCA. ▪ Communicate with the local importers and/or distributors to: - obtain quantities of the device available on the local market - coordinate the recall of all distributed stock - ensure quarantine of stock in storage

	- get list of any health institutions that may have been the end-users of the device in question and inform them accordingly ▪ Ensure that the notified body is notified by the manufacturer, if applicable ▪ Communicate with the manufacturer on all the coordinated details of the recall process ▪ Input all the progress details of the recall process in the recall database.
iv.	The competent authority should expect a final report from the manufacturer, with a summary of all the CAPAs carried out. This should be inputted in the recall database.

8.2.2 Mandatory Recall by the Competent Authority:

i.	If the competent authority identifies a serious risk to public health related to a medical device, and the manufacturer has not yet initiated a voluntary recall, a mandatory recall order may be issued. [(EU) 2017/745 Article 95, Article 98 and (EU) 2017/746 Article 90, Article 93]
ii.	The competent authority should formally notify the manufacturer and other relevant stakeholders [authorised representative/s, importer/s, distributor/s, notified body] of the mandated recall. The risk level resulting from the risk assessment should be notified to the stakeholders.
iii.	The competent authority must notify the European Commission and the other Member States of the risk assessment carried out on the device and the mandated recall.

iv.	The manufacturer and other economic operators involved with the device in question must execute the recall, following the competent authority's instructions. A clearly defined timeframe for the recall should be communicated.
v.	The local importers and/or distributors are asked to: - Confirm quantities of the device available on the local market - coordinate the recall of all distributed stock - ensure quarantine of stock in storage - provide list of any health institutions that may have been the end-users of the device in question and inform them accordingly
vi.	The manufacturer should issue a FSN immediately to inform the end-users.
vii.	The manufacturer should provide progress updates to the competent authority.
viii.	The competent authority may publish recall information on its website [until EUDAMED is fully functional].
ix.	When risk level is high, and there is a public health threat, direct warnings are issued from the competent authority to the end-users.
x.	The competent authority inputs all the progress details of the recall process in the recall database.
xi.	When the CAPAs are deemed sufficient, the competent authority can close the recall.
xii.	If the economic operator refuses to take the mandated corrective action within the timeframe defined by the competent authority, the competent authority can escalate enforcement measures, as per (EU) 2017/745 Article 95 and (EU) 2017/746 Article 90, to recall or withdraw the device, and restricting its availability on the market.

xiii.	In such cases of refusal, the competent authority should notify the European Commission and other Member States immediately of the enforcement measures. This notification should include: - all details required for the identification and tracing of the device - the origin of the device - the reasons for the non-compliance - the risk - the nature and duration of the national enforcement measures taken - the arguments put forward by the economic operator to justify refusal [(EU) 2017/745 Article 95 and (EU) 2017/746 Article 90]
xiv.	Other Member States should inform the European Commission and other Member States of any relevant information regarding the device. In cases of disagreement with the notified enforcement measures, the Member States should inform the European Commission and other Member States immediately. If no objection is raised within two months from notification, the enforcement measures are considered justified.
xv.	All Member States should now ensure that the enforcement measures for the non-compliant device are also taken on their own territory without delay.

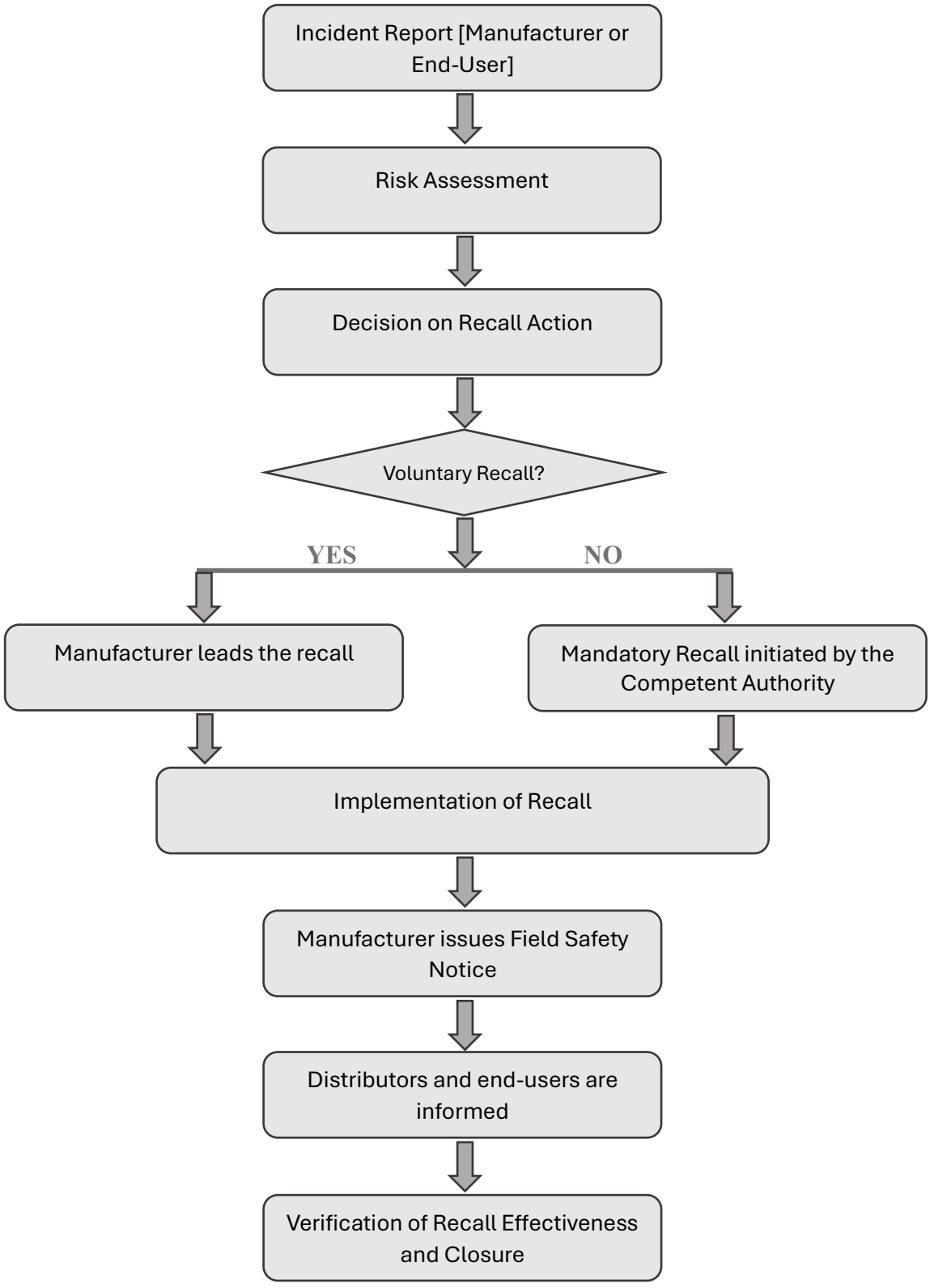

Figure 5. Recall Process

8.3 Monitoring Trends

In Article 88, the MDR emphasises the need for a proactive system that analyses any statistically significant increase in the frequency or severity of non-serious incidents, when compared to anticipated levels as documented in the technical documentation of the device. Manufacturers are required to monitor and report these trends because they may impact the benefit-risk analysis of the device. Details on how to monitor and manage these trends should be included in the Post-Market Surveillance Plan of the manufacturer.

