



# The United Kingdom and Ireland association of forensic toxicologists forensic toxicology laboratory guidelines (2018)



Simon P. Elliott<sup>a,\*</sup>, Duncan W.S. Stephen<sup>b</sup>, Sue Paterson<sup>c</sup>

<sup>a</sup> Alere Forensics, Malvern Hills Science Park, Geraldine Road, Malvern WR14 3SZ, UK

<sup>b</sup> Department of Clinical Biochemistry, Link Building, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZD, UK

<sup>c</sup> Toxicology Unit, Division of Investigative Science, Imperial College, London W6 8RP, UK

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## ABSTRACT

In 2010, the United Kingdom and Ireland Association of Forensic Toxicologists (UKIAFT) created forensic toxicology laboratory guidelines. This represents a revision of those guidelines as a result of the changing toxicological and technical landscape.

## 1. Introduction

The UK & Ireland Association of Forensic Toxicologists (UKIAFT) consists of representatives from each of the main laboratories in the United Kingdom and Ireland offering Forensic Toxicology Services. In the absence of national guidelines for forensic toxicology, the UKIAFT approached the board of the Society of Forensic Toxicologists [10] with a view to amending the Laboratory Guidelines published jointly by SOFT and the American Academy of Forensic Sciences (AAFS). The SOFT/AAFS Forensic Toxicology Laboratory Guidelines (Version 2006) were reviewed and amended to better reflect toxicology standards and practices within the UK & Ireland. This resulted in the publication of the first UKIAFT laboratory guidelines in 2010 ([1], “The United Kingdom and Ireland Association of Forensic Toxicologists Forensic toxicology guideline (2010)”, *Sci Justice*. 50:166–176). Since then, there have been various changes in laboratory testing, not least the wider use of liquid chromatography mass spectrometry, including high resolution mass spectrometry and is reflected in this revision.

The UK & Ireland Association of Forensic Toxicologists Forensic Toxicology Laboratory Guidelines (version 2018) acknowledge the following international standards:

- BS EN ISO/IEC 17025:2017 for testing laboratories,
- ILAC G-19:8/2014 guidelines for forensic science laboratories and,
- BS EN ISO/IEC 15189:2012 for medical laboratories

These guidelines do not necessarily reflect opinions about the minimum requirement for any laboratory, nor do they have any regulatory purpose; rather, they are intended to assist laboratories engaged in the practice of forensic toxicology in achieving future goals. These

guidelines are also in the processing of forming an Appendix for forensic toxicology in the UK Forensic Regulator's Codes of Practice and Conduct for forensic science providers and practitioners in the Criminal Justice System [8].

A list of the organisations from the United Kingdom and Ireland that have contributed to the UKIAFT Forensic Toxicology Laboratory Guidelines 2018 is found in [Appendix 1](#).

## 2. Scope

These guidelines are primarily for use in the practice of Forensic Toxicology encompassing post-mortem toxicology, human performance toxicology and criminal toxicology. There are separate guidelines available in relation to workplace drug-testing in the UK and Europe [5].

## 3. Definitions

*Forensic Toxicology* - determining the presence or absence and role of alcohol, drugs and their metabolites as well as other toxic substances in human fluids and tissues for Court and other legal purposes (including medico-legal matters).

*Post-Mortem Toxicology* - the determination of toxicological elements in death investigations.

*Human Performance Forensic Toxicology* - used to elucidate the absence or presence of substances modifying human performance or behaviour.

*Criminal Toxicology* - the determinants or toxicological factors in the investigation of criminal offences.

*Reference Material (RM)* - a material or substance containing target

\* Corresponding author.

E-mail address: [simontox@yahoo.co.uk](mailto:simontox@yahoo.co.uk) (S.P. Elliott).

analyte(s), one or more properties of which, such as analyte concentration(s) are established sufficiently well to be used for calibration of an apparatus, assessing a measurement or assigning values to material. (AOAC Official Methods of Analysis (1984)).

