PIPA UK Medical Device Vigilance Guidelines

January 2021

PIPA
Pharmaceutical Information & Pharmacovigilance Association

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1 Introduction

This document is provided only for guidance purposes and is not legally binding. It seeks to promote best practice in the pharmaceutical industry regarding medical device vigilance reporting and requirements.

Legislative framework:

Medical devices are currently regulated under three EU Directives and the regulations that transposed these Directives into UK law. These are:

- **Directive 90/385/EEC on active implantable devices (EU AIMMD) [1]**
- **Directive 93/42/EEC on medical devices (EU MDD) [2]**
- **Directive 98/79/EC on in vitro diagnostic medical devices (EU IVDD) [3]**
- **The Medical Devices Regulations 2002, SI 2002 No. 618, as amended.[4]**

Guidance documents have been developed by the European Commission to assist in the implementation of these directives. These are known as the MEDDEV Guidance Documents (MEDical DEVices documents)[5]. These are not legally binding but were developed to aid uniform application of the relevant directive provisions. The guidance documents relating to medical device vigilance are:

- **MEDDEV 2.12-1 rev. 8 Guidelines on a medical devices vigilance system[6]**
- **Additional Guidance Regarding the Vigilance System as outlined in MEDDEV 2.12-1 rev. 8[7]**

On 5th April 2017, two new EU Regulations on medical devices were adopted, and entered into force on 25th May 2017 replacing the existing medical device directives.

- **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 (MDR)**
- **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) IVDR)[9]**

The MDR comes into effect on the 26 May 2021 and the IVDR comes into effect on the 26 May 2022.

Brexit

As the MDR and IVDR do not come into effect until after the end of the Brexit transition period, 31 December 2020, they will not be effective in Great Britain (England, Scotland and Wales). The current devices vigilance legislation therefore continues to be effective though the Medicines and Medical Devices Bill[10].

1. https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:31990L0385&from=EN
2. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31993L0042
3. https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:31998L0079&from=EN
4. https://www.legislation.gov.uk/uksi/2002/618/pdfs/uksi_20020618_en.pdf
5. https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_guidance_meddevs.pdf
6. https://ec.europa.eu/docsroom/documents/32305/attachments/1/translations
7. https://ec.europa.eu/docsroom/documents/36292
8. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2017.117.01.0001.01.ENG&toc=OJ:L:2017:117:TOC
9. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2017.117.01.0176.01.ENG&toc=OJ:L:2017:117:TOC
10. https://services.parliament.uk/Bills/2019-21/medicinesandmedicaldevices.html

The MDR and the IVDR will be effective in Northern Ireland as a consequence of the Northern Ireland Protocol [11], which requires that there be no regulatory border on the island of Ireland. For companies marketing and distributing medical devices in both Great Britain (GB) and Northern Ireland, these guidelines should be read in conjunction with the PIPA EU Medical Device Vigilance Standards.

Guidance on post-transition regulations for medical devices is posted on the MHRA's website[12].

Changes to medicines devices regulations, including those relating to device vigilance, will be developed by the MHRA. This is in response to The Independent Medicines and Medical Devices Safety Review (The Cumberlege Report)[13] which identified the need to strengthen regulations relating to medical devices.

Definitions

See Article 2 in The Medical Devices Regulations and the MEDDEV 2.12-1 rev 8 for a full set of relevant definitions.

Stakeholders

Medical device manufacturers placing products onto the market in the UK (England, Scotland, Wales and Northern Ireland) will require the services of the following:

- **Authorised Representative**

For GB companies (England, Scotland and Wales) placing medical devices on the market in Northern Ireland, this is a person based in either the EU or Northern Ireland. This person acts on behalf of the manufacturer in relation to tasks specified in the MDR and IVDR.

- **UK Responsible Person**

Medical device manufacturers, including those based outside of the UK, require a UK Responsible Person who must be based in the UK. The responsibilities of the UK Responsible Person include immediately informing the manufacturer about complaints and reports from healthcare professionals, patients and users about suspected incidents related to a device for which they have been designated as the UK Responsible Person.

Post-market Surveillance System

Medical device manufacturers are required to establish and maintain a post-market device vigilance surveillance system. The manufacturer is obliged to notify the MHRA of the following incidents immediately on learning of them:

- Any deterioration in the characteristics or performances, and any inaccuracies in the instruction leaflet for a device which might lead to or have led to the death of a patient or a deterioration in his state of health
- Any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.

The guidelines do not give any recommendations on what procedures should be in the post-market surveillance system to ensure the collection, recording, analysis and reporting of safety data. As a minimum, device manufacturers should have procedures in place for the following medical device vigilance obligations:

Device incident reporting

Manufacturers should have a process in place for the:

- Receipt and recording adverse incidents
- Assessment and analysis of the incident
- Expedited reporting of the incident.

