Medical Devices

SECTION EDITOR

Kelly Goodwin Burri
kellygoodwinburri@stryker.com

Editorial

After the cancellation of EMWA's Spring Conference this year, EMWA's Medical Device Special Interest Group stepped up to ensure that members did not miss out on the Expert Seminar Series (ESS) by organising a virtual version of the event. Cherry Malonzo Marty provides a summary of the virtual ESS where medical device experts weighed in on drug-device combination products and an update on the new Eudamed database. In other news, preparations for the Medical Device Regulation continue even with implementation postponed to May 2021. Kerstin Römermann and Wiebke Theilmann describe two new guidance documents for post-marketing clinical follow-up plan and report templates released earlier this year by the Medical Device Coordination Group that will guide you in preparing these new documents.

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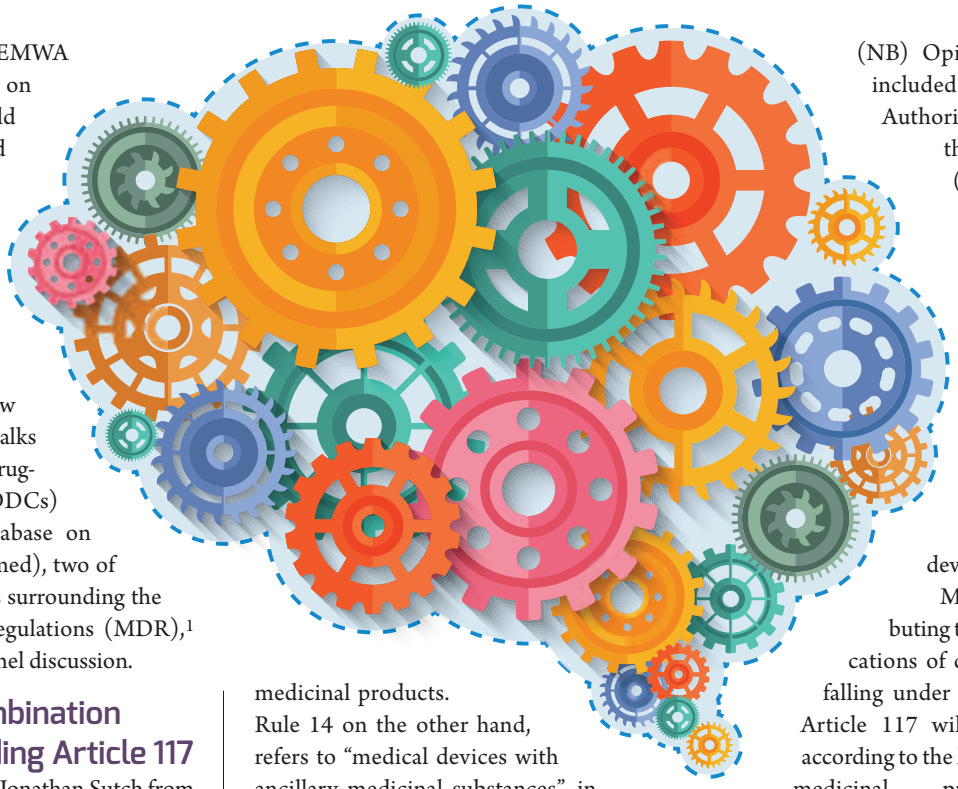
Virtual Expert Seminar Series



The first ever virtual EMWA Expert Seminar Series on Medical Devices was held on June 9, 2020. Attended by 39 participants, the majority having less than 5 years of professional experience in the medical device industry, the session was received positively with the new virtual format. The two talks in this series focused on drug-device combinations (DDCs) and the European Database on Medical Devices (Eudamed), two of the many open concerns surrounding the new Medical Device Regulations (MDR),[1] and concluded with a panel discussion.

Drug-device combination regulation including Article 117

The first presentation by Jonathan Sutch from BSI UK focused on DDC products classified under Rule 14 and Rule 21 of the MDR and products that fall under Article 117. Beginning with regulatory definitions differentiating medical devices under the MDR and medicinal products under the Directives 2001/83/EC,[2] the presentation continued by explaining the concept of the primary Mode of Action (MOA) that will determine the applicable regulatory pathways for these types of products.

Rule 21 refers to devices containing substances (e.g., paraffin dress) which need to comply to Directive 2001/83/EC for medicinal products.

Rule 14 on the other hand, refers to "medical devices with ancillary medicinal substances", in which the medical device acts as the primary MOA of the combination (e.g., drug-eluting stent), requiring compliance to the MDR. Though this type of product is sometimes referred to as "Device-Drug Combination" (also DDC), this is an informal name and should not be confused with integral DDCs falling under Article 117.

