Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Guidance for External Quality Assurance (EQA) scheme organisers on reporting known or suspected IVD performance issues

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Contents

1. Introduction

MHRA values the professional judgement and expertise of External Quality Assurance (EQA) scheme organisers and specialist advisory committees to facilitate the early identification of potential widespread performance issues with in vitro diagnostic medical devices (IVD MDs). As identified in BS EN 14136:2004 'Use of external quality assessment schemes in the assessment of the performance of in vitro diagnostic examination procedures' *'… EQAS is able to contribute to the post-marketing monitoring of IVD MDs as mentioned in Directive 98/79/EC on in vitro diagnostic medical devices to the benefit of both their manufacturers and users.'*

The purpose of this document is to propose a formalised route of reporting potential assay issues or adverse incidents identified by EQA scheme organisers to support MHRA in its regulatory role, ensuring medical devices are safe and fit for purpose. MHRA receives post-market reports from a variety of sources and uses these to find trends and signals within adverse incident records, to determine whether any regulatory action is required.

The term 'medical devices' used in this document encompasses IVD MDs – to qualify as an IVD MD (as defined in Article 1 paragraph 2(b) of the In Vitro Diagnostic Medical Device Directive 98/79/EC) the product must first fulfil the definition of a medical device (Article 1 paragraph 2(a)).

An adverse incident is defined in the In Vitro Diagnostic Medical Device Directive 98/79/EC (IVDMDD) as *'any malfunction, failure or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health'.*

2. EQA report submission

The IVDMDD mentions the contribution of EQA scheme organisers to post-market surveillance:

Article 11 paragraph 2 of the IVDMDD states:

> *2. Where a Member State requires medical practitioners, the medical institutions or the organisers of external quality assessment schemes to inform the competent authorities of any incidents referred to in paragraph 1, it shall take the necessary steps to ensure that the manufacturer of the device concerned, or his authorised representative, is also informed of the incident.*

Whilst paragraph 1 states:

a) *1. Member States shall take the necessary steps to ensure that any information brought to their knowledge, in accordance with the provisions of this Directive, regarding the incidents mentioned below involving devices bearing the CE marking is*

recorded and evaluated centrally: any malfunction, failure or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health;

b) *any technical or medical reason in relation to the characteristics or performance of a device for the reasons referred to in subparagraph (a), leading to systematic recall of devices of the same type by the manufacturer.*

MHRA encourages EQA scheme organisers to report suspected assay/method performance issues to MHRA as early as possible. When reporting, provide as much information as you can to enable MHRA to make an assessment, initiate an investigation and make appropriate enquiries. Where possible, indicate whether the issue may be clinically significant or clinically insignificant. Clinical risk to patients is not always well characterised at the time of reporting, but during the investigation the clinical risk and potential impact of sample material will be clarified.

MHRA does not require every incorrect EQA result or individual laboratory performance issues to be reported to us. It is not MHRA's intention to monitor the performance of individual labs, but to determine if there is a general performance issue with an assay/method that may require regulatory intervention. Please refer to Appendix 1 for examples of what and when to report.

Reporting can be done through the Yellow Card scheme outlined in the 'Reporting route' section and Appendix 1.

3. MHRA investigation procedure

Reports about medical devices are logged onto MHRA's Adverse Incident Tracking System and a unique reference number is allocated to ensure that information relating to the specific case is stored appropriately for case progression and future trending and signal detection. A signal indicates a concern in a particular area that justifies further investigation.

The case then undergoes a risk assessment and is assigned an investigation route, based on the information provided. Safety investigations are carried out by Medical Device Specialists within the Devices Safety and Surveillance unit (DSS) who have working knowledge and expertise in IVD MDs. Additional internal and external experts may be called upon as required. It is expected and desirable that the reporting EQA scheme organiser would remain involved in the investigation.

MHRA contacts the manufacturer of the device involved to inform them of the report. The information initially submitted to MHRA via the Yellow Card report (including any attachments) will be sent to the manufacturer to enable them to investigate.

MHRA and/or the manufacturer may contact the reporting EQA scheme organiser for further information about the issue. The manufacturer will review the adverse incident report to enable them to undertake any appropriate action.