*Certified Reference Material (CRM)* - a reference material, one or more of whose properties are certified by a valid procedure, or accompanied by or traceable to a certificate or other documentation which is issued by a certifying body (AOAC Official Methods of Analysis (1984)).

*Standard* - a reference material containing target analyte(s) possessing one or more properties such as analyte concentration(s) that are sufficiently well established so that it can be used to prepare calibrators.

*Calibrator* - a solution containing target analyte(s), either prepared from the reference material or purchased, used to calibrate the assay. Where possible, calibrators should be prepared in a matrix similar to that of the specimens to be analysed.

*Quality Control (QC)* - a solution containing target analyte(s) either prepared from the reference material (separately from the calibrators; that is, weighed or measured separately), purchased, or obtained from a pool of previously analysed samples subject to ethical approval and in accordance with the Human Tissue Act. Controls from any of these sources are used to determine the validity of the calibration; that is, the stability of a quantitative determination over time. Where possible, controls should be matrix-matched to specimens and calibrators, as indicated above.

#### 4. Personnel

Due to the variety of forensic toxicology service providers in the UK & Ireland, it is not possible to provide a prescriptive line-management structure for all laboratories and titles for generic roles may differ across the various organisations. However, the UKIAFT (through member consultation) has published recommendations for establishing best practice for professional training & development in forensic toxicology ([2], “The United Kingdom and Ireland Association of Forensic Toxicologists; establishing best practice for professional training & development in forensic toxicology”, *Sci Justice*. 57(1):63–71). Best practice is proposed using a blend of modular foundation knowledge training, continuing professional development, academic study, research & development and ongoing analytical practice. The need for establishing a professional career structure is also discussed within the publication along with a suggested example of a suitable model.

##### 4.1. Head of toxicology service

The forensic toxicology laboratory should be directed by a person who is qualified by reason of appropriate education and experience to assume the required professional, organisational, educational, managerial and administrative responsibilities.

Acceptable qualifications include a doctoral degree in one of the natural sciences and at least three years of full-time laboratory experience in forensic toxicology; or a Master's degree in one of the natural sciences and at least five years of full-time laboratory experience in forensic toxicology; or a Bachelor's degree in one of the natural sciences and at least seven years of full-time laboratory experience in forensic toxicology.

The Head of Toxicology Service should also have documented training and/or experience in the forensic applications of analytical toxicology (such as court testimony, research, participation in continuing education programmes, and/or peer review of appropriate manuscripts in the field), including a knowledge of evidentiary procedures that apply when toxicological specimens are acquired, processed, stored and disposed and when toxicological data are submitted as part of a legal proceeding.

The Head of Toxicology Service should be ultimately responsible for ensuring that the trained laboratory personnel are appropriately

qualified, experienced and competent to conduct their role in the work of the laboratory and that they participate in a scheduled continuous personal development programme.

The Head of Toxicology Service should be ultimately responsible for ensuring that the competency of laboratory personnel is monitored and maintained and skills verified. This training and competency assessment should be documented.

The Head of Toxicology Service should be ultimately responsible for ensuring the development of complete, up-to-date laboratory standard operating procedures (SOPs) that are available to and followed by all personnel carrying out tests.

The Head of Toxicology Service should be ultimately responsible for ensuring methods are fit for purpose and that procedures for validating new analytical methodologies and maintaining quality assurance programmes are in place to ensure the proper performance of methods and the reporting and interpretation (if required) of results.

Forensic toxicology laboratories handle controlled substances, generate results essential to the criminal justice system and have access to confidential information. The Head of Toxicology Service, to the extent practical or permitted by law, should exert reasonable efforts to ensure that all personnel meet high ethical and moral standards and that all personnel adhere to relevant legislation (e.g. Human Tissue Act and Misuse of Drugs Act) and other legal obligations.

##### 4.2. Other laboratory staff

The range and type of duties of other laboratory personnel will vary according to the size and the scope of the laboratory but recommendations are detailed in the UKIAFT professional training & development document.