Article 117 of the MDR is an amendment to Directive 2001/83/EC, which applies to so-called integral DDCs such as inhalers or pre-filled syringes. Under this amendment, such products will now require either CE Marking on the device component or a Notified Body (NB) Opinion (NBOp) to be included in the Market Authorisation Application of the medicinal product (Figure 1).[3] With the requirement of an NBOp, the medical device component of integral DDCs must conform to the relevant General Safety and Performance Requirements of Annex I of the MDR as justified by the device's intended purpose. Medical writers contributing to the pre-market applications of combination products falling under Rule 14, Rule 21, or Article 117 will have to document according to the EU MDR as well as the medicinal product Directives 2001/83/EC, keeping in mind that the reviewers as well as the requirements are different for each. Though this may be a challenge for medical writers accustomed to writing for only one sector and not the other, this would also be an opportunity to learn the regulatory language necessary to fulfil the requirements of such combination product submissions.

The new Eudamed under the MDR

The second talk was presented by Richard Houlihan, the technical IT manager for

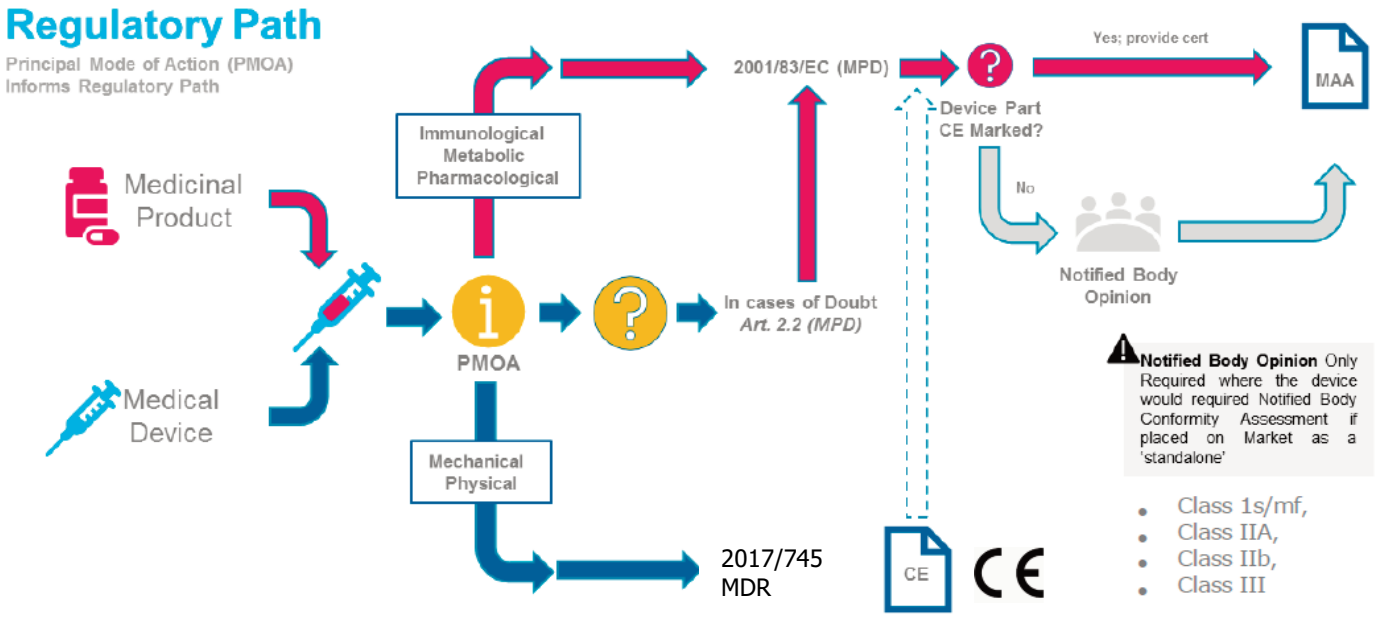


Figure 1. Future process (from May 26, 2021) for drug-device combinations under the Medical Device Regulation. Reprinted with permission from BSI UK.

Eudamed. This new database is now scheduled to go live in May 2022, when the new MDR and IVDR are already in place. The delay from the initial target date of May 2020 was announced earlier this year, citing the need for more time to ensure that the platform was fully functional before launch. The presentation covered the scope of the new Eudamed, an update of the Eudamed2 that is currently only accessible to competent authorities and the European Commission. Eudamed, in comparison, is being built to be accessible to all stakeholders, including the public, as a multi-purpose registration, collaboration, notification, and dissemination system.

