Süleyman Demirel Üniversitesi
Fen Bilimleri Enstitüsü Dergisi
Cilt 28, Sayı 3, 415-421, 2024

Süleyman Demirel University
Journal of Natural and Applied Sciences
Volume 28, Issue 3, 415-421, 2024

DOI: 10.19113/sdufenbed.1508221

A Novel Method for Monitoring Notified Bodies Designated under The European Union Medical Device Regulation

Tuncay BAYRAK[1*]

Turkish Medicines and Medical Devices Agency, 06520, Ankara, Turkey
Atılım University, Engineering Faculty, Computer Engineering, 06830, Ankara, Turkey

(Alınış / Received: 01.07.2024, Kabul / Accepted: 23.08.2024, Online Yayınlanma / Published Online: 23.12.2024)

Keywords
Monitoring,
digitalization,
medical device,
conformity assessment,
legislation,
notified body

Abstact: Notified bodies (NBs), which perform conformity assessments, play a crucial role in protecting patient health and providing access to safety products on the market. The EU 2017/745 Medical Device Regulation (MDR) brings stricter rules and responsibilities for notified bodies. Designating authorities (DAs), who are also responsible for monitoring notified bodies, have not been provided with any guidance documents or written procedures. In this study, for the first time, we proposed a methodology aided by a digital system to monitor notified bodies effectively. We conducted a need analysis based on the MDR requirements and the relevant guidance documents, and we introduced a six-component technique for monitoring of the medical device notified bodies. Then, we identified the subcriteria of each component and created business activity diagrams for the main processes to monitor the notified bodies. There are now forty-nine notified bodies available under the MDR. Our monitoring approach consists of six steps that cover all NB-related activities, such as review of technical documentation assessment, personnel authorization, and surveillance of the certified product on the market. The proposed system complies with the MDR requirements and handles all critical performance indicators of NBs. The new MDR requirements for NBs also require an advanced monitoring system for DAs. This study focused on the critical points for monitoring NBs. Member states should implement the proposed methodology and the activity diagrams to have an efficient monitoring system in accordance with MDR requirements. A similar system can be used for monitoring of the other conformity assessment bodies.

Avrupa Birliği Tıbbi Cihaz Yönetmeliği Kapsamında Yetkilendirilen Onaylanmış Kuruluşların İzlenmesi için Yeni Bir Yöntem

Anahtar Kelimeler
İzleme,
dijitalleşme,
tıbbi cihaz,
uygunluk değerlendirmesi,
mevzuat,
onaylanmış kuruluş

Öz: Uygunluk değerlendirmesi gerçekleştiren onaylanmış kuruluşlar, hasta sağlığının korunmasında ve piyasadaki güvenli ürünlere erişimin sağlanmasında çok önemli bir rol oynamaktadır. AB 2017/745 Tıbbi Cihaz Yönetmeliği (TCY), onaylanmış kuruluşlar için daha katı kurallar ve sorumluluklar getirmektedir. Onaylanmış kuruluşların izlenmesinden de sorumlu olan atama otoriteleri için herhangi bir rehber doküman veya yazılı prosedür yoktur. Bu çalışmada, ilk kez, onaylanmış kuruluşların etkin bir şekilde izlenmesi için dijital bir sistemle desteklenen bir metodoloji önerilmiştir. TCY gerekliliklerine ve ilgili rehber dokümanlara dayalı bir ihtiyaç analizi gerçekleştirilmiş ve tıbbi cihaz onaylanmış kuruluşlarının izlenmesi için altı bileşenli bir teknik ortaya koyulmuştur. Ardından, her bir bileşenin alt kriterleri belirlenmiş ve onaylanmış kuruluşların izlenmesine yönelik ana süreçler için iş aktivite diyagramları oluşturulmuştur. Şu anda TCY kapsamında kırk dokuz onaylanmış kuruluş bulunmaktadır. İzleme yaklaşımımız, teknik dokümantasyon değerlendirmesinin gözden geçirilmesi, personel yetkilendirmesi ve sertifikalı ürünün piyasada gözetimi gibi onaylanmış kuruluş ile ilgili tüm faaliyetleri kapsayan altı adımdan oluşmaktadır. Önerilen sistem TCY

*Corresponding author: bayraktuncay@gmail.com

gerekliliklerine uyumludur ve onaylanmış kuruluşların tüm kritik performans göstergelerini ele alır. Onaylanmış kuruluşlar için yeni TCY gereklilikleri, atama otoriterleri için de gelişmiş bir izleme sistemi gerektirmektedir. Bu çalışma onaylanmış kuruluşların izlenmesi için kritik noktalara odaklanmıştır. Üye devletler, TCY gerekliliklerine uygun etkin bir izleme sistemine sahip olmak için önerilen metodolojiyi ve faaliyet diyagramlarını uygulamalıdır. Benzer bir sistem diğer uygunluk değerlendirme kuruluşlarının izlenmesi için de kullanılabilir.

