The periodic safety update report and post market surveillance report under the new EU Medical Device Regulation

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Abstract

The new EU Medical Device Regulation 2017/745 (MDR) requires companies to provide a periodic safety update report (PSUR) and a post market surveillance report (PMSR). Creating these reports will strengthen the post market surveillance and vigilance system of medical devices by improving quality and patient safety. The first compliance deadline 1 year after the date of application of the regulation is around the corner, but a guidance document on PSUR requirements has yet to be officially released. The guidance draft has been re-worked several times in the last few years, becoming a very lengthy document outlining more detailed and precise information on high-level points described in the MDR regulation, thus introducing more ambiguity in certain sections. It is quite evident that creating PSURs and PMSRs is not a small task and should not be underestimated by manufacturers. Companies should seriously consider investing in the automation of report authoring to reduce the cost of manually creating the PSUR and PMSR.

Introduction

The periodic safety update report (PSUR) and post market surveillance report (PMSR) are two reports that are now required for post market surveillance (PMS) under Articles 86 (PSUR) and 85 (PMSR) of the new EU Medical Device Regulation 2017/745 (MDR)[1] with May 26, 2021 as date of application (DoA). The PSUR is not a new concept and has long been a requirement in pharmacovigilance (PV), and is now an obligation required for medical devices. Like the pharmaceutical industry,[2] the objective of creating such reports is to have a more robust PMS system. The aim is to strengthen the effectiveness of PMS activities and use the reports as a source for identifying new safety signals, monitoring the success of such mechanisms, updating the benefit-risk profile, and having an effective and transparent dialogue between manufacturers, regulatory bodies, and patients. As described in the MDR Article 83[3], the PMS system should be used to update device design, clinical evaluation, the Summary of Safety and Clinical Performance (SSCP), labelling, among other related interfaces.[1]

The PSUR and PMSR requirements

The PSUR is the summary of the results and conclusions of the PMS data gathered through the PMS activities outlined in the PMS plan (Article 84), the manufacturer's conclusions inferred from such PMS activities that may result in any corrective and preventive action (CAPA), and the conclusion of any changes in the benefit-risk profile. The PMSR has similar content to the PSUR but with fewer requirements and is a slimmer document compared to the PSUR. Several conferences on this topic, medical device blogs, online articles, and white papers[4-9] have summarised the requirements and differences between the PSUR and PMSR based on the published MDR and their current understanding of its implementation. Table 1 presents an overview of the MDR requirements. However, the description in the regulation is still somewhat high-level, leaving a fair amount of interpretation for the manufacturers and notified bodies (NB).

MDCG guidance on PSUR requirements

Guidance documents developed by the Medical

Device Coordination Group (MDCG) are drafted in collaboration with many parties and aim at implementing a common understanding of the legislation and increased harmonisation of documents in the medical device industry.[10] The European Commission (EC) has been working for several years on a guidance to assist manufacturers in creating PSURs compliant to the MDR. Nonetheless, up until now, only drafts have been shared to collect comments, and the guidance on the PSUR is still showing as "MDCG work in progress" on the EC's website even though the expected date of MDCG endorsement is listed as Q4-2021.[10] MDCG guidances are not legally binding[10] but are used as reference documents (checklists) by NBs to review and audit, thus, are incredibly relevant. Quite concerning is that the first PSURs for class IIb (including implantables) and class III devices are due on May 26, 2022, 1 year after DoA. At the time of writing, the medical device sector and the NBs do not have an "official guidance" as a reference and cannot expect manufacturers to follow the MDCG PSUR draft guidance to the letter. Consequently, it is highly recommended to have regular conversations and agreements with the NBs regarding submissions and content of the PSURs.