With the large scope and six main modules that no other medical registration system implements to date, the challenges of develop-

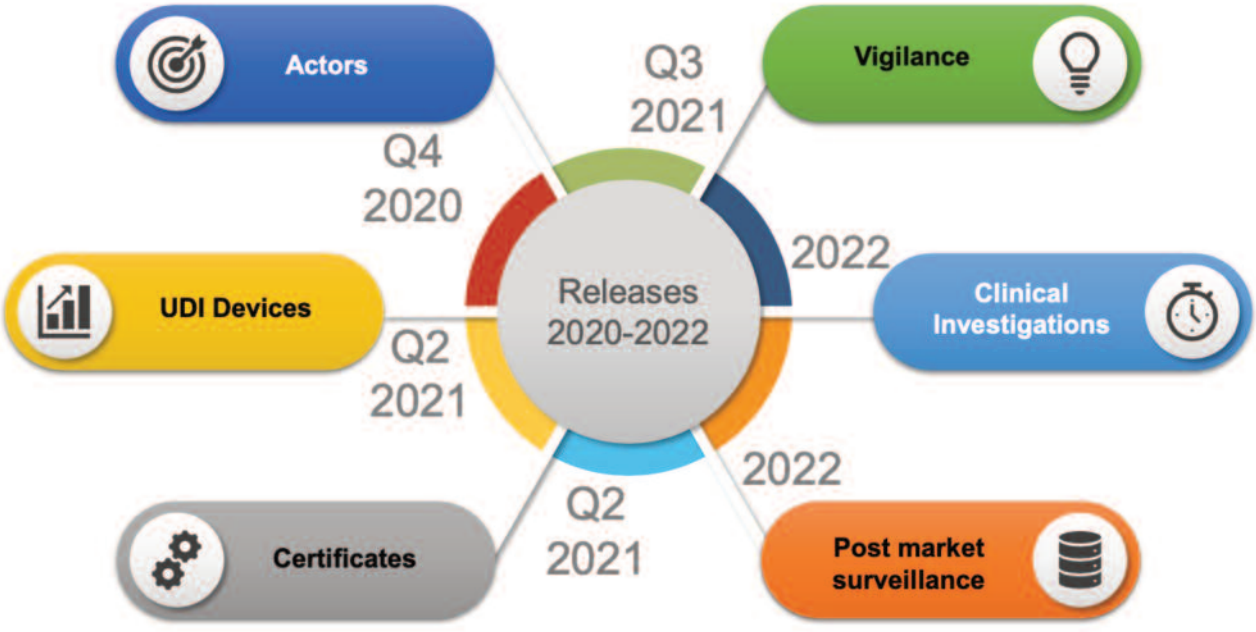


Figure 2. Timeline of Eudamed module releases. Reprinted with permission from Eudamed Ltd.

ing and implementing the interoperable system are multifaceted. Namely, the decisions of the Medical Device Coordination Group (MDCG) to Eudamed were referenced,[4] including decisions on legacy devices and nomenclature to be implemented in the new system. Emphasis was made on the technicalities of the new Unique Identification Number (UDI) that will be implemented with the new EU MDR, as well as the need for all stakeholders to review relevant guidance documents, in order to understand the functionality and requirements for uploading data into the database.

Figure 2 shows the Eudamed timeline with a staggered release of the different modules until the database is fully functional in 2022.[5] Though the MDR application date has been postponed 1 year, Eudamed still intends to release the first module at the end of 2020 and latest by May 2021 in time for the new MDR application date. The presentation emphasised the extensive amount of preparation that will be required for the large data submissions into the Eudamed modules. Though the specifics of the modules cannot be publicly disclosed yet, early preparation could not be overstated in order to collate all the Eudamed data in time for submissions when the modules go live. From web-based forms to bulk uploads and machine-to-machine inputs, preparation and understanding of the requirements is key to streamline the efforts of reporting. For medical writers, the potential of the EUDAMED system will not be optimised if data and documents do not fulfil the requirements in time for digital submissions.

Expert panel Q & A

The ESS was concluded by panel discussions where the experts were joined by Jane Edwards from BSI and Gillian Pritchard from Sylexis. The presentations had shed some light on the fundamental concepts of DDCs and the importance of preparing for Eudamed submissions in time for the MDR application date. However, it is also apparent that there are still ongoing developments. Even a survey poll conducted during the ESS returned unsurprising results; the participants believed the MDR delay of a year was appropriate. Though the ongoing COVID-19 pandemic has led to the postponement of MDR implementation, giving stakeholders in industry more time to prepare for the transition, many questions remain regarding MDR-readiness. Until May 2021, we may expect demand for more sessions like these being conducted across industry to aid in the crucial preparations of all stakeholders for the inevitable transition.