#### 5. Standard operating procedures

The laboratory should have standard operating procedures (SOPs) that are complete, up-to-date, and available to all personnel who are carrying out tests.

SOPs should include detailed descriptions of procedures for sample receiving, accessioning, chain-of-custody, analysis, quality assurance and quality control (including validation of methods), review of data, reporting and sample disposal as well as IT and security protocols.

SOPs should be available for administrative procedures as well as analytical methods and be reviewed, signed, and dated whenever they are first placed into use or changed.

The SOP should include, for each analytical procedure if appropriate, the following: a) theory and principle of the method, b) instructions for preparation of reagents, c) details of the analytical procedure, d) instructions for preparation of calibrators and controls (including use of blanks), e) information about any special requirements for handling reagents or for ensuring safety, f) validation parameters (e.g. LOQ, linearity) or reference to the appropriate validation document, g) criteria for the acceptance or rejection of qualitative or quantitative results, h) references and i) instrumentation to be used.

Please refer to relevant sections of ISO 17025:2017, ISO 15189:2012 and ILAC G19:2014 for further guidance on the requirements for document control.

A SOP or protocol for the performance or outsourcing for infrequently requested assays is recommended.

The laboratory Quality System should contain a record of sample signatures and initials of all staff handling specimens and carrying out analytical work (i.e. a “signature page”). This should be updated as needed to reflect staffing changes.

All SOPs should be reviewed as outlined in the laboratory Quality System but should be at least once every two years and the laboratory should maintain out-dated copies of all SOPs and provide a means for their retrieval from archival storage.

## 6. Samples and receiving

### 6.1. Specimen collection and labelling

The proper selection, collection (sampling), labelling and submission of specimens for toxicological analyses is of paramount importance if analytical results are to be suitable and their subsequent interpretation is to be scientifically sound and therefore useful in forensic casework. These guidelines can apply equally to investigations by Coroners, Procurators Fiscal, Forensic Medical Examiners and to investigation by law-enforcement agencies of civil and criminal matters and cases involving human performance issues.

The laboratory should develop and provide detailed guidelines and instructions to all agencies or parties the laboratory serves and consider this in conjunction with guidance documents already in circulation e.g. “*Guidelines for handling medicolegal specimens and preserving chain of evidence*” published by the Royal College of Pathologists in March 2017.

Instructions should state the types and recommended amounts of specimens needed to accomplish the requisite analyses and subsequent interpretations.

Whenever possible, the amount of specimen collected should be sufficient to ensure that enough remains for subsequent re-analysis if required.

Instructions should include specific requirements for the type and size of specimen containers and, if appropriate, the type and amount of preservative.

Instructions for labelling individual specimen containers, and acceptable conditions for packing and transportation, should also be provided.

Submitting agencies should be instructed to indicate relevant medical history on living subjects or decedents who may carry a highly infectious disease such as tuberculosis, hepatitis or human immunodeficiency virus. However, laboratories should adopt “universal precautions” when handling biological specimens, regardless of reported medical history.

Each specimen should be identified by type. For post-mortem blood, the anatomical site of collection should be stated. When ante-mortem and/or peri-mortem specimens are available from a deceased individual, each specimen should be labelled with the time and date of collection and whether the specimen is a separated aliquot from an original container. It should be noted that gel in containers can absorb drugs and affect analysis (especially quantitative) so should be avoided if possible, or noted.

The name of the subject from whom the specimens were collected should appear on each label, if known, together with other appropriate identification; for example, the customer number/exhibit reference (as appropriate) and/or the subject's date of birth.

### 6.2. Specimen handling and receipt

A chain-of-custody form should be designed that will accompany specimens from the place of collection to the laboratory. This information may be incorporated in the laboratory request form.

Handling and transport of a specimen from one laboratory or place to another should always be appropriately documented as part of a chain-of-evidence record.

The chain-of-custody section should be properly completed by responsible personnel at the time the specimens are collected and received.

Every effort should be made to minimise the number of persons handling a specimen.