Several draft versions of the PSUR guidance have been circulated since 2020, and what started as a lean, high-level document has evolved into a very dense, intricate, and extensive manuscript, still unclear and ambiguous in certain sections. The draft guidance breaks down what is shown in Table 1 in more detail. It provides more information on what CAPAs to present in the

Table 1. PSUR and PMSR requirements and differences by device class according to EU MDR

Report	PMSR (low-risk devices)	PSUR (medium to high-risk devices)	
Device class MDR	Class I	Class IIa	IIb and III
		Class IIa and IIb implantables	
Periodic update cycle	As needed, determined by the manufacturer	At least every 2 years	yearly
Common requirements	Results and conclusions of the analyses of the post market surveillance data gathered as a result of the post market surveillance plan referred to in Article 84		
	Rationale and description of any preventive and corrective actions taken		
Specific requirements based on MDR Articles 84, 85, 86, and Annex III	Complaint handling and AE reporting (vigilance): serious incidents and non-serious incidents (Art. 88)		
	Recalls and field safety notices		
	Scientific and technical literature. If applicable, based on the class and type of the device		
	Customer feedback and other proactive PMS activities (e.g., satisfaction survey, user survey, social media listening, focus groups, expert panels, etc.). If applicable, based on the class and type of the device		
		• Information on similar devices from AE and FSCA databases (e.g., MAUDE, MHRA, IMDD, etc.) • Registries (e.g., National Joint Arthroplasty Registries, etc.) • Main findings of the PMCF activities (e.g., specific literature, hospital registries, patient databases, specific clinical customer surveys, PMCF studies, etc.) • The volume of sales of the device and an estimated evaluation of the size and other characteristics of the population using the device and, where practicable, the usage frequency of the device • Conclusions of the benefit-risk determination	
Regulatory requirements	To be maintained and available to EU competent authorities upon request, but it does not need to be submitted regularly	The PSUR for Class III and implantable medical devices must be submitted via EUDAMED	

Abbreviations: AE, adverse event; EUDAMED, European Database for Medical Devices; FSCA, field safety corrective action; MAUDE, Manufacturer and User Facility Device Experience; MHRA, Medicines and Healthcare products Regulatory Agency; IMDD, Investigational Medical Device Dossier; PMCF, post market clinical follow-up; PMS, post market surveillance

Table 2. Overview of the MDCG PSUR draft guidance and associated challenges

Topic	Content	Additional Details & Challenges
Executive summary	Background information related to the benefit-risk profile	• If applicable, brief status description of actions taken by the manufacturer in the previous PSUR • If applicable, brief status description of the action taken by NBs in the previous PSUR • Data collection period • Based on the main results of the current PSUR, a clear statement indicating if the benefit-risk statement has been impacted positively or negatively
Description	General	Device classification, CE date (or first availability in the market), the status of the device in the market, intended purpose (instructions for use), indications, contraindications & target population
	MDR devices (BUDI-DIs)	Information provided according to BUDI-DIs groups, outlining device changes within the groups compared to previous PSURs, if applicable.
	Legacy devices & custom-made devices	Information provided by device model/device groups
Grouping of the devices	Grouping rules and additional considerations	• Multiple BUDI-DIs (or device families) may be covered in one PSUR as long as they have the same NB • In case the device is marketed with successive certificates of different NBs, a cross-reference should be added in the PSUR • In case of Multiple BUDI-DIs, performance should be clearly identified per BUDI-DI group • Introduction of "leading" device and "secondary" device concepts and changes in "leading" device **Challenges** • In case a PSUR includes several BUDI-DIs, the data must be presented in a way that the performance of each BUDI-DI can be followed. • Can become very complex depending on the manufacturer portfolio and number of medical devices
Sales volume	Volumes of sales, units shipped, or units implanted or another suitable method	All devices placed on the market, presented in a yearly format, providing devices information (sizes, models & configurations) **Challenges** • To determine sales or shipments for multiple-use instruments can be challenging since many instruments are supplied in loner kits (directly sent to the hospital and then returned to the manufacturer). For example, an alternative is to use implant sales as a reference to indicate the number of surgeries.
Size and other characteristics of the population using the device	The population for which the device has been used considering the device claimed intended purpose	Reported on the extent which is possible for the manufacturer **Challenges** • The size and characteristics of the actual population using the device are often tough to obtain. Patient information is sensitive and can only be shared on a high-level basis. Also, the hospital/ surgeon usually does not report such information.

