Guidance for Laboratories

Investigating and Communicating Assay Performance Issues

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1. Introduction

Ensuring the quality of diagnostic assays is crucial for patient safety, clinical decision-making, and maintaining confidence in laboratory services. This document provides guidance to laboratories on how to investigate assay performance issues, communicate findings effectively, and implement corrective actions. It applies to both public and private laboratories. All investigations should be recorded in the laboratory's quality management system.

2. Identifying and Scoping Assay Performance Issues

2.1 Initial Investigation

Assay performance issues may be identified through various routes, all of which should be given equal weight when considering whether to initiate an investigation. Outside of traditional markers of assay performance - such as internal Quality control (IQC), External Quality assurance (EQA) and field safety notices (FSN) - consider feedback from clinical users, or laboratory clinical review. Unexpected queries from primary or secondary care clinicians can be valuable indicators, highlighting performance issues through diagnosis rates or clinical experience.

Investigations should begin at the point when results are first queried. The initial steps should follow established good laboratory practice.

Where IQC and EQA data do not provide useful information, or are not available:

- Consider supplier performance claims, third-party (or additional) IQC comparisons, and replicate testing of samples.
- Further assessment may include the review of patient mean data over set time periods and proportions of results above or below the reference range and/or diagnostic threshold(s). Consider using a well-defined patient population, such as GP patients to help reduce biological / pathological variation.
- Consult suppliers/manufacturers and other users to identify any known or potential issues, including global reports. Clarify the supplier's intended use for the assay.
- Monitor performance over set periods (daily, weekly, monthly) to build a profile of assay behaviour. This should be retrospective as well as during the investigation period. This add confidence to the laboratory that the assay is being monitored rigorously.
- Review historical verification data to identify changes in performance since the assay's introduction.

- Consider using clinical outcomes or biological variation models to determine acceptable performance specification of the assay. Consider whether biological variation is contributing to perceived assay performance. EFLM Biological Variation
- Utilise EQA schemes for additional data on known assay performance trends. Scheme providers will be able to provide a further breakdown of assay performance and trends.
- It is also important to understand the development of diagnostic cutoffs and their clinical implications at these points. This enables the laboratory to understand the challenge points in the assay, and the likely clinical impact and the clinical use of the assay results.
- As part of business continuity and contingency planning, the laboratory should have in place a protocol to guide decision making on actions to take whilst assay performance is being investigated. This includes temporary suspension of the clinical service, or immediate additional protocols to mitigate the potential for poor assay performance (for example, increased maintenance or IQC periods, additional testing or introduction of result review by a senior scientist/clinician).
- The investigation of assay performance should use accepted statistical approaches; these should be defined as part of the initial investigation. This allows for objective, evidence-based decision making and can be used to support resolution and mitigation steps if required.

3. Triage and Risk Ranking

All assays have unique application(s), volume of tests, clinical urgency, and their contribution to the diagnostic answer. Laboratories should establish a system to ensure they understand the clinical impact upon the patient user group and how any poor performance might affect the clinical service. Patient risk must remain the primary consideration when determining appropriate and proportionate actions during the investigation period.

- Establish criteria to rank issues by clinical impact, number of patients affected, and financial impact on the NHS.
- A formal risk assessment can help guide the investigation and ensure that appropriate controls, mitigations and actions are identified.
- It may be helpful to use big data analytics proactively to detect emerging issues early, particularly for assays with known or potential performance issues and to review all assays at suitably frequent intervals. This may include monitoring diagnosis rates or clinical classifications within the local population.
- Determine whether changes in patient demographics, requesting patterns (e.g. introduction of new clinical guideline) or system modifications are affecting performance. This can be critical when new services are introduced or activity from new patient populations is added to the laboratory service.

4. Responding to Assay Performance Issues

A prompt response to suspected or known assay performance is critical to patient safety and maintaining confidence among clinical users in the laboratory service. Laboratory actions directly impact wider health systems and must reflect this responsibility. Responses should be proportionate and focused on delivering a safe service.

The individual laboratory is responsible for this decision-making and should escalate issues to the appropriate governance and clinical teams. Decisions must be transparent, clearly communicated to the clinical teams and service users promptly. Ensure appropriate documentation of investigations.

4.1 Addressing Assays Outside Clinical Tolerances

- Laboratories should have flexible decision-making processes reflect the specific context. Registered scientists and clinicians should be empowered to make initial, informed decisions as to immediate actions to ensure patient safety.
- Options include additional or alternative testing, temporary suspension of services, outsourcing tests, or modifying cut-offs with appropriate clinical oversight. It is unlikely that the laboratory can unilaterally implement these, so key stakeholders must be identified early.
- Consider the impact on sample integrity and stability, the consequences of service suspension, and the number of patients affected.
- In cases of uniform bias, cut-off adjustments may be made in consultation with clinical teams. These changes should be communicated clearly - both with the result and as a separate update.
- Issues should be reported to the assay manufacturer or supplier, EQA providers and via the MHRA Yellow Card system, UKAS and EPPR routes.
- As patients increasingly receive laboratory reports directly, report wording and footnotes should reflect this and be accessible.

4.2 Clinical Communication and Advice

- Stakeholders across the care pathway, including primary care providers, must be engaged. Rapid, transparent communication with clinical users is essential.
- Consider when to involve non-clinical stakeholders such as risk management teams, communication teams, IT departments, EPRR, supply disruption, contracts and other service managers.

- Laboratories should not hesitate to suspend services if assay performance is uncertain. This decision should be communicated to relevant clinical users and senior laboratory leaders.
- Use clear, accessible language and provide evidence-based explanations.
- Pre-agreed lines of communication should be in place to support timely and effective alerts across all domains primary and secondary care. Service users should be encouraged to have a low threshold to report suspicious results or unusual trends, particularly those identified at the patient interface.
- Educate users on expected assay performance, reference ranges and cut-off points (e.g., diabetes cutoffs based on retinopathy risk, method specific cortisol thresholds for synacthen tests) This will aid interpretation of results during the investigation stage.

5. Lessons Learned and Preventative Measures

Once the investigation is complete and appropriate mitigation or resolution has been implemented, it is vital that all users and clinical teams are informed. This includes confirming whether users can return to pre-investigation protocols or should continue using updated procedures.

Although the following actions are listed as post-investigation steps, laboratories should also consider them during the investigation where appropriate.

5.1 Post-Investigation Actions

- Laboratories should involve a wider team beyond pathology to review lessons learned. Findings should be shared across networks to support awareness and future learning.
- Issues and their resolutions should be reported through the MHRA Yellow Card system, UKAS and EPPR routes. Yellow Card | Making medicines and medical devices safer
- Risk management should consider patient-level risks, including diagnostic errors, delays or incorrect interventions. This may require involving the wider health system in a look-back exercise to assess the impact on affected patients. Particular attention should be given to access and equity, including the effects of social inequality.

6. Quality assurance

6.1 Quality Control and Monitoring

- Best practices around IQC and EQA should be followed to detect performance shifts at the earliest opportunity. EQA scheme providers should be informed and consulted so they are aware of any known or suspected performance issues.
- Investigations of unsatisfactory EQA performance should begin immediately, with clear action and risk assessment documented.
- Both biological and analytical variations must be considered in evaluations. This applies from the validation and verification stage through to assay introduction. Combined with the manufacturer's performance claims, these evaluations can highlight areas of risk that should be monitored regularly during routine use.

By following this guidance, laboratories can ensure that assay performance issues are investigated systematically, communicated clearly, and addressed in a way that safeguards patient care and maintains the quality of diagnostic services.

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