Individual specimens should be transported and stored in such a manner as to minimise the possibility of degradation, contamination, tampering and/or damage in shipment.

Acceptable means of transporting specimens to the laboratory may include hand-delivery, national postal service, or a private courier

service. Guidance on the requirements for transport of potentially infectious substances can be found through consultation of the regulation UN3373 [13].

The means of delivery of specimens should be recorded by the receiving laboratory.

The condition of the external package should be documented upon receipt at the laboratory, either on the requisition form that accompanies the specimen(s), in the log book, on the external chain-of-custody form, or on other documents that constitute normal laboratory records.

Shipping containers should be opened only in a secure area and only by an individual designated to record receipt of specimens. A “secure area” may be defined as an area to which unauthorised individuals do not have access without escort by authorised personnel.

A copy of the specimen-receipt record should be permanently maintained; this record may be computer-generated, typed, or handwritten, or a combination.

Specimens should be logged-in at the earliest opportunity. Pending login, the specimens must be stored under conditions of appropriate environment and security.

The integrity of the individual specimen container should be checked, as should the condition of each specimen. Discrepancies and actions taken should be recorded.

### 6.3. Recommended amounts of specimens

#### 6.3.1. Post-mortem forensic toxicology specimens

In death investigations, the types and minimum amounts of tissue specimens and fluids needed for toxicological investigation are frequently dictated by the condition of the body and the analyte or analytes that must be identified and quantified. The toxicologist should also be made aware of any embalming undertaken.

Many deaths involve ingestion of multiple drugs, necessitating larger amounts of tissue and fluids to be collected at post-mortem for toxicological examination. The following is a suggested list of specimens and amounts to be collected at post-mortem in such cases:

- Femoral Blood - 10 mL (site specified and suitably isolated)
- Urine - All Available
- Vitreous Humour\* - All Available
- Cavity/Heart Blood\* - 25 mL (if femoral blood is limited or not available)
- Hair\* - to be collected at the start of the autopsy prior to body evisceration. Cut from the vertex region of the scalp (additional sample pulled from vertex region) maintaining alignment with orientation of strands clearly indicated.
- Bile\* - 10 mL
- Liver\* - 10-20 g (if low volume of blood available)
- Stomach Contents\* - All Available (or specify if an aliquot) and any examples of undigested tablets/drug material (including potential plant toxin material)
- Brain\* - 10-20 g (for volatiles)
- Lung\* - 10-20 g (for volatiles)
- Skeletal Muscle\* - 10-20 g (if low volume of blood available)

Samples identified with an \* should only be submitted for analysis following discussion and agreement with the toxicology laboratory. Unique poisons and situations may dictate the need for other specimens, e.g. kidney and spleen. Such cases should be addressed on an individual basis. However, the amount of specimen routinely collected should be sufficient to allow re-analysis for one or more analytes at a later time, should the need arise.

#### 6.3.2. Sample preservatives

It is recommended that as a minimum, blood and urine samples collected for alcohol (ethanol) analysis should be stored in a vial

containing sodium fluoride. A number of drugs are unstable and where possible samples should be stored in a vial containing sodium fluoride ( $\geq 1.5\%$ ).

### 6.3.3. Human performance forensic toxicology specimens

As defined earlier, this activity encompasses the identification and quantification of ethanol and other drugs and substances in blood, breath or other appropriate specimens for evaluation of their role in modifying human performance and behaviour. The analysis of breath ethanol was not considered by the UKIAFT.

Although in many instances the analytes are clearly specified in advance in human performance forensic toxicology testing, the spectrum of drugs and chemicals may potentially approach those encountered in post-mortem toxicology. As a consequence but remembering the difficulties involved in obtaining samples from living persons, it is recommended that minimum volumes of blood and urine are requested as guidance and to provide sufficient sample volume to carry out a range of analyses. A minimum of 5 mL of blood and 20 mL of urine should be collected but lower volumes should still be accepted with the caveat that this will restrict what analyses can be completed. Forensic toxicology laboratories should develop their analytical methods such that a reasonably complete drug screen can be completed on no more than 5 mL.

