American Board of
ABFT
Forensic Toxicology ™

Guidelines for Performing Corrective Action for Deviations in Proficiency Test Results

Introduction

The performance of a laboratory in proficiency tests is one of the few reliable ways to effectively evaluate the quality of work of the laboratory. Historically, many laboratories have taken the viewpoint that while good performance is their goal, deficiencies may be overlooked with the thought that "*hopefully we'll do better next time*" or, "*the result was an outlier/aberration and there is no need for corrective action*", or "*the sample must have been bad because our calibration looked OK*".

However, it is a critical component of any quality assurance program that all apparent deficiencies should be investigated soon after the receipt of the report from the PT provider. The purpose of this document is to give guidance for the type and extent of investigation expected of the laboratory by the ABFT Accreditation Program. That may be dependent on the seriousness of the deficiency. To the extent possible, it is important that the investigation include determination of the root cause of the deficiency and corrective action to minimize or prevent reoccurrence of the same or a similar problem.

False positives

This is the most serious type of error and usually requires rigorous investigation. Potential sources can include carryover from another sample through pipettes, evaporator tips, reusable glassware, or most commonly carryover from a preceding sample containing a very high concentration of the same analyte (e.g. from a GC or LC injection), as well as processing errors (e.g. sample misidentification during accessioning or transfers). There are various ways to safeguard against all of these sources that toxicologists should be familiar with.

Other causes can be over zealous staff in "calling" a GC/MS peak positive based on a dubious mass spectral match or a tiny GC or LC peak close to the LOD of the assay.

Some types of false positives are less serious, although still require investigation and, as necessary, review and modification of analytical methods and reporting procedures. Examples include reporting ephedrine when pseudoephedrine was present, reporting a metabolite as present when it was not (but which may have been produced as an artifact of the analytical procedure - such as methylation of a target analyte when methanol is present in the sample or extraction solvent).

False negatives

Generally, false negatives fall into two categories - those where the analytical methods simply do not detect the target analyte (or detect it at the spiked concentration) - and those where the laboratory's methods should have detected the substance at the spiked concentration, but did not.

Not detecting a drug that should have been detected by the laboratory's procedures

This suggests a method failure - either a method with poor precision, one where the analytical instrumentation was operating below the expected level of sensitivity or analyst error (e.g., poor extraction). At the very least, the particular run where the failure occurred should be reviewed, including the performance of calibrators and controls and any pre-run column checks. If the analyte should have been detected, the PT sample should be repeated. Re-evaluation of the detection limit of the assay may be appropriate.

Not detecting an analyte that is not usually detected, or one that has been spiked at a concentration below the LOD of the laboratory's method, or failure to report an analyte (e.g., metabolite) that the laboratory does not usually report, does not require corrective action UNLESS in the opinion of the Accreditation Committee, detection and reporting of the analyte would reasonably be expected, consistent with the mission of the laboratory. Even so, the laboratory should document the reason in its corrective action documentation.

It is not practical to expect any laboratory to detect any and all analytes that have been spiked into a PT sample. Some analytes are either unusual (e.g., oxaprozin) or are of limited forensic significance in most cases (e.g., ranitidine, cimetidine, NSAIDS). If a laboratory may detect, but as a matter of policy does not report certain analytes, these are not usually regarded as a false negative by the ABFT program (e.g. not reporting a carbamazepine metabolite or a desalklyl metabolite; not reporting nicotine and caffeine if the concentrations do not appear to be unusually high).

However, failure of an ME/coroner laboratory to detect potentially fatal concentrations of a relatively common opiate such as hydromorphone, oxycodone or fentanyl deserves at least administrative review and evaluation to determine, for example, if screening methods should be improved or changed (e.g., use of immunoassay procedures on blood using cut-offs more suitable for urine is not usually appropriate). Other examples include the failure to detect some common depressants in DUID cases (e.g., meprobamate, carisoprodol), or some of the more potent benzodiazepines and related anxiolytics in DFSA cases (e.g., alprazolam, lorazepam). In this latter case, and as an example, failure to detect and report a hydroxybenzodiazepine in a DFSA urine sample when the parent was not detected would be regarded as a deficiency that should be investigated as either a method failure, or, an administrative investigation as to whether a new test should be introduced that is more appropriate for the mission of the laboratory.

Quantitative errors

Quantitative errors can usually be investigated on an "escalating basis". For most analytes in a forensic laboratory an acceptable error is regarded as 2 SD or ±20% for drugs similar analytes (2 SD or ±10% for ethanol). For relatively minor and isolated deviations outside these ranges a ***documented*** administrative review of the analytical method and quality control may be sufficient.

For more significant deviations (e.g., approaching 3 SD or +/-30%) a review of the analytical run in question followed by repeat analysis of the PT sample is warranted, at a minimum. It is usually appropriate to review prior performance of the assay by looking at the QC results for that analyte.

More serious deviations are usually symptomatic of an analytical error (calibrator error, isolated internal standard pipetting error, dilution error or similar error), *or an inherently bad procedure with poor precision*. If the error has been caused by the analyst it could be an isolated incident, however, review of that analyst's work and technique may sometimes be appropriate. If the assay has inherently poor precision, further method development is warranted.

What is not acceptable corrective action?

1. Simply re-analyzing a PT sample for an analyte with a significant deviation, and going no further if the result is now close to the PT target, is not appropriate. While this is better than "no action", it does not address the issue of why the result was out of range the first time.

2. Simply re-making a calibrator stock and re-running the assay to get a result that is in-range, is not appropriate in isolation. This is commonly done, but is not consistent with good laboratory practice. The assumption has been made that either the original calibrator solution was prepared incorrectly, or it has deteriorated. If the original calibrator solution was prepared incorrectly, that should have been evident from use of an independently prepared control. If the original calibrator stock had in fact deteriorated and been remade for the repeat test, the original material should have been run in parallel with the new calibrator to verify that deterioration. If in fact deterioration had occurred this should trigger further action such as shortening the expiry date or better storage conditions.

3. In either situation, if the original deficiency is major (e.g., >50 - 150% or > 4 SD) this should be

treated almost as seriously as a false positive and rigorous corrective action undertaken. The only exception might be if the deficiency was due to a reporting error, but even then action should be taken to improve accuracy of the reporting process.

Review of Affected Casework

Where a deficiency is identified the laboratory director must undertake a review to determine the potential impact of the deficiency. If that deficiency is likely to have resulted in misinterpretation of toxicology results in casework, the laboratory must notify the client. The extent of the review and any decision to re-analyze casework is a matter of discussion between the laboratory and the client. All such reviews, discussions and any reanalyzes must be documented as part of the laboratory's quality assurance program, and that documentation made available to ABFT at the earliest opportunity.

ABFT Accreditation Committee
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