8.3.1 Trend Analysis Strategy for Competent Authorities

Competent authorities can adopt a comprehensive strategy for systematic data collection, statistical evaluation, and proactive monitoring of trends.

Reference to regulatory documents, including:

- Regulation (EU) 2017/745 [MDR] Article 88, Article 90, Annex III
- Regulation (EU) 2017/746 [IVDR] Article 83, Article 85, Annex III
- ISO 14971:2019 *Medical Devices – Application of risk management to medical devices*
- ISO/TR 24971:2020 *Medical Devices – Guidance on the application of ISO 14971*

i.	Document all non-serious incidents, complaints, adverse events and feedback systematically in a database.
ii.	Choose the appropriate statistical tools based on the type of device and on the data available. (e.g. Regression Analysis, Weibull Analysis (ISO 24971), Nelson Rules (ISO/TR 20416), Mann-Kendall Test)

	This step is carried out by an expert statistician.
iii.	Define a baseline using historical data, and establish thresholds for statistically significant changes, that when exceeded, trigger further analysis.
iv.	When establishing thresholds, try to avoid overfitting models that capture all kinds of noise apart from actual trends, or overly simplistic models that can miss significant patterns in your data.
v.	Set regular intervals for evaluating trends.
vi.	Automated trend detection tools can be implemented in the authority database to monitor post-market surveillance data on a continuous basis.
vii.	Acquiring feedback from healthcare professionals and from other clinical studies can give real-world context to the trend analysis by adding qualitative assessments.
viii.	Acquiring information from other competent authorities on their systems of trend analysis would be of benefit when setting up the database (e.g. during JAMS 2.0).
ix.	Document all actions taken by stakeholders involved in response to identified trends.
x.	Share trend reports and associated corrective actions with other competent authorities, the European Commission, and the notified body.
xi.	Employees that work within the post-market surveillance and vigilance team should be provided training on how to use statistical tools and on how to interpret trend analysis reports effectively.

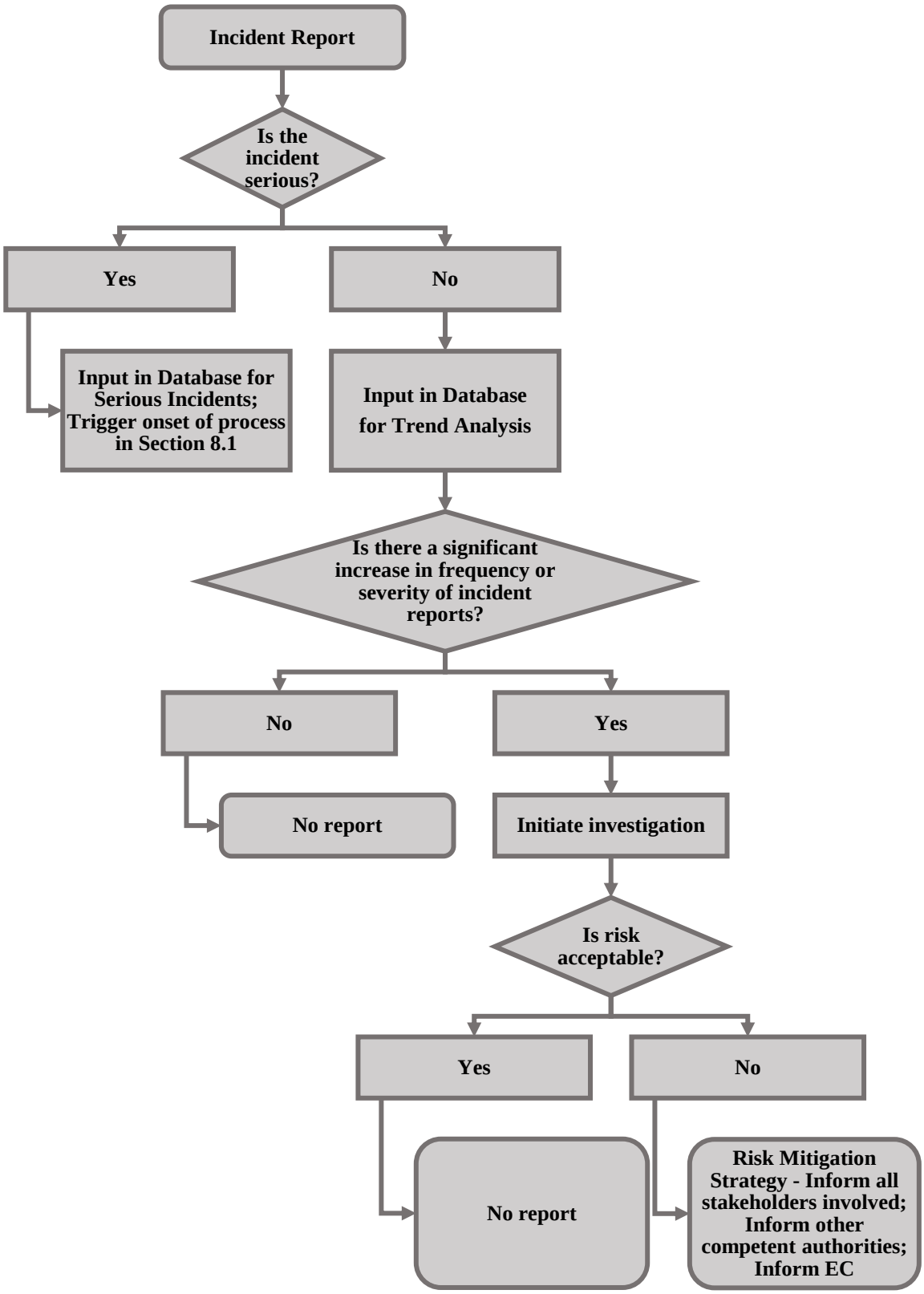

Figure 6. Process of Risk Assessment in Trend Analysis

8.4 Risk Analysis and Risk Management

Legal requirements such as the MDR/IVDR and ISO 14971:2019 *Medical Devices – Application of risk management to medical devices,* mandate that manufacturers implement robust risk management systems to identify, evaluate, and mitigate risks throughout the lifecycle of the device. ISO/TR 20416:2020 *Medical Devices – Post-market surveillance for manufacturers - Technical Report* helps the economic operator to provide deliverables to these legal requirements.

- "Manufacturers shall establish, document, implement and maintain a system for risk management as described in Section 3 of Annex I." [(EU) 2017/745 Article 10 (2)]

- "The *manufacturer* shall establish, implement, document and maintain an ongoing *process* for:

  a) identifying *hazards* and *hazardous situations* associated with a *medical device*;

  b) estimating and evaluating the associated *risks*;

  c) controlling these *risks*, and

  d) monitoring the effectiveness of the *risk control* measures.

  This *process* shall apply throughout the *life cycle* of the *medical device*.

