Medicines & Healthcare products Regulatory Agency

The Medical Devices (Post-market Surveillance Requirements) (Amendment) (Great Britain) Regulations 2024

Guidance on periodic safety update reports (PSUR) (regulation 44ZM) for approved bodies

Note: for the interpretation of this guidance, any references to classification of devices, annexes etc. refer to the rules set out in Directives 93/42/EEC, 90/385/EEC and 98/79/EC

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Scope

While the manufacturer is required to produce a PSUR for all devices it places on the Great Britain (GB) market unless regulation 44ZL applies, approved bodies only have obligations regarding PSUR under regulation 44ZM when they have a contract with a medical device manufacturer and have issued a UK Conformity Assessed (UKCA) conformity assessment certificate for a device which has been placed on the GB market. See Appendix II for a glossary of the regulation numbers and topics.

Exclusions/not included in the PSUR requirements for approved bodies

Approved bodies are not required to review PSURs:

- where the manufacturer is placing their device on the Great Britain (GB) market after fulfilling the requirements of MDR 2002 Regulation 19B, 19C, 30A, 44ZA or 44ZB (the device bears the CE mark)
- Any IVD which is not included in the lists of Directive 98/79/EC Annex II
- When the device is a system or procedure pack in accordance with MDR 2002 Regulation 14, unless the system or procedure pack contains one or more component device which is not UKCA-marked (or CE marked) or is to be used outside its intended purpose and therefore be required to undergo an appropriate conformity assessment procedure, in which case the approved body is required to review the PSUR

Responsibilities of the approved body (AB)

Approved bodies have the following responsibilities:

1. To receive all (initial and updated) PSUR documents submitted by manufacturers to their approved body
2. To review the PSUR documents:
    - for Class III devices, implantable devices of any risk class and List A and B IVDs, according to timelines (see Figure 1)

- for Class IIa and Class IIb devices which are not implants according to a sampling plan which may be aligned with the ongoing surveillance activity of the AB

3. To produce a report setting out the conclusions of the review conducted for the following devices:

- all Class III medical devices and active implantable medical devices
- all Class IIa and IIb implantable devices
- Annex II List A and List B IVDs

4. To make a decision on whether certification has been impacted and any subsequent actions

Competency requirements

The AB should have procedures for defining the competency required to undertake the PSUR review.

The review of the PSUR to be conducted by the approved body

The AB should have a procedure to describe the PSUR review activity, including the issuing of an AB PSUR report as per Regulation 44ZM(11)(b) for Class III devices, all implants and List A and B IVDs. The approach should be risk proportionate and should include details of when the PSUR will be a standalone activity, when it may take place during review of technical documentation or during other surveillance and monitoring activity of the AB.

The purpose of the PSUR review is for the AB to consider the data included in the PSUR “to determine whether there is any impact on the certification issued for the device” (regulation 44ZM(11)(a)).

The PSUR review has 3 objectives:

- to verify that the PSUR meets the requirements of the regulations
- to ascertain whether the risk benefit profile has changed and whether there is any impact on the certification issued

- to document the decision on whether action is required by the AB and to determine what the action(s) should be

The AB reviewer must ensure that the manufacturer has provided the necessary data in accordance with MHRA guidance, (Standardised format for PSUR). This data should be reviewed for its adequacy and compliance. Furthermore, the manufacturer should, if requested by the AB, supply an up-to-date iteration of their post-market surveillance (PMS) plan.

In the event the manufacturer has offered a rationale for the omission of any required data, the AB reviewer should also verify the acceptability of such justification. Instances where the MHRA may consider data exclusion appropriate include, but are not limited to cases where:

- there are no serious incidents reported to the manufacturer that occurred in the UK; however, serious incidents involving the same device have occurred in 3rd countries - these are summarised and an explanation on absence of UK data is provided

- data summary and conclusions from a post-market clinical follow-up (PMCF) study are not included due to an unanticipated delay in enrolment of subjects - an explanation and revised timetable is provided.

- no comparison with similar devices has been presented with regards to state of the art because the device is so novel that there are no comparable devices on the market - an explanation has been provided alongside a comparison with the nearest devices and/or alternative treatment methods

- there have been no field safety corrective actions (FSCA) conducted for the device

- sales data cannot be provided for the UK as the device has not been sold in this market

Failure to provide the minimum information in the contents of the PSUR may result in the PSUR being rejected by the AB reviewer and the manufacturer may be requested to resubmit a revised version within a timeframe agreed between the AB and the manufacturer. Failure to continually submit the minimum required information in the PSUR or failure to submit a PSUR may lead to actions that could result in suspension and/or withdrawal of the certificate.