It must be emphasised that urine concentrations of drugs and/or drug metabolites (with the exception of alcohol) should be interpreted with caution. In general, urine drug/metabolite concentrations should not be used to interpret the effect of a drug or chemical on human behaviour. In some cases a second urine sample may be useful for accurate alcohol (ethanol) interpretation. This should be taken at a stated interval after the first urine and the time of collection should be noted. If other specimens are submitted and analysed, any conclusions regarding drug use or effects on human behaviour should be based only on appropriate validated scientific studies.

### 6.3.4. Drug facilitated sexual assault (DFSA)

Guidelines for the collection and analysis of samples for DFSA cases are defined elsewhere

- Drug-Facilitated Sexual Assault – A Forensic Handbook. [3] Academic Press ISBN-13: 978-0-12-440261-4
- Guidelines by the Society of Hair Testing [11]
- Royal College of Physicians (The Faculty of Forensic & legal Medicine) – Recommendations for the Collection of Forensic Specimens from Complainants and Suspects [6].

## 7. Security and chain-of-custody

### 7.1. The laboratory

Access to the forensic toxicology laboratory should be limited. The Head of Toxicology Service should authorise and document the personnel able to enter designated areas.

Unauthorised personnel should be escorted and should be required to sign a log book upon entry and departure from the laboratory, recording the time, date and purpose of the visit.

The physical layout of the laboratory must be such that unauthorised personnel cannot enter without detection.

### 7.2. Specimens

Receipt should be indicated by handwritten or electronic signature (or initials) of individuals receiving the specimens; at a minimum the date of receipt should also be included.

Specimens received should be labelled with the name of the donor, suspect, complainant or witness case number, specimen type (e.g. blood) or unique identifier, date specimen taken and identification of

the individual taking the sample.

Specimens must be stored in a secure manner.

For the maintenance of specimen security it is recommended that, where possible, the laboratory has a separate accessioning area. In this area, specimens are received, assigned accession numbers, aliquots removed and/or stored in refrigerator/freezers.

Any transfer of specimens, or portions thereof that are removed for analysis, must be documented as part of the permanent laboratory record.

It is recommended that the chain of custody documentation reflects not only the receipt of the specimen from an outside source, but also transfers of the specimen or an aliquot thereof, within the laboratory. If multiple specimens are involved, a batch form may be used.

An aliquot or a batch of aliquots' chain of custody form may be used for indicating the transfer of portions of specimens for testing. This form should indicate the date, the test for which the aliquot was taken, the laboratory accession numbers, the identity of the individual obtaining the aliquots and the identity of the individual to whom the aliquots were given, if applicable.

Specimens may be transferred to a secure long-term refrigerator/freezer after analysis. Transfers between storage areas and other laboratories and/or subsequent disposal should be documented. The laboratory should develop a SOP for retention and disposal of specimens. This procedure should reflect regulations recommended or adhered to by the instructing authority and should comply with the necessary legislation (e.g. Human Tissue Act).

The laboratory should maintain a written policy and instructions pertaining to retention, release and disposal of specimens, complying with the necessary legislation and client requirements where appropriate.

## 8. Analytical procedures

### 8.1. Presumptive screening tests

In most instances where a laboratory is asked to look for drugs in biological specimens, screening tests are employed. Screening tests may be directed towards a class of drugs, such as opiates, or may be a broad-based screen. A presumptive screening test is one that provides an indication of the presence of a drug or drug class but does not provide unequivocal identification, thereby requiring the use of a further and more specific test for confirmation of the result or identification of a specific drug.

Presumptive screening tests such as immunoassay or colour tests must be appropriate and validated for the type of biological specimens being analysed. With regards to immunoassays used on whole blood they must be appropriately validated for that purpose, especially if using post-mortem blood. If a reporting cut-off is used, the precision of the assay around that cut-off must be demonstrated. Specimens spiked at the cut-off concentration must be clearly distinguishable from specimens that do not contain the target analyte.