  This *process* shall include the following elements:

  — *risk analysis*;

  — *risk evaluation*;

  — *risk control*; and

  — production and *post-production* activities." [ISO 14971:2019 Section 4.1]

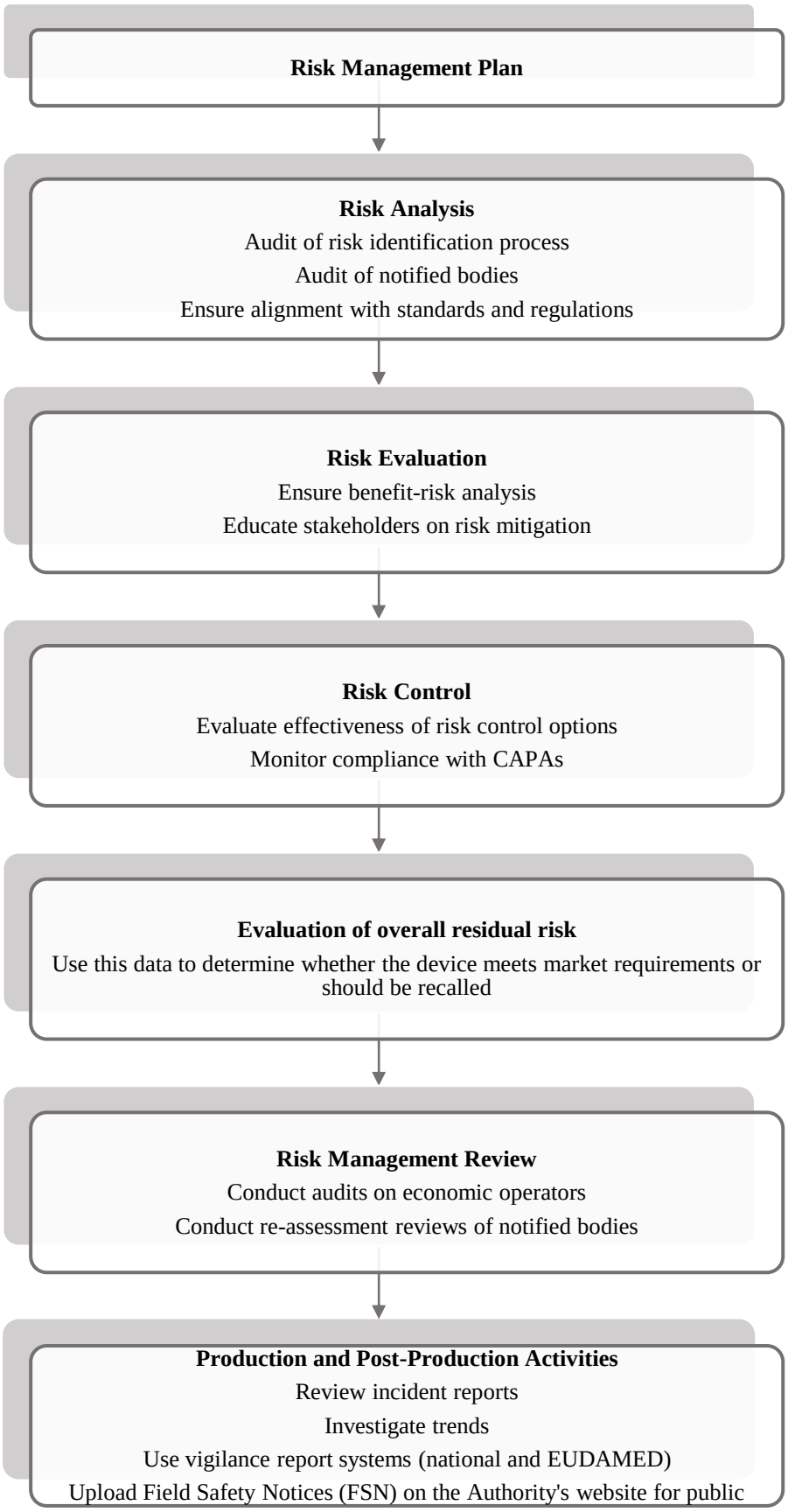

Figure 7. Risk Management Responsibilities of Competent Authorities
[Adapted from Figure 1 - A schematic representation of the risk management process of ISO 14971:2019]

Risk management responsibilities of the competent authority include:

i.	The competent authority must oversee that the manufacturer's risk management system is continuously updated, based on new data, incident reports, or changes and modifications in device design or intended use.
ii.	The competent authority must expect a thorough risk analysis for medical devices, with any identified potential risks, the likelihood of their occurrence, and the evaluation of the severity of any potential harm. Risk management activities need to be integrated in the post-market surveillance plan and in the post-market clinical follow-up (PMCF).
iii.	The competent authority needs to assess whether risk control measures taken by the manufacturer are appropriate in reducing the risks within acceptable levels. Any residual risks must be justified.
iv.	The competent authority needs to monitor the safety and performance of devices by documenting data on adverse events, and collecting user feedback and other relevant information on the device.
v.	The competent authority is responsible for being proactive in keeping trend analyses, to enable timely interventions if any trends or emerging safety concerns are identified.
vi.	The competent authority is responsible for requiring field safety corrective actions (FSCAs) for risk mitigation, in cases of identified safety concerns with a device. Take into account: - Threat to public health - Causality

	- Detectability - Probability of recurrence of the issue - The frequency of use of the device - Probability of occurrence of direct or indirect harm to patients - Severity of any direct or indirect harm to patients - Clinical benefit of the device - Intended and potential users of the device - The population affected by the FSCA - The adequacy of the FSCA undertaken by the manufacturer - The need for further FSCA [as per (EU) 2017/745 Article 89 and (EU) 2017/746 Article 84]
vii.	The competent authority is responsible to audit and oversee conformity assessment bodies that it has designated as notified bodies, to ensure that their assessment of the manufacturer's risk analysis and risk management is robust and compliant to MDR/IVDR and ISO 14971 standards.
viii.	During re-assessments of notified bodies, the competent authority must verify that risk management processes are aligned with the technical documentation of the manufacturers. Notified bodies are assessed on audits they have carried out on manufacturers, to confirm that risk management is integrated into post-market surveillance and vigilance activities. The competent authority assesses whether any CAPAs that arise after risk analysis are followed up by the notified body.
ix.	The competent authority may offer training sessions to economic operators on a regular basis, to inform them on the regulatory expectations related to risk analysis and risk management involved in post-market surveillance and

	vigilance activities throughout the lifecycle of the device that they have made available on the market.
x.	The competent authority is responsible to maintain transparency with healthcare professionals and other end-users in communicating any findings from risk assessments and vigilance activities.
xi.	The competent authority is responsible to carry out market surveillance inspections of the facilities of economic distributors (manufacturers, importers, distributors) and audit their quality management systems to assess compliance with risk management requirements.
xii.	The competent authority is responsible in carrying out risk assessments on received incident reports. The authority is also responsible in justifying this risk classification whenever there is disagreement between the manufacturer and the authority. [See Figure 8]

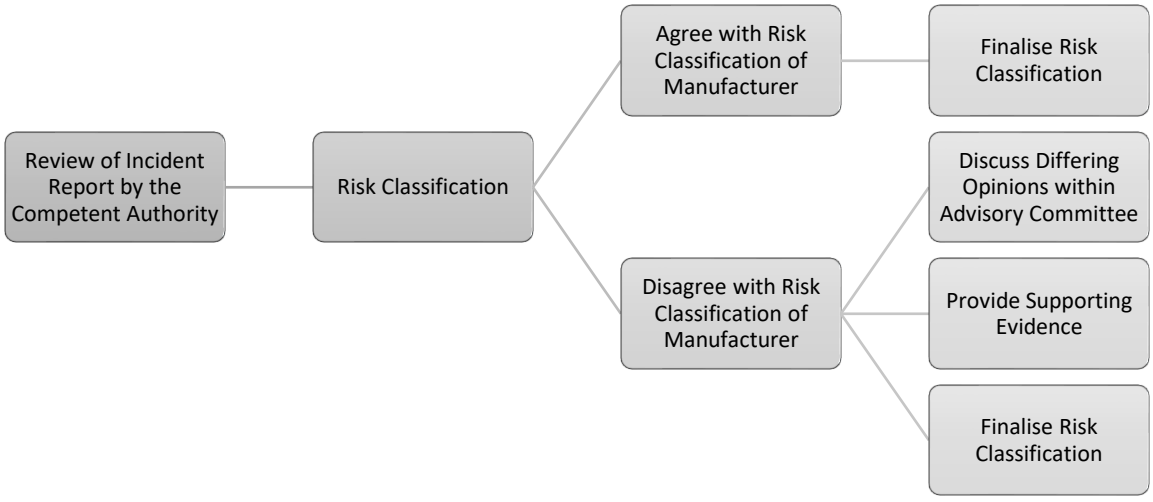

Figure 8. Risk Assessment and Classification
The risk assessment and risk classification carried out by the competent authority upon receiving an incident report. This is compared with the risk assessment carried out by the manufacturer. If there is misalignment between the two results, the risk assessment is discussed within the advisory committee for vigilance, to ensure the best outcome for patient safety. All the steps of the resolution process should be documented in detail.