If a reported device incident meets all four of the following criteria, it should be reported in an expedited manner to the MHRA:

11. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/840230/Revised_Protocol_to_the_Withdrawal_Agreement.pdf
12. https://www.gov.uk/guidance/regulating-medical-devices-from-1-january-2021
13. https://www.immdsreview.org.uk/

1. An incident has occurred such as (but not limited to) a malfunction or deterioration in performance, unanticipated adverse reaction, interaction with other device or medicine, degradation of the device, or inaccuracy in labelling
2. The device is suspected to be causally related to the incident. Take into consideration the opinion of the reporter, the initial assessment by the manufacturer, previously reported incidents, other relevant information held by the manufacturer
3. The incident was fatal or considered as serious. Serious incidents include:
    - Life-threatening
    - Result in permanent impairment or damage
    - Requires surgical or medical intervention
    - Indirect harm from an incorrect diagnostic or in vitro device test result, or the correct use of an in vitro fertilisation or artificial reproductive technology device
    - Foetal distress, foetal death or any congenital abnormality or birth defects
4. The incident occurred in the UK
    - Note: If the incident occurred in Northern Ireland, this will require centralised reporting once EUDAMED goes live.

If the incident meets all four of the above criteria, it should be reported to the MHRA within the following timelines:

- Serious public health threat: 2 days
- Death or unanticipated serious deterioration in state of health: 10 days
- Other reportable incidents: 30 days.

Device incidents can be reported to the MHRA using the Manufacturer Incident Report form[14].

Non-reportable incidents

There are a number of scenarios where the reporting of incidents is not normally required. These include:

- Device deficiency identified before use. For example, device damaged in its packaging and therefore discarded before use in the patient
- Event caused by the patient's underlying medical condition
- Device used after the expiry of its shelf-life or service life
- Correct functioning of a fail-safe. For example, alarm activated following an infusion pump failure and no injury to the patient
- Expected and foreseeable side effects. These should meet all of the following criteria:
    - Listed in the manufacturer's labelling
    - Clinically well known as being foreseeable and having certain qualitative and quantitative predictability when the device is used correctly
    - Documented in the device master record maintained by the manufacturer
    - Clinically acceptable in terms of individual patient benefit

  Note: medical review of such events is recommended
- Likelihood of death or serious deterioration in patient state of health is considered as negligible.

Even though these events are not normally reportable, the manufacturer should have a trending procedure in place to monitor for any changes in the frequency and severity of device incident and complaint reports received by the manufacturer (see Trend reports).

14. https://ec.europa.eu/docsroom/documents/41681/attachments/1/translations/en/renditions/native

Periodic summary reports

Device incidents may be reported to the MHRA in periodic summary reports (PSR) rather than as individual incident reports. The preparation and submission of a PSR can only be done with the agreement of the MHRA.

PSRs may be prepared for the reporting of incidents where a field safety corrective action (*qv*) has been implemented, or for common and well documented incidents. The frequency of submission of a PSR must be agreed with the MHRA, including any incident report thresholds that may require the submission of an interim PSR. The MEDDEV PSR template may be used[15].

Device manufacturers should therefore have a procedure in place for PSRs that should include guidance on when and how to approach the MHRA, collation of appropriate incident reports, review and approval of the report, its submission, and implementation of any assessment report.

Trend reporting

Trend reporting is used by a manufacturer when there is a significant increase in events not considered to be individually reportable but for which there are predefined trigger levels used to determine the threshold for reporting.

A trend report should be prepared and submitted to the MHRA, irrespective of whether a PSR has been agreed, where there is a significant increase in:

- Already reportable incidents
- Incidents that are usually reportable
- Events that are not usually reportable.

The MEDDEV guidelines do not define significant increase nor how to determine the threshold for reporting.

Trend reports can be submitted to the MHRA using the MEDDEV template[16].

The manufacturer should therefore have a procedure in place for trending device incident and complaint reports received to determine if there are any changes to the number and severity of such reports received. The procedure should also give guidance to the manufacturer on what they consider to be a significant increase in such reports and what they consider to be the threshold to trigger the submission of a trend report to the MHRA.

The procedure should also include guidance on how to prepare, review and approve the report, and how to track its subsequent submission to and assessment by the MHRA, including the implementation of any assessment recommendations.

Field safety corrective actions

Field safety corrective actions (FSCA) are actions taken by the manufacturer to reduce the risk of a death or serious deterioration in the patient's state of health. It may require the recall or withdrawal from the market of the device, or issuing revised instructions for use. Reasons for implementing such an action include deterioration in the characteristics or performance of the device, or inadequate use instructions.