When reviewing the data presented in the PSUR to ascertain whether there is any impact on certification or action required, the AB may take into consideration the MHRA guidance for manufacturers on the content of the PSUR. For example:

- does the presentation and quality of the data and evaluation conducted by the manufacturer suggest any deficiency in their ability to conduct robust post-market surveillance activity?
- has the sales, population and vigilance data been presented appropriately, and an analysis presented?
- has the manufacturer considered any new clinical data, including any limitations in the data and/or its evaluation?
- has a new specific PMCF/ post-market performance follow-up (PMPF) been initiated?
- has the data obtained from a concluded PMCF/PMPF activity been considered?
- have they considered whether the data has an impact on the benefit risk profile of the device?
- have new or emerging risks or common occurrence of poor performance been identified in the data and been assessed for seriousness, clinical impact, acceptability when weighted against the benefits of the device?
- has there been a consideration of the current state of the art, through a comparison with other similar devices?
- has the manufacturer identified and implemented corrective and preventative actions which are effective in reducing risk as far as possible?

The approved body PSUR report

For Class III devices, all implants and Annex II List A and B IVDs, the AB is required to issue a report to the manufacturer (and if applicable the UK responsible person) setting out the conclusions of its review.

Active implantable, Class III and Class IIb implantable devices and Annex II List A IVD

The AB reviewer should document comments or observations on the appropriateness of the data presented in the PSUR and provide a summary of the findings of the review including any actions identified.

The AB should have a procedure which sets out how findings of the PSUR review should be addressed with the manufacturer.

If the AB determines that there is an impact on certification and they are proposing action, the report should set out the concerns identified, including a rationale, and list the actions to be taken by the AB.

Where there are improvements needed to enhance the data within the PSUR, but no immediate concerns on the data, conclusions or the benefit/risk determination, the AB reviewer may provide feedback in the PSUR report requesting the manufacturer provides additional information/data for future PSUR submissions. It is critically important that the manufacturer addresses this feedback for the next PSUR submission to avoid potential suspension and/or withdrawal of the certificate.

The AB report and the conclusion drawn must be specific to the GB legislation requirements, demonstrating that the review has considered the UK data and any impact on UKCA certification.

See Appendix I for general information related to the presentation and review of the PSUR.

Class IIa implantable devices and List B IVDs

Devices in these risk classes are subject to representative sampling of the technical documentation at conformity assessment. In some cases, at the time of PSUR submission to the AB, the technical documentation may not have been reviewed, and the AB would not have had sight of the data used to support certification.

In these cases, PSUR reviews can be conducted:

- during scheduled sampling of the technical documentation
- during ongoing surveillance and monitoring activity such as quality management system (QMS) audits

- as a standalone review activity

If the AB review of the device technical documentation is not scheduled to be conducted within the prescribed PSUR cycle for a Class IIa implantable device (2 years) or a List B IVD (1 year), the AB may review the PSUR during other ongoing surveillance and monitoring activity. In this scenario the AB may focus their review on the manufacturer's compliance with requirements for PSUR (for example, content and procedures). The AB should carry out a more detailed review of PSUR when technical documentation review takes place.

To support the standalone review of PSURs when technical documentation has not previously been assessed, the AB may require the manufacturer to submit the PMS plan.

The AB report should document whether the technical documentation review has been completed before the PSUR review, and any actions identified.

Class IIb and IIa non-implantable devices

Class IIa and IIb non-implantable medical devices do not require the AB to issue a report. The AB may provide feedback about their review of PSUR and any outcomes to the manufacturer and their UK responsible person in line with their own internal procedures.

Whilst it is acknowledged that each approved body operates different systems and processes, the MHRA recommends that the AB keeps a documented record of the completion of PSUR reviews.