8.4.1 The Risk Matrix

Using a 5 x 5 Risk Matrix template can help to identify the combination of probability of the risk (likelihood) with the impact of the identified risk (severity). It gives 25 risk levels, leading to more flexibility in risk tolerance levels, allowing for more accurate ranking of risks. The colour coding of the matrix shows high risks in red, moderate risks in yellow, and low risks in green.

The probability of the risk to occur (y-axis) is rated:

Rare (Least Likely)	1
Unlikely	2
Moderate	3
Likely	4
Almost Certain (Most Likely)	5

The probability of risk considers criteria such as:

- the causality of the adverse event – Un-assessable (1), Possible (2), Probable (3), Likely (4), Certain (5)
- the probability of occurrence of direct or indirect harm – Negligible (1), Low (2), Moderate (3), Likely (4), Highly Likely (5)
- the risk class of the device – Class I (1), Class [Is, Im, Ir] (2), Class IIa (3), Class IIb (4), Class III and implantable devices (5) (MDR)

  Class A (1), Class A[sterile] (2), Class B (3), Class C (4), Class D (5) (IVDR)
- the quantities of devices affected by the incident report – One (1), Two - Five (2), Six - Ten (3), Ten – Twenty (4), More than Twenty (5)

The Impact that the risk can have (x-axis) is rated:

Insignificant	1
Minor	2
Significant	3
Major	4
Severe	5

The impact of risk considers criteria such as:

- any past incident reports on the same device – None (1), One (2), Two – Five (3), Six – Ten (4), More than Ten (5)
- the number of batches affected by the adverse event – One batch (1), Two batches (2), Three batches (3), Four batches (4), More than Four batches (5)
- the affected population – General population (1), Healthy Adults population (2), Healthy Paediatric population (3), Immunocompromised Adults/ICU Adults population (4), Immunocompromised Paediatric/ICU Paediatric/Elderly population (5)
- the level of harm assumed by the reporter - Negligible (1), Low (2), Moderate (3), Likely (4), Highly Likely (5)

Prioritising risks this way can guide decision-making by focusing on higher risks.

Keep in mind that some risks may be overlapping.

When there are doubts, it is always safe to go to the next higher level of risk and carry out further risk analysis.

Multiplying the value of Probability by the value of Impact determines the risk level.

Table 1. Differentiating between risk levels

Probability x Impact	Risk Level	Mitigation Measures
1 – 2	Very Low Risk	No further action may be required but monitoring is still advised
3	Low Risk	Monitoring advised
4 – 9	Medium Risk	Further risk analysis may be required
10 – 12	High Risk	Implement immediate risk mitigation measures
13 - 16	Very High Risk	Implement immediate risk mitigation measures
17 - 25	Extremely High Risk	Implement immediate risk mitigation measures and cease activities

	Insignificant 1	**Minor 2**	**Significant 3**	**Major 4**	**Severe 5**
Almost Certain 5	Medium 5	High 10	Very High 15	Extreme 20	Extreme 25
Likely 4	Medium 4	Medium 8	High 12	Very High 16	Extreme 20
Moderate 3	Low 3	Medium 6	Medium 9	High 12	Very High 15
Unlikely 2	Very Low 2	Low 4	Medium 6	Medium 8	High 10
Rare 1	Very Low 1	Very Low 2	Low 3	Medium 4	Medium 5

Figure 9. The 5 x 5 Risk Matrix
[Adapted from: Puder et al. Threat Assessment and Risk Analysis (TARA) for Interoperable Medical Devices in the Operating Room Inspired by the Automotive Industry. Healthcare. 2023; 11:872. Available from URL: https://doi.org/10.3390/healthcare11060872]

8.5 CASP Tool for Vigilance Skills

A Critical Appraisal Skills Programme (CASP) tool, which was originally designed for the critical appraisal of research evidence, is adapted to determine the regulatory personnel's ability to critically assess data and decision-making processes in post-market surveillance and vigilance activities. This tool aims to improve critical analysis of incident reports and clinical data received by the competent authority, and to enhance risk assessment and management and signal detection. It could be utilised in the training program to refine vigilance skills.

CASP-Based Critical Appraisal Checklist for Medical Device Vigilance	
Assessor Name	
Incident Report Reference No.	
Appraisal Date	
Section 1: Validity of Incident Report and Data Received by the Competent Authority	
1.4 Source Reliability	
Is the MIR complete and accurate?	Yes ☐ No ☐ Can't tell ☐
Is data sourced from a verified system? [e.g. IMDRF, EUDAMED…]	Yes ☐ No ☐ Can't tell ☐
Was the MIR sent within the regulatory timelines?	Yes ☐ No ☐ Can't tell ☐
1.5 Causality Assessment	
Is there uncertainty about the link between the device and the reported adverse event?	Yes ☐ No ☐ Can't tell ☐

Are there no other factors, such as patient comorbidities, that could contribute to the adverse event?	Yes ☐ No ☐ Can't tell ☐
1.6 Consistency of Data	
Is there only one incident reported for this device or device group?	Yes ☐ No ☐ Can't tell ☐
Is it an expected adverse event?	Yes ☐ No ☐ Can't tell ☐
Section 2: Risk Assessment and Impact Analysis	
2.1 Severity of the Incident	
What is the impact of the incident?	☐ Public health threat – 3 points ☐ Death – 2 points ☐ Deterioration in health – 1 point
What is the probability of direct or indirect harm to the patient being caused by the device?	☐ Negligible – 1 point ☐ Low – 1 point ☐ Moderate – 2 points ☐ Likely – 3 points ☐ Highly Likely – 3 points
2.2 Risk-Benefit Analysis	
Have appropriate risk mitigation measures been initiated by the manufacturer?	Yes ☐ No ☐ Can't tell ☐
2.3 Signal Detection and Trend Analysis	
Is there an emerging pattern of non-serious incidents?	Yes ☐ No ☐ Can't tell ☐
Do signals and trends indicate that an FSCA is not necessary?	Yes ☐ No ☐ Can't tell ☐
Section 3: CAPA Evaluation	
3.1 Root Cause Analysis	
Has the manufacturer conducted a comprehensive root cause analysis?	Yes ☐ No ☐ Can't tell ☐
Are the identified root causes plausible and evidence-based?	Yes ☐ No ☐ Can't tell ☐