1. Introduction

Medical devices are defined as various tools, apparatuses, software, machinery, and similar products that are used for the prevention, diagnosis, treatment, and prognosis of disease in humans and that show a mechanism of action electrically, physically, or mechanically, unlike medicines [1]. The EU 2017/745 Medical Device Regulation (MDR) aims to regulate the market in which high-quality and safe medical devices are available in place of the directives[2,3]. Conformity assessment is the main activity for accessing safe and quality products on the market. It is defined as the process of demonstrating whether the requirements of the MDR relating to a device have been fulfilled. Manufacturers shall apply to third parties (notified bodies in the MDR) for conformity assessment of higher risk class devices (class IIa, IIb and III). Designating authorities designates the notified bodies in accordance with MDR Art 38-42. Notified bodies should be independent, impartial and objective when assessing the conformity of devices [4]. Manufacturers and notified bodies are the primary actors in the market. Therefore, the EU released several guidelines for these actors after the MDR was published [5]. The number of notified bodies designated under the MDR is forty-eight [6]. The MDR defines new rules for manufacturers and notified bodies. Notified bodies assess many technical issues within conformity assessment procedures, as manufacturers of higher risk devices are under the supervision of notified bodies. Similarly, notified bodies are under the supervision of the relevant designating authority. According to MDR Art 46, designating authorities should effectively monitor notified bodies under their supervision. This monitoring activity plays an important role in ensuring continuity in the placement of safe products on the market. There are many parameters for monitoring the performance of notified bodies, but a limited number of personnel and written documents are available for designating authorities. Currently, no guidance documents are available for designating authorities, while the European Commission provides useful information for manufacturers and notified bodies through guidance documents. Designating authorities need to improve their assessment criteria because of the increased responsibilities of notified bodies and the proactive surveillance approach of the MDR.

2. Material and Method

In this study, first, we analysed the relevant requirements and performance indicators for monitoring notified bodies. Second, we conducted a needs analysis in which the necessary roles in the system were identified. Third, we identified the processes and the relevant documentation. We also created business activity diagrams of the activities in NB monitoring using DIA software [7]. Figure 1 shows the inputs that are used in the need analysis. MDR Chapter IV, which describes the rules for the designation authority and notified bodies, is the basis of the monitoring system. MDR Annex VII describes the requirements that notified bodies must meet. We determined the user profiles in the monitoring system based on this chapter, which also defines the relevant roles of notified bodies. The NBOG 2017-2 [8] describes the minimum qualifications of conformity assessment personnel of notified bodies. We reviewed the employment of new personnel of notified bodies in accordance with this guidance. Our digital-based model is able to notify personnel authorization to the designating authority. NBs carry out conformity assessment procedures in accordance with MDR Annexes IX, X, and XI and the conformity assessment routes explained in MDR Chapter V. We defined the relevant functions as receiving customer files prior to surveillance assessment, resource allocation, medical device technical files, consultation, and document sharing within the framework of the information in these annexes.