The FSCA is communicated to the MHRA via the FSCA form[17] and to users via a field safety notice (*qv*).

Communication of the FSCA to the MHRA should allow time for the MHRA to review the FSCA and agree with the proposed actions.

The manufacturer should have a procedure in place that ensures the prompt review of any reported incidents that could precipitate the preparation of an FSCA. This should include its submission to the MHRA, agreements with the MHRA on the proposed actions, and the implementation and reconciliation of the actions agreed in the FSCA. This should be linked to the field safety notice procedure (*qv*).

15. https://ec.europa.eu/docsroom/documents/32305/attachments/7/translations
16. https://ec.europa.eu/docsroom/documents/32305/attachments/7/translations
17. https://ec.europa.eu/docsroom/documents/32305/attachments/4/translations

Field safety notices

A field safety notice (FSN) is a communication to users, which can mean healthcare professionals or patients, in relation to an FSCA.

The draft FSN should be submitted to the MHRA along with the FSCA. There should normally be 48 hours before the manufacturer distributes the FSN, the only exception is if the safety concern requires a shorter timescale, for example, a serious risk to public health.

The manufacturer should use the MEDDEV FSN template[18].

FSNs should be distributed by the manufacturer but are also distributed by the MHRA via email and on their website .

Manufacturers should have a process in place for the preparation, review and internal approval of FSNs, their approval by the MHRA, and their distribution. This should be linked to the procedure for FSCAs, or be integrated into the FSCA procedure.

18. https://ec.europa.eu/docsroom/documents/32521/attachments/1/translations/en/renditions/native
19. https://www.gov.uk/drug-device-alerts?

Annex. Comparison between UK and the EU MDR and IVDR

Requirement	MEDDEV 2.12-1	MDR	IVDR
Person Responsible for Regulatory Compliance	Not required	Required	
When to report reportable incidents	• **2 days in the case of serious public health threats** • **10 days in the case of death or unanticipated serious deterioration in health which has remained unchanged** • **15 days for all other events**		
Who to report to	MHRA	Centralised reporting to EUDAMED, including incidents from Northern Ireland	
Periodic summary reports	When agreed with the MHRA • **For similar incidents with a known root cause or implemented FSCA** • **For common, well documented incidents**	When agreed with the coordinating competent authority in the EU • **For similar incidents with a known root cause or implemented FSCA** • **For common, well documented incidents**	

Periodic safety update report	Not required	• **Class I devices**
		  • Not required
		• **Class IIa devices**
		  • When necessary and at least every 2 years
		• **Class IIb devices**
		  • When necessary and at least every year
		  • Made available to notified body and upon request to a competent authority
		  • Notified body evaluation to be added
		  • PSUR and notified body evaluation to be made available to competent authorities via Eudamed
			• **Class A and B Devices**
			  • Not required
			• **Class C Devices**
			  • When necessary and at least every year
			  • Made available to notified body and upon request to a competent authority
			• **Class D devices**
			  • When necessary and at least every year
			  • To be submitted electronically to notified body via Eudamed
			  • Notified body evaluation to be added
			PSUR and notified body evaluation to be made available to competent authorities via Eudamed

Requirement	MEDDEV 2.12-1	MDR	IVDR

		• **Class III devices**
		  • When necessary and at least every year
		  • To be submitted electronically to notified body via Eudamed
		  • Notified body evaluation to be added
		PSUR and notified body evaluation to be made available to competent authorities via Eudamed	

Trend Reporting	If a significant increase in events not normally considered to be incidents or reportable incidents and for which predefined trigger levels are used to determine the threshold for reporting	Mandatory reporting by the manufacturer required for: • **Statistically significant increase in frequency or severity of non-serious incidents or expected side effect that could impact risk/benefit ratio** • **'Statistically significant increase' should be predefined for the device** The EU Commission will perform trending and signal detection based on the data in Eudamed.	
Field Safety Corrective Action	The details of FSCAs are communicated by manufacturer to the MHRA via FSCA form and to the users in FSNs	• **The details of FSCAs are communicated by manufacturer to the national competent authorities via FSCA form and to the users in FSNs** The national competent authorities may perform their own risk assessment, manufacturer has to provide the supporting documentation. • **The national competent authorities may intervene in the manufacturer's investigation.** • **The FSN needs to contain the unique device identifier and the manufacturer's single registration number and needs to be uploaded in Eudamed.** National competent authorities may ask manufacturers for corrective actions and will inform the notified body, other manufacturers and the EU Commission.	

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