An example of the content of a PSUR review record includes:

- date review was completed
- name and role of AB reviewer with appropriate competency demonstrated
- what was reviewed (including device or device group, certificate number, PSUR document identifiers, revision and data validity period)
- conclusion statement on whether the UKCA certification was impacted with justification
- confirmation of whether action(s) taken and what they were

Timeline for the AB review

Regulation 44ZM (5) requires the manufacturer to produce the PSUR annually for Class III, IIb, active implantable medical devices and Annex II List A and B IVDs, whereas Regulation 44ZM (7) requires the manufacturer to produce the PSUR at least every 2 years for Class IIa devices.

Each PSUR is submitted to the AB by the manufacturer or their UK responsible person. Submission dates and method should be agreed between the AB and the manufacturer.

The AB is required under Regulation 44ZM(11)(a) to review the PSUR as soon as is reasonably practicable. When determining the timing of the review of the PSUR, the AB may take into consideration a range of factors, including but not limited to:

- operational efficiencies, for example, alignment with activity under other regulatory frameworks or schemes
- other scheduled surveillance and monitoring activities of the AB with the manufacturer of the device, such as QMS audits
- knowledge or awareness of compliance or safety concerns
- proposed grouping of devices in a single PSUR by the manufacturer
- representative sampling of technical documentation for devices, where applicable

Note, PSUR reviews outside of schedule may be triggered via vigilance, field safety corrective actions, regulatory intelligence or MHRA prompt.

Figure 1 Risk-based guide for the timing of the AB review following receipt of a manufacturer's PSUR

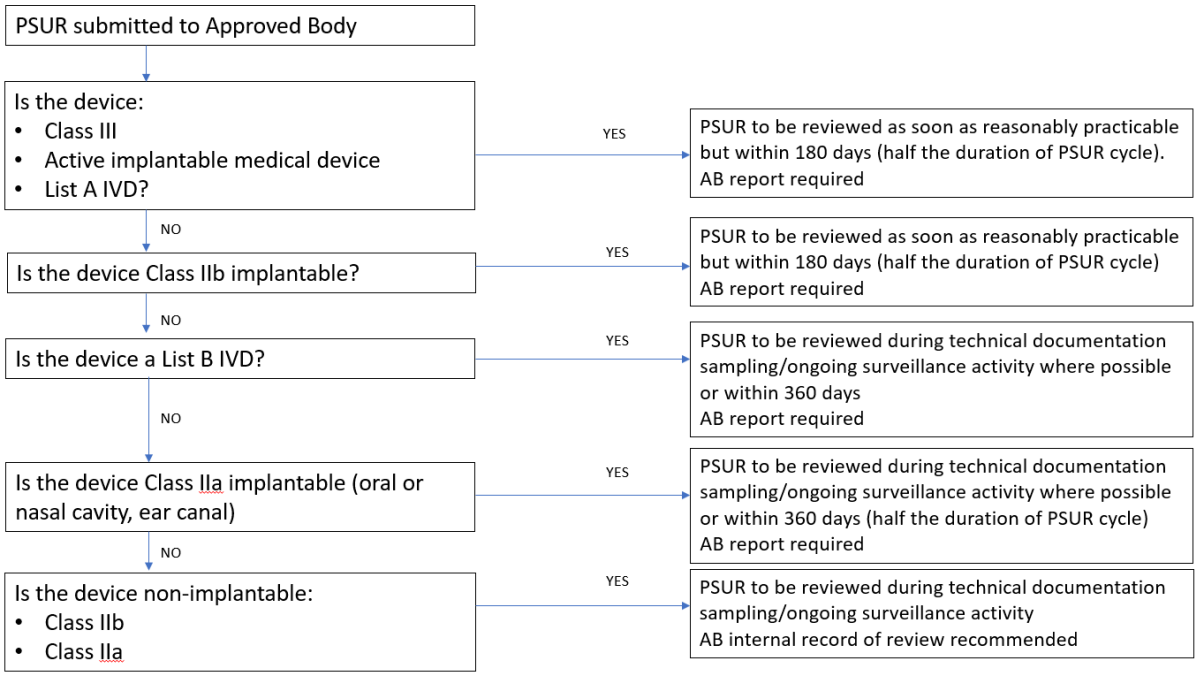

Table 1: Risk-based guide for the timing of the AB review following receipt of a manufacturer's PSUR. Note, this is Figure 1 in an alternative format

Device type	Timing of the AB review following receipt of a manufacturer's PSUR
Class III Active implantable medical device List A IVD	PSUR to be reviewed as soon as reasonably practicable but within 180 days (half the duration of PSUR cycle). AB report required.
Class IIb implantable	PSUR to be reviewed as soon as reasonably practicable but within 180 days (half the duration of PSUR cycle). AB report required.
List B IVD	PSUR to be reviewed during technical documentation sampling/ongoing

	surveillance activity where possible or within 360 days. AB report required.
Class IIa implantable (oral or nasal cavity, ear canal)	PSUR to be reviewed during technical documentation sampling/ongoing surveillance activity where possible or within 360 days. AB report required.
Class IIb non-implantable Class IIa non-implantable	PSUR to be reviewed during technical documentation sampling/ongoing surveillance activity. AB internal record of review recommended.