MHRA recognises that EQA scheme organisers will continue with their own investigations in parallel with the one initiated by MHRA. To avoid duplication of effort or repeat questions being asked of the manufacturer, you should keep MHRA informed of any findings that may have an impact on the MHRA investigation. This includes any information that may change the clinical risk decision. Please use the unique reference number you will be provided with once the issue is logged.

MHRA will advise EQA scheme organisers of any developments and keep you informed of the progress of any investigation that has been initiated. Please be aware that investigations may be resolved very quickly or they may take several months.

If a Field Safety Corrective Action is required MEDDEV 2.12-1 rev 8 outlines the roles and responsibilities of manufacturers, national competent authorities, notified bodies and the European Commission. MHRA may also consider it necessary to issue additional safety messages e.g. medical devices alerts.

On conclusion of an investigation, and within our confidentiality restrictions, MHRA will send a closure letter to the submitting EQA scheme organiser and manufacturer. The information is retained on MHRA's database and is available if it is needed to support any future investigation. Any comments or queries about the investigation outcome should be addressed to MHRA at the earliest opportunity.

MHRA is bound to observe the confidentiality clause outlined in Article 19 of the IVDMDD. This is also subject to the Enterprise Act 2002, in particular, Part 9 'Information' which covers the rules on disclosure.

Every report MHRA receives enables us to build a better picture of the reported problems associated with devices. The importance of reporting is highlighted in the Biomedical Scientist Article in February 2016 issue. This can be accessed through the following link.

http://content.yudu.com/A3ylnn/BMSfeb2016/resources/index.htm?referrerUrl=http%3A%2F%2Fcontent.yudu.com%2FhtmlReader%2FA3ylnn%2FBMSfeb2016%2Findex.html

Please see the Appendix 2 for links to additional information about adverse incident reporting and other information relating to IVD MDs. You can also refer to the devices information section of the gov.uk website https://www.gov.uk/mhra.

For those wishing to access information about the role and aims of the Joint Working Group and EQA scheme organisers links to the relevant websites are also provided in the Appendix.

4. Reporting route

Yellow Card scheme

https://www.gov.uk/report-problem-medicine-medical-device

The Yellow Card scheme is the MHRA's online system for reporting problems with medical devices and medicines in the UK. This online scheme was formally extended for reporting adverse incidents and performance issues relating to medical devices in 2015.

This scheme is vital in helping MHRA monitor the safety of all healthcare products in the UK to ensure they work and are acceptably safe.

This is the preferred reporting route for EQA scheme organisers and their subscribers.

Appendix 1 gives details of what, when and how to report. It also outlines what information to include in your report, also how to contact a Medical Device Specialist should you require assistance in determining whether an issue should be reported. This informal discussion is not a substitute for a Yellow Card report, or an alternative route for reporting.

5. MHRA recommendations

- The route for reporting is via the online Yellow Card scheme.
- Submitters are encouraged to report potential device issues as early as possible.
- Submitters are encouraged to indicate whether the reported issue is, or may be, clinically significant.
- Please keep MHRA informed of any developments or updates relating to your report by contacting us on aic@mhra.gov.uk quoting the unique MHRA reference number.

Appendix 1

What to report
(please note this is not an exhaustive list)

- Where there is an actual or potential clinical impact/safety risk where the device is suspected to be a contributory cause.
- Where a device is working outside its intended purpose and there is a potential clinical impact/safety risk.
- When a device is not meeting its performance claims.
- When a device is working within specification but there is a shift which may lead to an adverse event/safety risk.
- When a manufacturer makes a change to their device that may affect performance with native samples which may have a clinical impact/safety risk.
- Where there is a significant change in performance, persistent or unexpected, which may have a clinical impact/safety risk.
- When the IFU requires a modification to make it clearer to users how they should be using the device.
- When the IFU appears clear but some users do not understand the limitations of the assay or how to interpret the results. This may require the manufacturer to provide additional clarification in the IFU.
- When a change has been made to the device or labelling/documentation to address a safety issue.
- Where a device is not traceable to an available primary reference material or method.

What not to report
(please note this is not an exhaustive list)

- When a device is performing within specification with no actual or potential clinical impact.
- Individual lab performance issues.

When to report
(please note this is not an exhaustive list)

- When there has been harm.
- When there is the potential for harm.
- Inform MHRA at the same time the manufacturer is contacted.
- If in doubt report.

How to report

Via the online Yellow Card system.