References

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Cherry Malonzo Marty, MD, MSc BME
cherrymalonzo@m3writing.com

Post-market clinical follow-up plans and evaluation reports

In April 2020, the Medical Device Coordination Group (MDCG) endorsed post-market clinical follow-up (PMCF) plan and PMCF evaluation report templates as a guidance for manufacturers to ensure compliance with the relevant requirements. Here we aim to provide an overview of the contents of the MDCG template documents.

As PMCF plans and reports are reinforced under the Medical Device Regulation (MDR), uncertainties exist regarding which information has to be documented and how. Even though Annex XIV Part B of the MDR[1] provides the minimum requirements for a PMCF plan, the description is rather short and lacks detailed information. With the purpose to guide manufacturers in complying with the requirements of the MDR, the MDCG created a template PMCF plan and PMCF evaluation report with detailed instructions on format and content. The MDCG template documents are not European Commission documents and not legally binding. They were designed to simplify the work of both, the manufacturer in complying with all relevant standards and the notified bodies or competent authorities in data extraction. Manufacturers who have already prepared their own PMFC plan templates might need to update them in order to capture any missing elements from the MDCG guidelines.

The PMCF plan and the PMCF evaluation report are similar in content and section structure. The templates are structured into seven sections (Table 1). Both documents shall be stand-alone documents and therefore,

Table 1. Sections of the MDCG PMCF plan and PMCF evaluation report template documents from MDCG 2020-7 and MDCG 2020-8

	Template section heading	
Section	**PMCF plan template**	**PMCF evaluation report template**
A	Manufacturer contact details	Manufacturer contact details
B	Medical Device description and specification	Medical Device description and specification
C	Activities related to PMCF: general and specific methods and procedures	Activities undertaken related to PMCF: results
D	Reference to the relevant parts of the technical documentation	Evaluation of clinical data relating to equivalent or similar devices
E	Evaluation of clinical data relating to equivalent or similar devices	Impact of the results on the technical documentation
F	Reference to any applicable common specification(s), harmonised standard(s) or applicable guidance document(s)	Reference to any common specification(s), harmonised standard(s) or guidance document(s) applied
G	Estimated date of the PMCF evaluation report	Conclusions

Source: MDCG 2020-7[2] and MDCG 2020-8.[3]

the manufacturer details as well as device description and specification need to be documented in the first two sections. The PMCF plan contains a definition of the specific objectives as well as general and specific methods and procedures that will be conducted in the post-market period. This could be a screening of scientific literature and other sources of clinical data, post-market studies (e.g., prospective case series, retrospective patient record reviews, nested registry studies), analysing data in registries, surveys from health care professionals or patients/users, or reviews of case reports which may reveal misuse or off-label use. The choice of methodology should be based on the level of risk associated with the device, e.g., literature screening might be a sufficient PMCF activity for low risk, non-implantable devices with sufficient clinical evidence. Each PMCF method and procedure is described in detail in specific subsections. Within these subsections, the manufacturer will provide:

- A definition where the need of conducting the PMCF activity is coming from
- A description of activity and if it is a general or specific method/procedure
- A definition of the aim of the respective activity
- A description of the respective methods
- A rationale for the appropriateness of the chosen methods/procedures. This includes and is not limited to justifications for sample size, endpoints, comparators, study design or statistics
- A detailed and adequately justified time schedule for all planned PMCF activities

Furthermore, a PMCF plan must document the evaluation of the clinical data related to equivalent or similar devices as defined in the clinical evaluation plan. These data may be used to update state of the art information or identify relevant safety outcomes. Nevertheless, the device under evaluation itself should deliver the data to demonstrate continuing safety and performance.

In the penultimate section, the PMCF plan and the PMCF evaluation report shall reference to the relevant parts of the clinical evaluation report and to the risk management (referred to in Section 4 and Section 3 of Annex I)[1] and to any relevant common specifications, harmonised standards, and relevant guidance on PMCF, if applicable. The results of the manufacturer initiated PMCF analyses are stated in the PMCF evaluation report document. The overall conclusion of the findings is provided and related to the aims of PMCF in the last section of the PMCF evaluation report. Moreover, the conclusion focusses on necessary implementations of corrective and preventive actions. The conclusion will also be part of the following clinical evaluation, the risk management file, and gives input into the next PMCF plan.

Still, several uncertainties exist regarding which and how PMCF information must be documented under the MDR. Thus, the MDCG templates provide a helpful tool to simplify and accelerate the work of manufacturers and notified bodies.

References

1. European Commission. 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/EE. [cited 2020 Jul 1]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX: 32017R0745
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Kerstin Römermann, PhD
Roemermann@tr-medicalwriter.de

Wiebke Theilmann, PhD
Theilmann@tr-medicalwriter.de