3.2 Effectiveness of CAPA	
Are the corrective actions appropriate?	Yes ☐ No ☐ Can't tell ☐
Are preventive measures in place to avoid recurrence?	Yes ☐ No ☐ Can't tell ☐
3.3 Stakeholder Communication	
Has the manufacturer issued a FSN?	Yes ☐ No ☐ Can't tell ☐
Were healthcare professionals and other end-users adequately informed?	Yes ☐ No ☐ Can't tell ☐
Section 4: Decision Making	
4.1 Regulatory Compliance	
Is the manufacturer compliant with MDR (EU 2017/745) and IVDR (EU 2017/746)?	Yes ☐ No ☐ Can't tell ☐
Have all reporting and documentation requirements been met?	Yes ☐ No ☐ Can't tell ☐
4.2 Regulatory Action Plan	
Was further investigation or on-site inspection initiated?	Yes ☐ No ☐ Can't tell ☐
Were the economic operator's decisions consistent with the competent authority's assessment?	Yes ☐ No ☐ Can't tell ☐
4.3 Continuous Monitoring and Improvement	
Are post-market follow-up (PMCF) activities in place?	Yes ☐ No ☐ Can't tell ☐
Are periodic safety update reports (PSUR) being submitted?	Yes ☐ No ☐ Can't tell ☐

Evaluation Rating System		
Yes	1 point	
Can't Tell	2 points	
No	3 points	
57 - 72 points	High Confidence Level (67 – 100%)	Strong evidence; Effective regulatory action is recommended
41 - 56 points	Moderate Confidence Level (34 – 66%)	Moderate evidence; Additional monitoring is required
24 – 40 points	Low Confidence Level (Below 34%)	Insufficient evidence; Request for additional data is required

Figure 10. CASP-Based Critical Appraisal Checklist for Medical Device Vigilance
[Adopted and modified from a Critical Appraisal Skills Programme tool used for the critical appraisal of research evidence in cohort studies and case-control studies]

Artificial Intelligence	The development of systems that can perform tasks that typically require human intelligence and behaviour, such as problem-solving, decision-making, language processing, and learning from experience. [WHO *Regulatory considerations on artificial intelligence for health 2023]*
AI System	A machine-based system that is designed to operate with varying levels of autonomy and that may exhibit adaptiveness after deployment, and that, for explicit or implicit objectives, infers, from the input it receives, how to generate outputs such as predictions, content, recommendations, or decisions that can influence physical or virtual environments [(EU) 2024/1689 AI Act]
Machine Learning	A branch of artificial intelligence, where algorithms allow machines to learn from data, identify patterns, and improve performance over time without being reprogrammed. [ISO/IEC 23053:2022 *Framework for Artificial Intelligence (AI) Systems Using Machine Learning (ML)*]
Deep Learning	A subset of machine learning, where algorithms allow a machine to mimic the thought processes of a human being through artificial neural networks that process large amounts of data, identify patterns and make predictions with high accuracy. [ISO/IEC 23053:2022 *Framework for Artificial Intelligence (AI) Systems Using Machine Learning (ML)*]

Medical Device Software (MDSW)	Software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a “medical device” in the MDR or IVDR.
Softare as a Medical Device (SaMD)	Software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device. [IMDRF - *Software as a Medical Device (SaMD): Key Definitions*]

9.1 The AI Act and Post-Market Monitoring

The European Artificial Intelligence Regulation (EU) 2024/1689 [AI Act] entered into force on the 1st of August 2024 and will be fully applicable by 2027. One of its main aims is to encourage AI research in healthcare, which may increase the pace at which AI is being integrated into clinical settings. The MDR/IVDR and the AI Act are both risk-based regulations. To ensure compliance with both the MDR/IVDR and the AI Act, manufacturers and competent authorities must integrate AI-specific risk management, performance evaluation, and continuous monitoring into existing regulatory frameworks.

i.	Medical devices and *in vitro* diagnostic medical devices that require conformity assessment by a notified body (Class Is, Ir, Im, IIa, IIb, III under the MDR; Class As, B, C, D under the IVDR) are classified as high-risk in the AI Act.
ii.	Medical devices incorporating an AI system should conform to both Regulations since there may be risks specific to AI systems that are not addressed through the MDR/IVDR. Testing and documentation processes of the AI Act could be integrated into the procedures required under the MDR/IVDR.
iii.	The risk-management system should be a continuous process throughout the entire lifecycle of the high-risk AI system.
iv.	Article 72 of the AI Act - *Post-market monitoring by providers and post-market monitoring plan for high-risk AI systems* mandates that providers of high-risk AI systems establish a post-market monitoring system to ensure continuous compliance and risk management.

	▪ Providers must create a systematic monitoring framework tailored to the risks of the high-risk AI ▪ This system must collect, document and analyse data on AI performance, including real-world feedback ▪ If applicable, post-market monitoring should include interactions with other AI systems but must exclude sensitive operational data of competent authorities ▪ Providers will be expected to document a post-market monitoring plan as part of the technical documentation, as mandated in Annex IV; a template for this plan is planned to be established by the EC by February 2026 ▪ Providers can integrate the AI monitoring requirements into their existing post-market surveillance frameworks, ensuring equivalent levels of protection
v.	Article 73 of the AI Act – *Reporting of serious incidents* establishes reporting requirements for serious incidents involving high-risk AI systems. ▪ Providers of high-risk AI systems must immediately report serious incidents to the competent authority of the Member State where the incident has occurred ▪ If a causal link between the AI system and the incident is confirmed or suspected, the report must be made within 15 days ▪ If the incident involves a death, the report must be made within 10 days ▪ In the case of widespread infringement or serious incident, the report must be made within 2 days

	▪ Providers may submit an initial incomplete report to meet deadlines, followed by a full investigation report ▪ Following the report, the provider must do a full investigation with risk assessment and corrective actions ▪ The provider must cooperate with the competent authority and the notified body ▪ The provider must not alter the AI system in a way that would affect the investigation ▪ The competent authority shall take appropriate measures within 7 days of receiving the report [further guidance on this should be issued by the EC by August 2025] ▪ Incident reporting for AI systems that are safety components of devices or are themselves devices, must comply with both the MDR/IVDR and the AI Act Article 73 ▪ The national competent authority has to immediately notify the EC about serious incident reports received