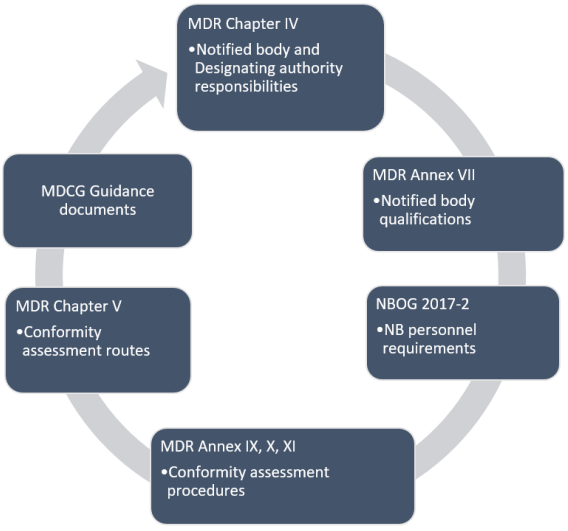

Figure 1. The inputs of the needs analysis for monitoring notified bodies

MDR Art 44 requires an annual plan for monitoring and evaluating notified body activities, and the designating authority (DA) shall provide this plan to the European Commission. This plan includes an observation of the NB's personnel during the quality management system audit at a manufacturer's facility. The DA also performs systematic follow-up for complaints, vigilance, postmarket surveillance by the manufacturer, and market surveillance. DA may conduct short-notice, unannounced or 'for-cause' reviews if needed to address a particular issue or to verify compliance. In addition, the DA reviews the assessments by notified bodies of manufacturers' technical documentation, including clinical evaluation documentation regarding MDR Art 45.

3. Results

3.1. The proposed system

We propose a system for monitoring MDR Art 44 in NBs that explains the main requirements for monitoring NBs explained in the previous section. Our monitoring system consists of six components: (1) project-based monitoring, (2) review of NB assessment of technical documentation, (3) analysis of data obtained from postmarket surveillance and vigilance, (4) outcomes of the other assessments (unannounced, short notice, etc.), (5) review of personnel authorization, and (6) annual on-site assessment activity. Figure 2 shows the components of the proposed monitoring system. The DA can report the results of these six subprocesses and make decisions such as suspending, restricting, or fully or partially withdrawing the designation, depending on the seriousness of the failure of the NB to comply with the MDR. The proposed system provides a systematic assessment scheme to report evidence and justification for NB decisions. The notified body competency is explained with a code system containing active medical devices (MDA), non-active medical devices (MDN), specific characteristics of the device (MDS) and technologies or processes (MDT). Conformity assessment personnel is authorized with the appropriate codes according to some special requirements in educational background, training and work experience.

Project-based monitoring covers all main parts of a certification project carried out by NBs, such as receiving an application from the manufacturer, offering prices and making a contract between the NB and the manufacturer, planning, resource allocation, technical file assessment, assessment of a clinical evaluation report (CER), observation of site audits in the manufacturer's facility, specific procedures such as consultation (if applicable), final review and decision making. The conformity assessment process requires site auditors, product reviewers, special experts, final reviewers, and decision makers, who are the main roles described in the MDR and NBOG 2017-2. The performance of these personnel must be assessed in accordance with the conformity assessment body (CAB)'s procedures. The main activities are explained in MDR Art 52, Annex IX, Annex X, Annex XI and NBOG 2017-2. The DA assessor should have a control list and good knowledge about the legal requirements for these activities. A NB receives a formal application and signs an agreement with the manufacturer regarding MDR Annex VII Article 4.3. In notified body, project leader introduces an audit program and allocates the resources for the certification project of the proposed device that is defined with a basic unique device identification-device identifier (UDI-DI). Audit program includes surveillance and unannounced audits for those devices. In general, audit duration is determined using the International Accreditation Forum Mandatory Documents (IAF MD) 5:2019 [9]. Effective number of personnel and the manufacturing sites impact the audit duration. As a general rule, a lead auditor cannot lead audits of the same manufacturer for more than 3 consecutive years, or cannot participate in audits regarding MDR Annex VII Article 3.6. The personnel who makes the decision to grant certification and the conformity assessment personnel are different from each other. The DA assessor should control these rules.