PSUR, the grouping of the devices, PMS requirements for medical devices remaining under Medical Device Directives , until when a PSUR is required (i.e., device lifetime), data collection periods, subsequent updates of the PSUR, and finally regulatory aspects (e.g. timelines, and submission to the European Database for Medical Devices [EUDAMED] and in the absence of EUDAMED).[11] Also, six annexes with additional information such as a content checklist, additional information on requirements, data reporting, data evaluation and submission, terminology, and a PSUR form to be filled for EUDAMED submissions are part of the draft. One of those annexes suggests ways of presenting data in several proposed table templates, all of which make evident how time-consuming authoring a PSUR according to this guidance will be and the probable expectations of regulatory bodies. Table 2 summarises the content of the MDCG PSUR requirements based on last year's draft[11] and the main associated challenges from the authors' perspective.

Associated challenges

In agreement with Ben-Menahem et al. 2020, the MDR brings substantial improvement to patient safety by consolidating the requirements on vigilance and PMS, clinical investigations, conformity assessments and adds significant changes to the roles of NBs in terms of audits and certifications.[12] It emphasises a more rigorous risk management process by establishing a stronger relationship between the clinical evaluation and PMS processes. Nevertheless, it also introduces several layers of complexity

Table 2. Continued

Topic	Content	Additional Details & Challenges
Post Market Surveillance (PMS) data including general PMCF data	Vigilance data	• Complaints and statistical analyses (trend reports) • Serious Incidents reported to competent authorities • Non-serious incidents (Article 88 trend report) • IMDRF AE terminology **Challenges** • No guidelines or instructions are given on which statistical tools to be used for the trend analysis • Trending on IMDRF data might be challenging if not enough historical data is available • No templates or guidelines given on how to perform the trending according to Article 88
	General PMCF data	• Complaints: not reported in the vigilance section, IMDRF grouped or by internal event code, occurrence rates, justification for the exclusion of complaints • Scientific literature review, public registry data, public information on similar devices, other **Challenges** • For example, most national joint registries only collect data on hip and knee arthroplasty implants. Only a couple collect data on other anatomical joints like shoulder, wrist, ankle, etc. • Many registries have incomplete data and cannot provide special reports to industry • AEs identified in literature is challenging because product information is extremely limited or not available. Consequently, a proper investigation is hardly possible. Also, potential duplication of complaints may occur.
	Preventive or corrective actions (Article 83.4)	• CAPAs resulting from the PMS system • Quality management system related (CAPAs are excluded) unless they could have a direct impact on product safety, performance, or quality **Challenges** • Every CAPA can somehow directly impact product safety, performance, or quality. It is difficult to determine which CAPAs can be excluded.
	Preventive and corrective actions for safety reasons	(FSCA, Article 87) FSCAs resulting from the PMS system
Specific Post Market Clinical Follow-up (PMCF) data	Summary of data generated from PMCF activities	• Data not limited to PMCF studies, may include but not limited to, evaluation of suitable registers, manufacturer device registries, surveys, and real-world evidence analyses • PMCF Report may be referred to, but enough details should be outlined in the PSUR **Challenges** • Surveys might not provide specific enough information/ adverse events
Summary of the findings and conclusion of the PSUR	Data validity, overall conclusion and, if applicable, action(s) taken by the manufacturer	• Data limitations • If applicable, newly identified risks and their potential clinical impact as well as new identified benefits • A conclusion to determine if the benefit-risk profile has changed • Specific actions taken to address any identified unknown risks • Actions taken during the data collection period evaluated in the PSUR

Abbreviations: NB, notified body; BUDI-DI, Basic Unique Device Identification – Device Identifier; AE, adverse event; IMDRF, International Medical Device Regulators Forum; CAPA, corrective and preventive actions; FSCA, field safety corrective actions

because not only do challenges related to the PSUR content exist (Table 2), but there are also numerous steps involved in its creation process. Some concrete examples are data retrieval, data processing, data analysis, data consistency and accuracy, development and sustainability of proactive PMS activities, and building quality into the PSUR process. Furthermore, MDR requirements on PMS apply to "legacy" and "old" medical devices,[13] although some flexibility is allowed to create leaner documents for the latter. Also, if the "old" devices were not phased out from the market before DoA, the conditions of the MDR apply.[13]

All of the conditions mentioned above increase compliance costs throughout new product development, certification, and maintenance while also relying heavily on the

availability of adequate resources. Large companies with large product portfolios may absorb those expenses. Still, many of those large companies were forced to re-evaluate their product portfolio based on their company size, number of marketed products, number of sales, number of countries where the medical devices are marketed, the volume of complaints, type of indication(s) for which the medical device is specified and more. In comparison, smaller companies and start-ups, which represent 95% of the medical-technology sector and are considered a vital source of progress and innovation, may not fare as well due to an increase in regulatory compliance costs and longer times to market for new medical devices, all resulting from the new MDR requirements.[12] Furthermore, the introduction of the MDR has served as an example for many non-EU countries, resulting in an update of their medical device regulations with more strict PMS requirements. As a result, companies have started to receive requests for PMS reports that may or not require the same content, thus adding to the current workload introduced by the MDR.