Additional guidance on how to complete a Yellow Card for EQA reports:

- Essential Yellow Card fields to complete i.e. all red starred fields, reporter contact details, nature of defect/details of incident (section 5), details of any action taken (section 6).
- The date of incident can be left blank for EQA reports.
- For device description, use the best fit from the available list. Clarification can be made in the 'nature of defect/details of incident' free text box.
- Use the free text boxes (section 5 and 6) for information about the event and for relevant information that does not fit anywhere else on the form.
- Attachments can be included under section 7.
- The information initially submitted to MHRA via Yellow Card (including any attachments) will be sent to the manufacturer when they are contacted by MHRA and asked to investigate.

What information to provide in your Yellow Card report

- A clear statement on the form to indicate whether the report is just for information at this stage (as this will determine the level of investigation assigned to the report). If required, MHRA can change the level of investigation as more information becomes available.

- Product information
  Please provide as much information as you can, for example:
  - manufacturer details
  - device name, model, catalogue number, lot numbers (if known and relevant)
  - instrument the reported assay is being run on
  - software version (for applicable devices)
  - any data the manufacturer has provided to you during the course of your initial review.

- Clinical risk:
  - Include EQA scheme assessment or initial thoughts on the clinical risk. If you are still unsure, please indicate this.
  - Advise MHRA if the clinical risk assessment changes based on availability of additional information.

- Injury:
  - As the report will be related to EQA samples the risk will be NONE. However, there may be potential risk to patients.

- Indication of the scale and longevity of the issue:
  - how long the bias/change in performance has been evident
  - whether the bias/change is across the linear range

- number of subscribers
- it would be helpful if you could provide copies of the scheme results showing the reported event.

Communication

- If in doubt we encourage you to report.
  - If you'd like to have an informal chat to a Medical Device Specialist to see if the event should be reported please contact Medical Devices Adverse Incident Centre (AIC) on 020 3080 7080 – this will enable you to be forwarded to the most appropriate person in the IVD team.
  - Please be aware this informal discussion DOES NOT constitute an adverse incident report and will not be logged on our adverse incident database.

Ongoing communication

- Keep MHRA informed of the progress of your investigation and any additional information that comes to light e.g. change in clinical risk, data provided by the manufacturer, changes proposed and agreed with the manufacturer etc.
- Provide updates using the unique MHRA reference number assigned to the report.
- Send updates to us on: aic@mhra.gov.uk
- MHRA will keep the reporter informed of investigation progress (unless level of MHRA investigation has been assigned as Trending and Surveillance).
- If you do communicate directly with the assigned Responsible Officer (RO) please copy in aic@mhra.gov.uk
- On completion of the investigation MHRA will send a 'closure' report to the reporter and manufacturer (unless level of MHRA investigation has been assigned as Trending and Surveillance)
- Within confidentiality constraints, there should be bi-directional communication between MHRA and EQA scheme providers where there is a suspected device issue.

Appendix 2

Useful links

- Reporting site for the Yellow Card scheme: https://yellowcard.mhra.gov.uk/
- Council Directive 98/79/EC on In Vitro Diagnostic Medical Devices (IVDMD) (1998)
- Guidance document: Market surveillance - Guidelines on a Medical Devices Vigilance System - MEDDEV 2.12/1 rev.8: http://ec.europa.eu/DocsRoom/documents/15506/attachments/1/translations
- Medical devices: guidance for manufacturers on vigilance: https://www.gov.uk/government/collections/medical-devices-guidance-for-manufacturers-on-vigilance
- Medical devices regulation and safety: https://www.gov.uk/topic/medicines-medical-devices-blood/medical-devices-regulation-safety
- Guidance: In vitro diagnostic medical devices: procurement, safety, quality and performance https://www.gov.uk/government/publications/in-vitro-diagnostic-medical-devices-procurement-safety-quality-and-performance
- Guidance: In Vitro diagnostic point-of-care devices https://www.gov.uk/government/publications/in-vitro-diagnostic-point-of-care-test-devices
- EQA Scheme Organisers (this list is not exhaustive): https://www.rcpath.org/profession/committees/jwgqa.html

  https://uknegas.org.uk/

  http://www.wegas.com

  http://www.rigas.com/

  https://www.emqn.org/

  https://www.genqa.org/

Links last checked April 2019