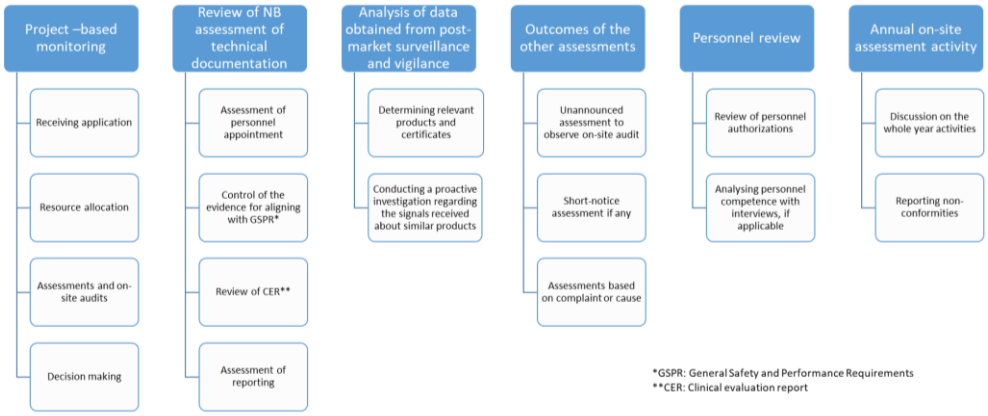

Figure 2. The proposed monitoring system components

The second component is a review of the NB's technical documentation assessment. This can be carried out within project-based monitoring. However, the DA should introduce a sampling plan for the review of technical documentation assessment based on risk classes. Thanks to the guidance documents (i.e., MDCG 2019-13 [10]) published for NBs, the DA can use this guidance to determine the critical points of the process to observe the performance of NBs. MDR requires two types of technical documentation regarding Annex-II and III. Annex II contains the relevant evidence demonstrating the conformity of the product in accordance with general safety and performance requirements, while Annex III requires a surveillance plan to be prepared by the manufacturer for the product after certification. The NB should assess both types of technical documentation. In this regard, the DA assessor should have sufficient technical background and complete at least some training programs, including biocompatibility, risk analysis, quality management systems and auditing principles. The third component is the analysis of postmarket surveillance data, including vigilance records. If there is any nonconformity that is related to the NB's activities, the DA may carry out unannounced or short-notice assessments. This may also include an observation of the quality management system (QMS) audit of the NB. During the one-year surveillance period, unannounced, short-notice or announced assessments for any reason may also be conducted. The DA should also review the personnel authorizations of the NB. It may sample or examine all of them. This depends entirely on the DA personnel capacity and workload. The MDR Annex VII explains the organizational, quality management, resource and process requirements for NBs. The DA should assess the NBs in accordance with this annex and combine the outcomes of steps 1-5 during the on-site assessment. After that, the NB has to implement a corrective and preventive action process to close the nonconformities, if any.

It is very important to ensure effective communication and document transfer between NBs and the DA during monitoring. To this end, a digital-based system can be implemented by DAs. In this respect, we produced business activity diagrams for surveillance and an unannounced assessment of NBs. Figure 3 shows the activity diagram of the surveillance assessment process. The main actors defined in the system are responsible for triggering the assessment process in the DA, assessors and final reviewers in the DA, users from the PMS department of the DA and the NB user. The system should allow for the sharing of documents between the DA and the NB. A final reviewer in the DA is very important to check the whole flow in the process. Figure 4 shows the steps of the on-site observation of an audit carried out by the NB. We can define this process as short-notice or unannounced assessment. The DA should have a monthly audit calendar for the NB to select the appropriate audit that will be observed. For this purpose, the DA can request monthly audit calendars from the NB throughout the year. This notification should involve the product details (i.e., name, risk class), the relevant MDR codes, the auditors appointed and the audit dates. The DA should review or check the audit details and observe the audit process on-site. The diagrams in Figures 3 and 4 can be easily implemented for other countries. The first designation, reassessment or other assessment types can be designed in the same way. This digital system can be used for monitoring other conformity assessment bodies.

The DA first informs the notified body about the dates for the surveillance assessment and the date by which it has to submit the updated QMS documentation. The NB makes the official application and pays the relevant fees. The DA requests selected customer files from the NB and conducts an office review. The DA then shares the assessment plan with the NB, conducts the surveillance assessment at the NB facility and reports nonconformities, if any. The NB submits a corrective and preventive action (CAPA) plan for these nonconformities. The NB carries out its CAPA actions in accordance with the plan approved by the DA. The DA makes the final decision in the surveillance assessment of the NB after these activities.