Provision of AB report to MHRA (Regulations 44ZM(13) and 44ZR)

The AB must provide the completed AB PSUR report(s) to the MHRA within 3 working days upon request. If the AB is unable to meet the 3 working day deadline, the MHRA has discretion to extend this to an appropriate date by which the AB will provide the MHRA with the AB report(s).

The MHRA may request submission of the AB PSUR report due to awareness of emerging safety or performance concerns or trends and, in cases where the latest PSUR has not been reviewed, the MHRA may request the AB brings forward the PSUR review schedule. The AB and the MHRA will agree an appropriate date by which the AB will provide the AB report.

Appendix I

General information related to the presentation and review of the PSUR

The MHRA recognises that a UKAB may be affiliated with an EU notified body and that a combined PSUR report format may be used. This is acceptable as long as it demonstrates that the GB requirements have been met.

The MHRA recommends that the AB PSUR report includes the following minimum information which may be used in the format below, or integrated into the UKAB's QMS in a different way:

Core data

A core data section to ensure it is clear to which PSUR the AB report refers. It should be aligned to the data listed in section 2 of the PSUR standardised format for manufacturers (manufacturer and device information). The AB may also include details of who has conducted the review and any other information required by their procedure and which is useful for audit purposes. Any personal data shall be redacted before release.

Verification of PSUR compliance with requirements

The report should document whether the information to be included in the PSUR is present and whether it is appropriate. This may be presented as a checklist or in a table.

Table 2 Example of how the information may be presented in a table format

PSUR content	**AB to indicate for each PSUR section whether the required information is provided and whether it is appropriate with a brief comment. Any missing data should be justified by the manufacturer.** **Points for consideration for the AB reviewer are provided below**
Executive summary	Has the manufacturer described and given the status of any actions arising from the previous PSUR? Has there been a change in the leading device and if yes, is the justification accepted?

	Is the clear statement declaring the impact on the benefit-risk profile included?
Description of the devices covered by the PSUR	Has the manufacturer followed the guidance provided by the MHRA on grouping and presented the data for the grouped device in a way that it can be reviewed for impact on certification for each device?
Device exposure information: volume of Sales (for the last 4 years presented per geographical region; UK, rest of world (ROW))	Reviewer should consider any trend and stage of product lifecycle of the device, state of the art (SOTA) and whether the manufacturer has made any links between sales volume/geographical region and corresponding PMS data
Device exposure information: size and other characteristics of the population using the device – verification that the PSUR considers the population using the device and estimate of people using the device in the UK	Reviewer should consider whether this is aligned to the intended purpose and use of the device as per the granted certificate. If there has been 'creep' in the intended purpose/use population, consider whether any action is required (for example, change notification process)
Device performance information: • verification that the PSUR contains (a summary of) • number and rate of serious incidents • trends • FSCAs including those undertaken in a third country	Consider whether the manufacturer has applied the IMDRF coding appropriately and that the choice of data presentation allows the data to be assessed/understood. Trends reported in the PSUR should include those which could have a significant adverse impact on the risk analysis in addition to those giving rise to a risk of serious injury. Have any new risks been identified? If so have they been assessed for clinical impact and weighed against benefit of the device? Reviewer should consider whether the manufacturer has fulfilled their contractual obligations (where applicable) by informing