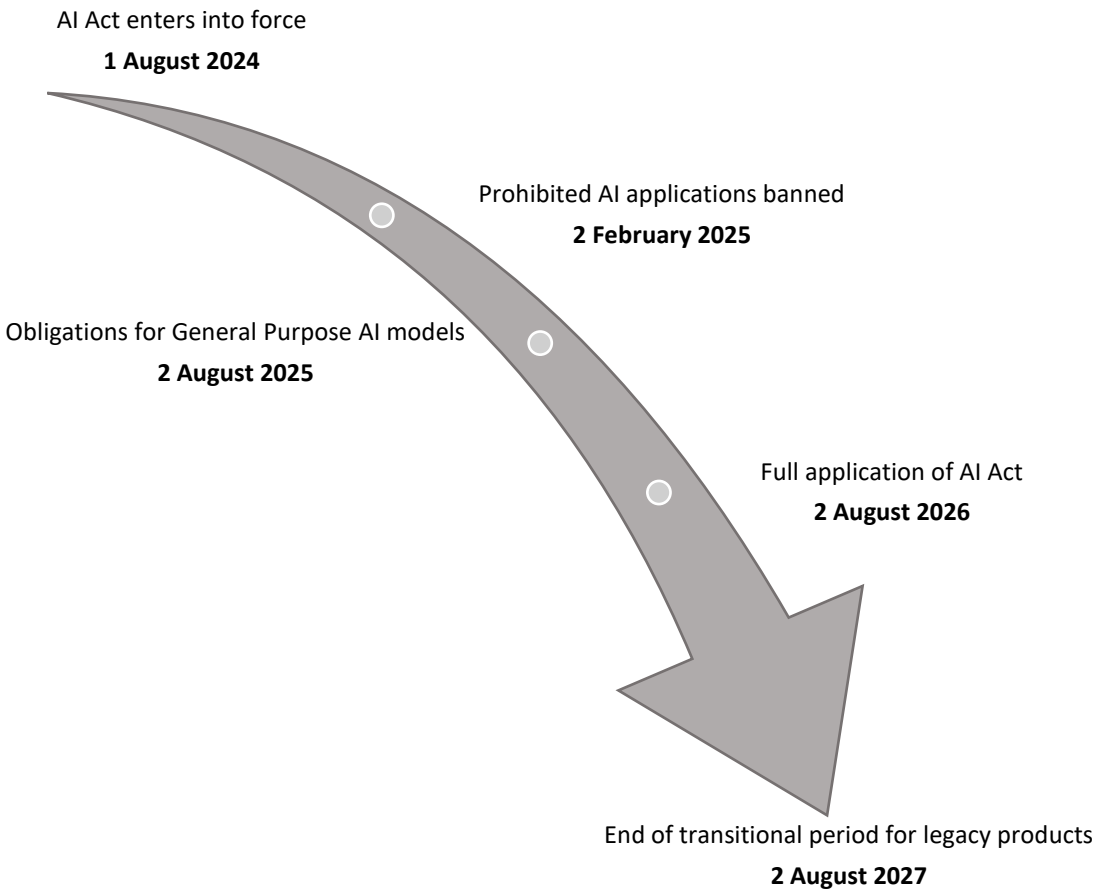

Figure 11. AI Act Timeline

[The AI Act entered into force on 1st August 2024. By 2nd February 2025, any AI systems that were deemed to pose unacceptable risk were banned. By 2nd August 2025, specific transparency and compliance requirements apply to providers of medical devices that incorporate or are built on a general-purpose AI. By the 2nd August 2026, AI-enabled medical devices, even those classified as high-risk under Annex III of the AI Act, must fully comply with the Regulation in addition to existing MDR/IVDR requirements. 2nd of August 2027 is the end of the transitional period for certain high-risk AI systems embedded in existing medical devices that were already on the market before August 2026, provided there were placed on the market compliant with the MDR/IVDR.]

9.2 Implementing AI in PMS Oversight and Vigilance

For competent authorities, leveraging AI in daily activities related to the oversight of PMS and vigilance can help detect safety issues faster, increasing efficiency and accuracy in managing medical device risks. AI does not replace human oversight, but it can be used as a tool to support decision-making in improving patient safety.

Integrating AI in regulatory processes – what the competent authority can do:

i.	Budgeting for innovative AI-powered regulatory systems, especially for vigilance
ii.	Investing in AI training for regulatory personnel
iii.	Using AI in predicting potential risks
iv.	Using AI for real-time monitoring Data is collected from various sources such as ▪ clinical databases ▪ wearable devices [can send continuous performance data] ▪ implantable devices [can send continuous performance data] ▪ global regulatory databases such as those of FDA and WHO ▪ social media platforms [although seen as mundane in the scientific world, the power of these platforms should not be overseen, because patients may discuss concerns online] ▪ scientific literature ▪ scientific current news
v.	Trend analysis to help identify any unusual patterns that could emerge from unpredicted risks

vi.	Detection of falsified devices due to blockchain systems that track device supply chains. This blockchain technology logs every step of the journey of the device from the warehouse to the end-user, ensuring traceability with tamper-free records. The UDI-DI is essential in this process, since if a scanned UDI does not match the blockchain records, the device needs to be assessed as potentially falsified. Blockchain systems also monitor for change in patterns in supply – if there are large quantities of devices at a point in the chain without any previous records, these need to be assessed. Since every economic operator under the new EU Regulations is accountable for the safety of devices, this blockchain technology aids transparency and leads to faster detection of any falsified devices.
vii.	Robotic process automation is more efficient than human intervention in streamlining repetitive tasks like data input and report creation, leaving more valuable time for surveillance and vigilance personnel to focus on other strategic work.
viii.	Building device databases to organise data on a national level, in view of the gradual roll-out of EUDAMED in the near future
ix.	Engagement with stakeholders on collaboration platforms such as AI-powered chatbots
x.	Large sets of data can be analysed more efficiently and with higher precision
xi.	Increasing traceability of all medical devices and *in vitro* diagnostic medical devices on the local market by having an AI-driven system that could combine the economic operator interface, the clinical setting interface and the user interface

xii.	Building a system that mimics the electronic medical record used for medicines, for patients who are using implantable medical devices This Electronic Medical Device Record (EMDR) could include: ▪ the UDI-DI of the device for traceability ▪ details of the manufacturer ▪ details of the device such as model, serial numbers and batch numbers ▪ dates when device was implanted, distributed, used, or underwent maintenance or updates ▪ management of recalls, withdrawals or disposal ▪ any operational parameters such as energy consumption and activity ▪ maintenance needs ▪ possibility of linking to the vigilance system of the competent authority
xiii.	Having the relevant expertise on AI in the advisory committee for vigilance, considering both AI integrated in the vigilance process and also AI in medical devices that are involved in adverse event reports
xiv.	Developing risk scoring models in vigilance database to help in prioritising incident reports received
xv.	Integrate General Data Protection Regulation (GDPR) practices to protect patients' personal data
xvi.	Provide training for patients and end-users on cybersecurity risks and mitigation measures to avoid these risks
xvii.	Implementation of AI-driven surveillance tools to keep track of economic operators (mainly distributors and importers in Malta)

xviii.	Collaborating with EU and global regulatory networks to increase expertise and skills in using AI to improve patient safety [such as JAMS 2.0]
xix.	Training on MDCG documents on software and other global guidance documents such as the IMDRF/CYBER WG/N60Final:2020 *Principles and Practices for Medical Device Cybersecurity* and the WHO report *Ethics and governance of artificial intelligence for health [2021]*
xx.	Using AI tools to analyse scientific literature to back real-world evidence for safety signals
xxi.	In the local scenario: ▪ set up meetings with the Malta Digital Innovation Authority, to incorporate the AI needs of the regulatory processes involved with medical devices and *in vitro* diagnostic medical devices into the national regulations that are being developed to align with the AI Act ▪ Collaborate with the Ministry for Health & Active Ageing to integrate data on the medical devices being used by patients on their *myHealth* portal ▪ Link the website of the competent authority on the *myHealth* portal so that patients can view Field Safety Notices and other important information regarding their devices

Training Modules on Post-Market Surveillance and Vigilance

10.1 Training for the Regulatory Personnel

Training for Regulatory Personnel in oversight of post-market surveillance and vigilance could be done through:

- Workshops led by senior staff and management of the competent authority for medical devices
- Modules and quizzes on online learning platforms
- Case studies
- Internal Audits
- Practical case evaluations during vigilance meetings
- Continuous evaluation of daily work

Identifying key learning points:

i.	All the new regulatory personnel responsible for the oversight of post-market surveillance and vigilance need to follow an induction training course and obtain a set pass mark.
ii.	All employees should have refresher courses on Chapter VII of (EU) 2017/745 / (EU) 2017/746 *Post-Market Surveillance, Vigilance and Market Surveillance,* all related Articles, and relevant national legal notices.
iii.	All appointed employees should have easy access to Standard Operating Procedures (SOPs) of the competent authority, and participate in the development of new SOPs.
iv.	The appointed employees need to become members of the EU working groups on post-market surveillance and vigilance, to gain and share expertise with other colleagues from different Member States.