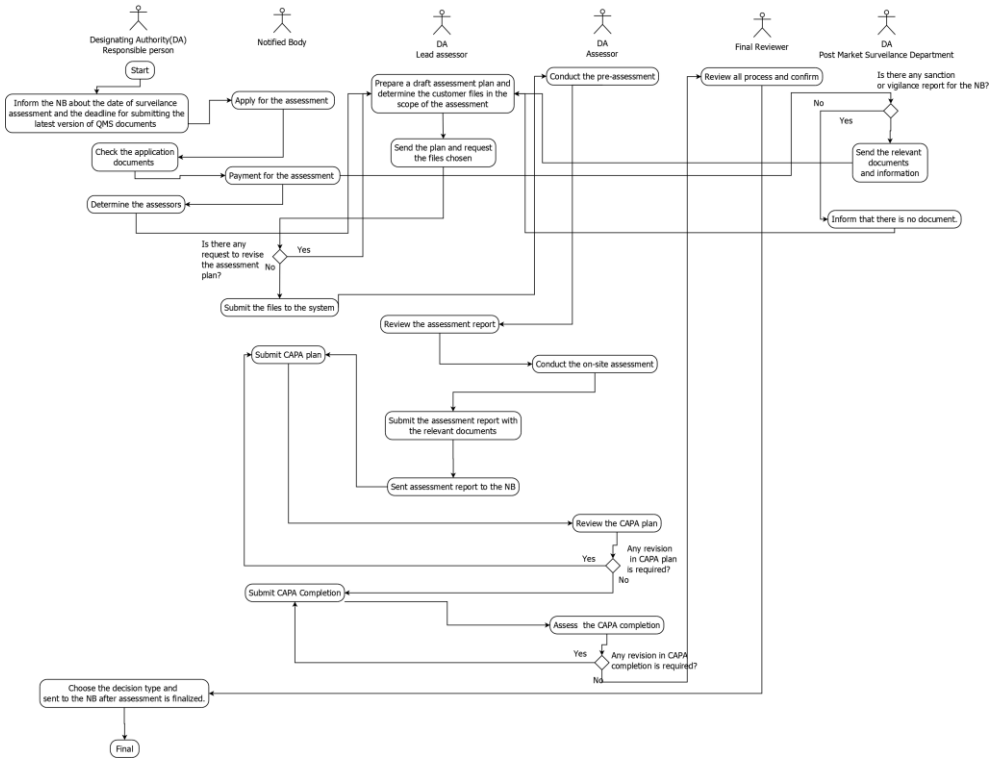

Figure 3. Surveillance assessment activity diagram

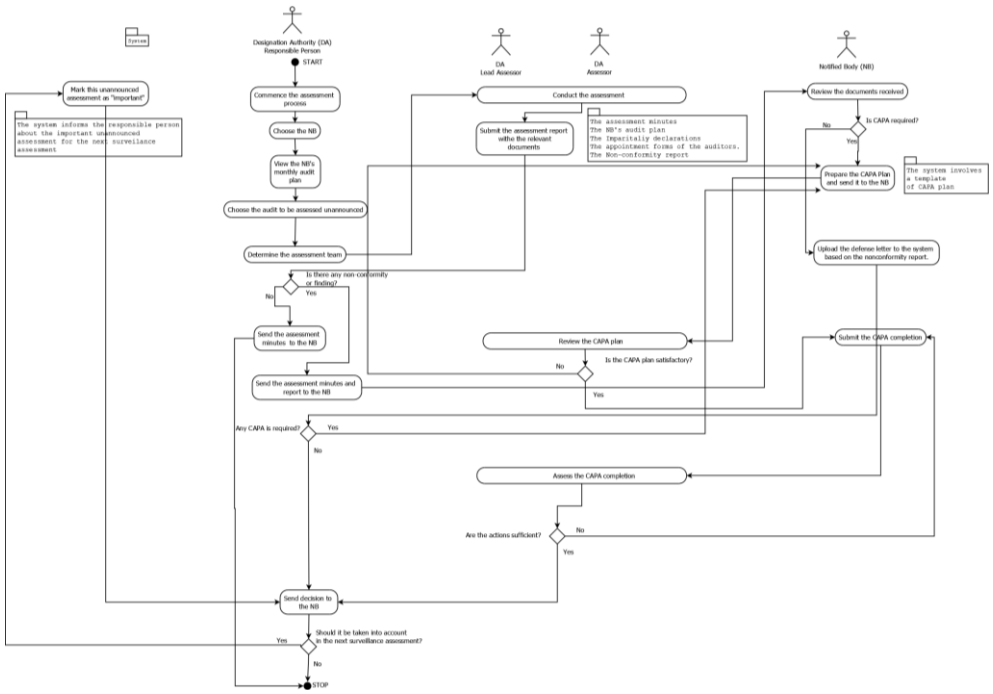

Figure 4. Activity diagram for unannounced/short-notice assessment

4. Discussion and Conclusion

Project-based monitoring can be an efficient method to observe the NB's conformity assessment procedure within the selected project, and it provides a proactive approach. The DA can review all the steps from resource allocation to decision making and observe the performance of the conformity assessment personnel (CAP) in the project. The DA assessor should combine MDR Annex VII and the relevant conformity assessment routes to verify the CAP's actions. The DA assessor should have sufficient information to review the technical documentation of the NB. For this reason, ISO standards that are applicable for the product and preclinical studies should be reviewed in accordance with the general safety and performance requirements (GSPR) of the MDR. A clinician or other relevant personnel who is familiar with the clinical aspects of the product can conduct a review of the NB assessment on a clinical evaluation report. In this respect, MDCG 2020-5 [11], MDCG 2020-6[12] and MDCG 2020-7[13] can be used

to review CER assessments. There is a relationship between the technical file and the manufacturer's facility. According to the technical documentation, the product reviewer must understand the critical points that are related to the production site. Subsequently, product reviewers should inform site auditors about these special processes, such as packaging, sterilization, metal processing, chemical processing or plastic processing. Site auditors should assess these processes on the manufacturer's facilities. The DA assessor should review this cooperation. Personnel appointment is the main activity in resource allocation carried out by the project leader of the NB. For example, the final reviewer and decision maker must be different from the product reviewer and site auditors in the same project. In addition, every NB has a designation scope that consists of MDA/MDN codes that reflect the design and intended purpose of the device, MDS horizontal codes that reflect the specific characteristics of the device and MDT horizontal codes that describe technologies or processes. The MDCG 2019-14 explains the MDR codes with device examples [14]. The NB must employ a sufficient number of personnel for each code. Every personnel is authorized for the relevant codes. A competency matrix that includes the responsibilities and authorizations of the personnel in the NB should be established in accordance with the MDR Annex VII Art 3.3.2. This is a useful tool for viewing the personal capacity of the NB for DA assessors. The project leader must appoint these personnel due to their authorizations for each project. The DA should assess these appointments for the selected projects. This is an indicator of the project leader's competency and performance. The DA should verify these