	the AB of for example reportable incidents FSCA, FSCA undertaken in a 3rd country. If not, consider what action or extraordinary measures may be required.
Proactive data analysis from defined populations: PMCF activities and findings – verification that the PSUR addresses these: • manufacturer sponsored PMCF studies or registries • independent clinical studies or registries/databases • information from review of scientific/specialist literature	Reviewer to consider whether the manufacturer has conducted the PMCF activity it intended to as per the PMS/PMCF plan and if not, has the manufacturer provided a sufficient justification. If it has, what are the data and have they been analysed appropriately? Consider whether clinical reviewer/expertise is required to assess impact of any new safety and performance data from PMCF studies included. Consider novelty of the device, PMS/PMCF plan if no results are included or if no PMCF action is planned, is manufacturer's justification sufficient?
Data from other sources including incidents not considered serious*:* • feedback and complaints • real-world data sources	Reviewer to consider whether the manufacturer has identified feedback and complaints from a range of sources and indicated what, if any, action has been taken as a result. Has the manufacturer identified other real-world data sources and listed the findings related to safety and performance?
Comparison with available information on similar devices	Reviewer to consider the appropriateness of the similar devices identified. Consider whether any safety and performance data presented about similar devices has any bearing on certification of the device or device group subject of the PSUR.
Preventive and corrective action	Reviewer to consider whether the list of CAPA and the current status and effectiveness has

	any impact on certification or whether any extraordinary surveillance measures by the AB are required.
Manufacturer's findings and conclusions: • validity of the data • overall conclusions from data analysis • actions taken to address conclusions	Has the manufacturer drawn valid conclusions relating to the risk-benefit profile of the device from the analysis of the data and are the actions appropriate?

Approved Body summary of findings from the review

In this section the AB should summarise the findings of the review of the complete data set presented by the manufacturer, including whether any actions are proposed and the corresponding rationale. For subsequent versions of the PSUR, the AB may consider any changes or developments or actions arising from previous PSUR submissions, for example, if the manufacturer has been advised that missing or poorly presented data is not acceptable and should be addressed for the next submission, the AB may refer to whether this was appropriately addressed.

The summary may address the following points:

- new or emerging risks for the device or similar devices
- changes to benefit-risk profile of the device
- has the manufacturer evidenced any cross-linking of data from different sections of the PSUR or between datasets gathered in the PMS plan? (for example, if PMS data indicates evidence of device use outside the intended population and vigilance data shows a corresponding rise in complaints amongst that population, has this been identified and considered by the manufacturer?)
- use of data from a range of sources to fulfil the PMS obligations such as vigilance, PMCF, feedback, complaints, real-world evidence
- impact on other processes such as risk management and clinical evaluation

- evaluate the manufacturer’s conclusions on the benefit-risk determination (based on suitable indicators and threshold values derived from the state of the art) - Regulation 44ZM (3c)

- evaluate if the results and conclusions of the analyses of the post-market surveillance data, gathered as a result of the post-market surveillance plan, are evident - Regulation 44ZM (3a)

Approved body conclusion and action(s) arising

The conclusion should state whether or not:

- the PSUR meets regulatory requirements

- any action(s) are being taken as a result of the review of the PSUR

- the UKCA certification was impacted based on the data reviewed (justification should be provided)

Any feedback to the manufacturer on the content or presentation of the PSUR can be included in this section.

The conclusion may be presented as series of statements which are selected as appropriate. Examples below:

- certification is not impacted - no action is needed as the periodic summary report does not identify any negative trends, new hazards, or occurrence/frequency excursions
- certification granted may be at risk, therefore extraordinary surveillance measures shall be performed
    - extraordinary surveillance measures to be performed:
        - unannounced audit
        - increased frequency of surveillance audits
        - changes to sampling plan
        - technical documentation review
        - informing/notifying the MHRA
        - other (specify)
- certification granted is at immediate risk, the certification suspension / withdrawal process shall be started immediately

Appendix II Glossary

Regulation numbers and topic covered:

Part 4A	**Post market surveillance requirement**
44ZC	Interpretation of Part 4A (definitions)
4ZD	Scope of Part 4A
44ZE	Post market surveillance system
44ZF	Post market surveillance plan
44ZG	Preventive and corrective action
44ZH	Initial reporting of serious incidents
44ZI	Investigation and final reporting of serious incidents
44ZJ	Field safety corrective actions and field safety notices
44ZK	Field safety corrective actions outside of Great Britain
44ZL	Post-market surveillance report
44ZM	Periodic safety update report
44ZN	Trend reporting
44ZO	Reports received by the Secretary of State
44ZP	Analysis of information received under Part 4A
44ZQ	Retention of post-market surveillance documentation
44ZR	Requests for post-market surveillance documentation