Is automated report authoring the future?

An article published in 2019 on trends in regulatory writing[14] mentioned how PV companies had recognised the importance of automation for data mining and artificial intelligence (AI) to address the volume of data availability, data collection cost, data assessment, data processing, and analysis. These aim to reduce execution time, labour cost, human error, increase consistency within the data and among different authors of documents. At the same time, the use of AI is left to the interpretation and analyses of data, thus moving towards predictive PV.[14] Currently, automation and AI are highly focused on retrieving and reviewing medical literature because it is considered a substantially time-consuming task. It involves developing consistent search strategies of scientific publications, their appraisal, the extraction of adverse events (AEs), and adequate analysis by subject matter experts (SMEs). However, a recent publication stressed[15] the utilisation of AI can go beyond data mining of literature to include analysis of safety data from various internal databases used within companies and external sources like AEs global databases or social media. The above aspects are also transferable to the medical device industry, specifically the automation of PSUR and PMSR authoring. Based on the content on the MDCG guidance on PSUR requirements, the author opines that companies should invest, especially those with large portfolios, in automating the creation of PSURs and PMSRs. The aim would be to reduce lead times in writing the reports, decrease workload, increase the number of reports produced, and meet submission deadlines while maintaining content quality and compliance to the MDR and other applicable regulations. This would definitely have a beneficial business and cost impact.

Pianka et al. (2021) developed an electronic platform for PV that populates a periodic safety update template. One of their first steps was to identify automatable content versus non-automatable content. Automatable content was defined as information that could be authored by extracting data from source documents or internal company databases (e.g. sales, distribution data, statistical analyses, etc.), and non-automatable content was defined as information that required discussion and interpretation by SMEs (e.g. benefit-risk conclusion). The result was a combination of fully automated, semi-automated, and non-automated sections. The authors reported that automation saved 25% of the time required to write a safety update report and an overall quality improvement, which translated into cost savings.[16] PSUR and PMSR automation is undoubtedly the future for the medical device sector. Nonetheless, challenges, risks, and limitations should be considered such as cost-benefit, ensuring source data consistency, errors pulling source data, maintenance of the tool to keep with regulation changes, amongst many others.

Conclusion and outlook

The MDR certainly improves patient safety. The PSUR and PMSR are undoubtedly some of its most effective tools to demonstrate cohesiveness among vigilance, PMS, clinical evaluation, risk processes, and regulatory bodies. Thus, they are crucial to determining benefit-risk profile changes. Challenges are inevitable whenever a new process is implemented for the first time because of the associated additional resources, workload, and high costs. This is also true for the first PSURs and PMSRs implementation, notably if data mining is involved. However, the constant re-drafting of the MDCG guidance on PSUR requirements without a final official version released to date poses additional hardships for manufacturers, especially when the first regulatory deadlines for PSUR readiness are around the corner. Furthermore, there is still lack of clarity in some sections of the draft due to certain complexities that can be interpreted

differently by manufacturers.

It is important not to underestimate the requirements of the PSUR. Future considerations should take into account proper resource planning (roles and responsibilities), adequate training of resources (an increase of expertise), metrics (number of late PSUR submissions, number of error and inconsistencies, audit observations, etc.), automation of data mining methods and the actual authoring of reports (reducing manual labour and human error) and finally clear and constant communication with the NB in terms of PSUR expectations and submissions (clarification of content and timelines).

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employer or EMWA.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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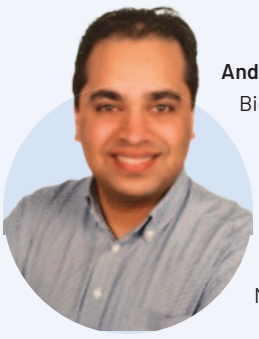

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