points in the selected projects. Another parameter is the determination of the audit time for the relevant project. In this case, the NB must use the approved procedures to calculate the audit time on the facility, which also depends on the number of effective personnel of the manufacturer. The DA assessor should review this time according to the NB's procedures and IAF MD 5 guidance document. As a result, the DA lead assessor should combine all findings to determine nonconformities, if any.

The capacity of the DA personnel is very important for achieving successful assessment of NBs. In the literature, there are no studies addressing this issue. The DA assessor should approach the technical files like a product reviewer. Considering the components of a medical technical file, many criteria can be determined to demonstrate compliance with the GSPR and special procedures.

MDR has new challenges for all stakeholders, including designating authorities, notified bodies and economic operators. Some studies have focused on the challenges of MDR [15-19] and the benefits of MDR [20]. The EU has also published many guidance documents for notified bodies and economic operators. NBs play a critical role in the medical device market, so monitoring NBs becomes crucial for patient safety. On the other hand, in the literature, very few studies address the designation of notified bodies. Farrugia proposed a methodology that consists of four phases for the designation of notified bodies, but this methodology does not involve monitoring NBs and provides sufficient detail about the assessment of notified bodies. The author reported general guidance for the designation and reassessment of NBs [21]. In contrast, our study, for the first time, proposes a monitoring approach aided by a digital framework. There are many data types for monitoring NBs, such as customer files, technical documentation of products, clinical evidence, and product design. Data security is another important issue, and the DA system should comply with the General Data Protection Regulation, which involves limitations on many data-based activities. Users should be informed about the DA's policy on data management.

The MDR imposes strict rules on conformity assessment processes for the safe supply of medical devices to the market. In the implementation of these rules, manufacturers, notified bodies and designating authorities with oversight responsibility for notified bodies have important responsibilities. Therefore, it is critical to establish methodologies and information sources that can be used by designating authorities to effectively monitor the processes of notified bodies. The methodology and digital-based monitoring approach proposed in this study can be applied by other countries.

Declaration of Ethical Code

In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.

References

[1] Anonym, 2017. (EU) 2017/745 Medical Device Regulation. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745 (Accessed date: 20.05.2024).