v.	Continuous professional development and knowledge-sharing initiatives should be highly promoted.
vi.	Required Tools: ▪ Training on IMDRF adverse event terminology ▪ Training on EMDN codes ▪ ISO standards such as ISO 13485 and ISO 14971 ▪ Training on reporting timelines ▪ Participating in EU programs such as JAMS 2.0 ▪ Risk analysis and management training ▪ Training on the classification of incident reports ▪ Using the *CASP-Based Critical Appraisal Checklist for Medical Device Vigilance* ▪ Training on handing of initial and final MIRs ▪ Training on handling incident reports from healthcare professionals and patients ▪ Training on using the vigilance database ▪ The AI Act
vii.	Appointed employees need to collaborate with the personnel responsible from the re-assessment of notified bodies when technical documentation of devices needs to be reviewed.
viii.	Appointed employees need to collaborate with the personnel responsible from clinical investigations and performance studies when there are incident reports regarding devices being used in clinical investigations as per Article 80 of the MDR and devices used in performance studies as per Article 76 of the IVDR.

ix.	Appointed employees need to collaborate with data analysts and statisticians for the development of a data system that integrates real-world evidence and analyses big sets of data for vigilance.
x.	The appointed employees should have training in international collaboration with other Member States and with the relevant notified bodies.
xi.	The appointed employees should attend any training sessions organised by the Directorate-General for Health and Food Safety of the EU.
xii.	The appointed employees should have at their disposal a list of useful resources on post-market surveillance and vigilance, such as: ▪ MDCG Guidance documents ▪ CIRCABC access to current publications on the subject ▪ Access to the relevant mailboxes on Microsoft Outlook ▪ Relevant ISO standards
xiii.	Global research and publications such as WHO Guidelines and IMDRF Guidelines should also be reviewed periodically.
xiv.	Training on the implementation of the AI Act and its consequences on post-market surveillance and vigilance of medical devices should be a priority at this current time. This training needs to address emerging risks from new technologies such as SaMD and ML devices.
xv.	Appointed employees need training in public communication strategies and engaging with patient advocacy groups and media groups, when there are high-risk incidents, recalls and withdrawals of devices, to avoid public alarm.
xvi.	Training is needed for responsible action in safety recalls of devices, when the decision is taken by the economic operator, and when the recall is refused by the

	economic operator but is mandated by the competent authority to ensure patient safety. Recalls need to be carried out in a controlled manner to avoid consequences to patients such as shortage of devices and procurement issues.
xvii.	Appointed employees should undergo training for risk minimisation strategies such as: ▪ proactive data collection from other adverse event databases ▪ getting user feedback ▪ signal detection systems ▪ trend analysis ▪ communication with other competent authorities ▪ informing end-users of any FSNs ▪ monitoring of post-recall situations ▪ international harmonisation initiatives [such as discussions for one common Incident Report Form among EU Member States]
xviii.	Appointed employees should be provided training on the 'vigilance and post-market surveillance' module on EUDAMED, since its use will be mandatory 6 months after being published [proposed date by EC is the first quarter of 2027].

10.2 Training for the Healthcare Professionals and other End-Users

Training for healthcare professionals in vigilance could be done through:

- In-person workshops led by the competent authority for medical devices
- Virtual group training workshops with interactive elements
- Modules and quizzes on online learning platforms, with certification
- Case studies for hands-on training on how to fill in the incident report form
- Webinars with experts in medical device vigilance
- Guidance documents provided on the website of the competent authority, or sent to individual recipients by email

Identifying key learning points:

i.	Provide an overview of medical device regulatory framework. [(EU) 2017/745 / (EU)2017/746 Chapter VII *Post-Market Surveillance, Vigilance and Market Surveillance*]
ii.	Explain the legal responsibilities for reporting incidents to promote patient safety.
iii.	Explain the different types of causes for adverse events with devices. [e.g. malfunction, misuse, poor performance…]
iv.	Use case studies and give examples of adverse events when presenting the case studies for better understanding.
v.	Guide healthcare professionals step-by-step through the process of using the incident report form for the reporting of adverse events.
vi.	Provide links to the reporting form, the website of the competent authority, and to other platforms providing information on vigilance.

vii.	Explain the necessity of providing as much information on the incident as possible. [Details of the device, the patient's condition, and the incident should be provided]
viii.	Emphasise the importance of an open communication between the healthcare professional and the regulator for the benefit of the patient.
ix.	It is important to highlight that incident reporting is not a waste of precious time, but a necessity in the holistic approach to safeguarding patients' lives.
x.	Provide a qualitative feedback tool such as a 'training satisfaction survey' where the healthcare professionals could communicate any barriers to reporting and any suggestions that they may have.

10.3 Training for the Local Economic Operators

Training for local importers and distributors in vigilance could be done through:

- In-person workshops led by the competent authority for medical devices
- Virtual group training workshops with interactive elements
- Modules and quizzes on online learning platforms, with certification
- Webinars with experts in medical device vigilance
- Guidance documents provided on the website of the competent authority, or sent to individual recipients by email

Identifying key learning points:

i.	Provide an introduction to post-market surveillance and vigilance activities as outlined in the MDR and the IVDR.
ii.	Emphasise the importance of patient safety and device performance all throughout the lifecycle of the device.
iii.	Define other regulatory standards such as ISO 14071 for risk management.
iv.	Highlight the importance of responsibility for: ▪ Device compliance with regulations ▪ Ensuring storage and transport conditions ▪ Traceability of all devices by keeping distribution records ▪ Cooperation and communication with competent authority ▪ Cooperation and communication with manufacturers ▪ Vigilance – incident reporting and follow-up
v.	Highlight the importance of risk assessment and risk classification of incident reports.

vi.	Ensure that the economic operators have a robust QMS that caters for post-market surveillance and vigilance procedures.
vii	Provide incident report templates for the economic operators to familiarise themselves with reading or filling in reports if necessary.

References

The references for this framework include:

11.1 EU Regulations on devices

- These incorporate the requirements of economic operators for a post-market surveillance system, the criteria for vigilance reporting, and EUDAMED
- Abiding by these requirements will provide traceability and active risk management throughout the whole lifecycle of the device

i. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
[Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02017R0745-20250110]

ii. Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU
[Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02017R0746-20250110]

11.2 EU Regulation on AI

i. Regulation (EU) 2024/1689 of the European Parliament and of the Council of 13 June 2024 laying down harmonised rules on artificial intelligence and amending Regulations (EC) No 300/2008, (EU) No 167/2013, (EU) No 168/2013, (EU) 2018/858, (EU) 2018/1139 and (EU) 2019/2144 and Directives 2014/90/EU, (EU) 2016/797 and (EU) 2020/1828 (Artificial Intelligence Act)
[Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32024R1689

11.3 The International Medical Device Regulators Forum (IMDRF) guidelines

- These guidelines allow harmonisation of adverse event terminology, and provide a standard for reporting that can be used across borders

- Standardisation facilitates sharing of information between countries

- Collaboration between multiple global regulatory authorities strengthens post-market regulation

i. for adverse event reporting:
   - GHTF SG2/N54R8:2006 – *Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices*
     [Available from: https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg2/technical-docs/ghtf-sg2-n54r8-guidance-adverse-events-061130.pdf]