[2] Anonym, 1990. Council Directive 90/385/EEC concerning active implantable medical devices. Official Journal of The European Communities, Luxembourg. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A31990L0385 (Accessed date: 20.05.2024).

[3] Anonym, 1993. Council Directive 93/42/EEC concerning medical devices. Official Journal of The European Communities, Luxembourg.

https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A31993L0042 (Accessed date: 20.05.2024).

[4] Anonym, The NANDO website. https://single-market-economy.ec.europa.eu/single-market/goods/building-blocks/notified-bodies_en (Accessed date: 20.05.2024).

[5] Anonym, MDCG Guidance documents. https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en (Accessed date: 20.05.2024).

[6] Anonym, The list of notified bodies under the MDR. https://webgate.ec.europa.eu/single-market-compliance-space/#/notified-bodies/notified-body-list?filter=legislationId:34,notificationStatusId:1 (Accessed date: 20.05.2024).

[7] Medvidovic, N., Rosenblum, D.S., Redmiles, D.F., Robbins, J.E. 2002. Modelling software architectures in the Unified Modelling Language [TOSEM]. ACM Trans Softw Eng Methodol;11(1):2–57.

[8] Anonym, NBOG 2017-2 Guidance on the Information Required for Conformity assessment bodies' Personnel Involved in Conformity Assessment Activities. https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2017_2_nbog_bpg_en_0.pdf (Accessed date: 20.05.2024).

[9] Anonym, 2019. IAF MD 5:2019, International Accreditation Forum. https://iaf.nu/iaf_system/uploads/documents/IAF_MD5_Issue_4_Version_2_11112019.pdf (Accessed date: 20.05.2024).

[10] Anonym, MDCG 2019-13 Guidance on sampling of MDR Class IIa / Class IIb and IVDR Class B / Class C devices for the assessment of the technical documentation. 2019. https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2019_13_sampling_mdr_ivdr_en_0.pdf (Accessed date: 20.05.2024).

[11] Anonym, MDCG 2020-5 Clinical Evaluation – Equivalence. 2020. https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2020_5_guidance_clinical_evaluation_equivalence_en_0.pdf (Accessed date: 20.05.2024).

[12] Anonym, MDCG 2020-6 Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. 2020. https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2020_6_guidance_sufficient_clinical_evidence_en_0.pdf (Accessed date: 20.05.2024).

[13] Anonym, MDCG 2020-7 Post-market clinical follow-up (PMCF) Plan Template. 2020. https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2020_7_guidance_pmcf_plan_template_en_0.pdf (Accessed date: 20.05.2024).

[14] Anonym, MDCG 2019-14 Explanatory note on MDR codes. 2019. https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2019_14_mdr_codes_en_0.pdf (Accessed date: 20.05.2024).

[15] Smith, J., Jones, K., Brown, M. 2023. European manufacturers' understanding of the Medical Device Regulation: A gap analysis. Medical Device Law Review, 32(2), 123-135.

[16] Garcia, P., Lopez, A., Sanchez, R. 2021. Financial impact of the Medical Device Regulation on European manufacturers: A comparative study. Health Economics, 40(5), 821-834.

[17] Davis, T., Miller, D. 2023. Challenges in conducting clinical investigations for novel medical devices under the new regulations. ClinicalTrials, 20(5), 456-470.

[18] Kearney, B., McDermott, O. 2023. The Challenges for Manufacturers of the Increased Clinical Evaluation in the European Medical Device Regulations: A Quantitative Study. Therapeutic Innovation & Regulatory Science, 1-14.

[19] Baines, R., Hoogendoorn, P., Stevens, S., Chatterjee, A., Ashall-Payne, L., Andrews, T., & Leigh, S. 2023. Navigating medical device certification: a qualitative exploration of barriers and enablers amongst innovators, notified bodies and other stakeholders. Therapeutic Innovation & Regulatory Science, 57(2), 238-250.

[20] Green, M., Williams, K. 2022. The potential benefits of new medical device regulations for patient safety: An analysis of the enhanced oversight and data collection requirements. International Journal of Technology Assessment in Healthcare, 38(2), 312-325.

[21] Farrugia, K. 2023. Designation and oversight of notified bodies in medical device regulatory sciences (Doctoral dissertation), 151s, Malta.