   - IMDRF/AE WG/N43 - *Terminologies for Categorized Adverse Event Reporting (AER): terms, terminology and codes*
     [Available from: https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-200318-ae-terminologies-n43.pdf]

ii. for field safety notices:
   - GHTF SG2/N57R8:2006 – *Guidance – Content of Field Safety Notices*
     [Available from: https://www.imdrf.org/sites/default/files/2024-05/ghtf-sg2-n57r8-2006-guidance-field-safety-060627_0.pdf]

iii. for information exchange:
   - IMDRF/NCAR WG/N14 - *Medical Devices: Post-Market Surveillance: National Competent Authority Report Exchange Criteria and Report Form*
     [Available from: https://www.imdrf.org/documents/medical-devices-post-market-surveillance-national-competent-authority-report-exchange-criteria-and-report-form-0]

iv. for post-market clinical follow-up:
   - IMDRF MDCE WG/N65
     [Available from: https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-210325-wng65.pdf]

v. for Unique Device Identification (UDI):
   - IMDRF UDI WG(PD1)/N48
     [Available from: https://www.imdrf.org/sites/default/files/2021-09/imdrf-cons-udi-system-n48-180712.pdf]

11.4 WHO Guidelines for post-market surveillance of devices and artificial intelligence

- These guidelines encourage alignment with international standards
- Global patient safety and equity are promoted
- Emphasis on linking risk management to surveillance of devices
- Roles of different stakeholders involved throughout the lifecycle of a device are explained
- Medical device issues are categorised as per IMDRF guidance

i. *Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics*
[Available from:
https://iris.who.int/bitstream/handle/10665/337551/9789240015319-eng.pdf?sequence=1]

ii. *MeDevIS 2024 v1.0 – Priority Medical devices information system including in vitro diagnostic, some assistive products and other related health products*
[Available from:
https://medevis.who-healthtechnologies.org/]

iii. *WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices*
[Available from:
https://cdn.who.int/media/docs/default-source/biologicals/ecbs/annex3-gmrf-who_trs_1045.pdf]

iv. *WHO Global Benchmarking Tool plus Medical Devices (GBT+Medical Devices) for Evaluation of National Regulatory System of Medical Products*
[Available from:
https://cdn.who.int/media/docs/default-source/medicines/regulatory-systems/gbt-medical-devices/gbt-md_rev_vi-md_ver_2-3.pdf?sfvrsn=ab243243_4&download=true]

v. *Regulatory considerations on artificial intelligence for health*
[Available from:
https://iris.who.int/bitstream/handle/10665/373421/9789240078871-eng.pdf]

11.5 MDCG Guidance Documents

- The Medical Device Coordination Group (MDCG) provides interpretative documents to help stakeholders to comply with the EU Regulations.

- Although not legally binding, these guidance documents clarify EU requirements and help in maintaining consistency across all Member States.

i. MDCG 2023-3 rev.2 *Questions and Answers on vigilance terms and concepts as outlined in the Regulation (EU) 2017/745 on medical devices and Regulation (EU) 2017/746 [Last updated January 2025]*
ii. MDCG 2022-21 *Guidance on Periodic Safety Update Report (PSUR) according to Regulation (EU) 2017/745 [Last updated December 2022]*

iii. MDCG 2024-1 *Device Specific Vigilance Guidance (DSVG) Template [Last updated January 2024]*

iv. MDCG 2024-1-1 *DSVG 01 on Cardiac ablation [Last updated January 2024]*

v. MDCG 2024-1-2 *DSVG 02 on Coronary stents [Last updated January 2024]*

vi. MDCG 2024-1-3 *DSVG 03 on Cardiac implantable electronic devices (CIEDs) [Last updated January 2024]*

vii. MDCG 2024-1-4 *DSVG 04 on Breast implants [Last updated January 2024]*

viii. MDCG 2024-1-5 *DSVG 05 on Urogynaecological Surgical Mesh Implants used for Pelvic Organ Prolapse repair and Stress Urinary Incontinence [Last updated June 2024]*

ix. MDCG 2020-7 *Post-market clinical follow-up (PMCF) Plan Template - A guide for manufacturers and notified bodies [Last updated April 2020]*

x. MDCG 2020-8 *Post-market clinical follow-up (PMCF) Evaluation Report Template - A guide for manufacturers and notified bodies [Last updated April 2020]*

xi. MDCG 2021-3 *Questions and Answers on Custom-Made Devices (& considerations on Adaptable medical devices and Patient-matched medical devices) [Last updated March 2021]*

xii. MDCG 2021-25 Rev.1 *Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC [Last updated October 2024]*

xiii. MDCG 2022-8 *Regulation (EU) 2017/746 - application of IVDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2022 in accordance with Directive 98/79/EC [Last updated May 2022]*

xiv. MDCG 2019-16 rev.1 *Guidance on Cybersecurity for Medical Devices [Last updated July 2020]*

[Available from:
https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en]

11.6 International Organization for Standardization (ISO) Standards

- ISO Standards provide global consistency in established processes used by stakeholders for the monitoring and evaluation of safety, quality and performance of medical devices.
- The below-mentioned ISO standards serve as a practical tool in ensuring compliance once devices have been placed on the market:

i. ISO 13485:2016 *Medical Devices – Quality management systems - Requirements for regulatory purposes* [Last reviewed 2020]

ii. ISO 14971:2019 *Medical Devices – Application of risk management to medical devices* [Edition 3 published 2019]

iii. ISO/TR 24971:2020 *Medical Devices – Guidance on the application of ISO 14971 [Edition 2 published 2020]*

iv. ISO/TR 20416:2020 *Medical Devices – Post-market surveillance for manufacturers - Technical Report* [Edition 1 published 2020]

v. ISO/IEC 62304:2006 *Medical device software – Software lifecycle processes* [Last reviewed 2021]

vi. ISO/IEC 23053:2022 *Framework for Artificial Intelligence (AI) Systems Using Machine Learning (ML)* [Edition 1 published 2022]

[Available from:
https://www.iso.org/home.html]

Appendix A ~ IMDRF Adverse Event Terminology

Annex	Terminology for adverse event reporting
Annex A	**Medical Device Problem** - Terms and codes to describe device issues such as malfunction, deterioration or failure - Coding System: A|00[00][00]
Annex B	**Cause Investigation** – Type of Investigation - Terms and codes to specify the type of investigation for the reported event - Coding System: B|00
Annex C	**Cause Investigation** – Investigational Findings - Terms and codes to describe findings from the device investigation - Coding System: C|00[00][00]
Annex D	**Cause Investigation** – Investigation Conclusion - Terms and codes to summarise the conclusion derived from the investigation - Coding System: D|00[00]
Annex E	**Health Effects** – Clinical Signs, Symptoms and Conditions - Terms and codes to describe patient symptoms or conditions resulting from the adverse event - Examples: Nervous System, Vascular System, Infections - Coding System: E|00[00][00]
Annex F	**Health Effects** – Health Impact - Terms and codes to outline the broader health impact on the individual affected - Examples: Death, Surgical Intervention, Foetal Harm - Coding System: F|00[00][00]
Annex G	**Component** - Terms and codes for describing the part or component involved in, or affected by, the adverse event - Examples: Biological & Chemical, Electrical & Magnetic, Safety - Coding System: G|00[000][00]

The updated Annexes of IMDRF/AE WG/N43Final:2025 [published 2025 March 03] are available on URL:

https://www.imdrf.org/documents/terminologies-categorized-adverse-event-reporting-aer-terms-terminology-and-codes

Find the relevant codes from Annex A to Annex G for the incident, to fill the Incident Report Forms.