As a general matter of scientific principle, the detection or initial identification of drugs and other toxins when detected by an immunoassay or enzymatic assay should be confirmed whenever possible by a second technique based on a different principle. Use of a second immunoassay system (e.g. RIA) to confirm another immunoassay (e.g. FPIA) is not regarded as acceptable, even if it is deemed to be a more specific assay.

Specifically for immunoassays, a laboratory should, at a minimum, be able to demonstrate that the blank or negative calibrator plus two standard deviations does not overlap with the cut-off or the lowest positive calibrator.

The reporting of preliminary, unconfirmed screening tests in a final report is discouraged and further confirmatory analysis should be performed where possible.

## 8.2. Chromatographic tests

Chromatography provides a chemical separation of analytes in a gaseous (GC) or liquid (LC) system, providing a retention parameter to allow identification of a compound. For greater selectivity, these systems are coupled with an appropriate detector such as GC/NPD, GC/FID, LC/DAD, GC/MS or LC/MS, for example. The detector selected should be appropriate to the analytes amongst other factors.

Such techniques can be used to confirm presumptive immunoassay findings but GC/NPD or GC/FID for drugs does not generally provide sufficient specificity for criminal casework. However, the rigorousness required of a confirmation depends to some extent on the importance of the analytical finding and circumstances of the case.

Confirmation using a different technique or system with different chromatographic retention time characteristics is recommended, whether through chemical derivatisation or use of different columns. However, in many circumstances, use of hyphenated techniques that possess at least two powers of identification (e.g. retention time and mass parameter – full scan mass spectrum and/or validated fragmentation ion ratios) is adequate. Nevertheless, a different technique or system should be applied if there is any doubt as to identity, especially if one of the parameters is compromised (e.g. retention co-elution, similar mass spectrum or ion fragmentation transitions).

For ethanol, although false positives are unlikely, confirmation using a second analytical system and matrix (e.g. vitreous humour if post-mortem) is encouraged. It is recommended that GC-FID with headspace (HS) be utilised for alcohol (ethanol) determination in a post-mortem setting. In performance testing (e.g. blood/urine Road Traffic alcohol), analysis utilising two different columns is recommended.

Volume permitting, it is good practice to confirm the identity of an analyte in a fresh aliquot. This will help to prevent contamination or sample mix-up of the first aliquot in the course of the testing process. Analysis of a completely different sample helps to strengthen the results.

The quantification of an analyte may serve as acceptable confirmation of its identity if it was initially detected by a significantly different method (e.g. LC/MS/MS quantification of a drug detected by immunoassay).

Where mass-spectrometry is used in selected ion monitoring (SIM) or selected/multiple reaction monitoring (SRM/MRM) mode for the identification of an analyte, whether as part of a quantitative procedure or not, the use of at least one qualifying ion for each analyte and internal standard, in addition to a primary ion for each, is recommended as a minimum. It is strongly encouraged that where possible 2 or more qualifying ions/transitions are monitored. Commonly used acceptance criteria for ion ratios is  $\pm 20\%$  relative to that of the corresponding control or calibrator. However, it is recognised that some ion ratios are concentration dependent and that comparison to a calibrator or control of similar concentration may be necessary, rather than an average for the entire calibration. Ion ratios for LC/MS assays may be more concentration and time dependent than for GC/MS and therefore acceptable ion ratio ranges of up to  $\pm 30\%$  are appropriate.

8.2.8 In routine practice, interpretation of GC/MS-EI and LC/MS full scan mass spectra is carried out by the instrument's software as a semi-automated search against a commercial or user-compiled library using appropriate reference material (certified where possible). The quality of the match or “fit” may be aided by the factor that is generated, either as a ratio or percentage, where 1.0 or 100% are “perfect” matches. However, such “match factors” must be used as guides only and are not sufficiently reliable to be used as the final determinant of identification. Final review of a “library match” must be carried out by a toxicologist with considerable experience in interpreting mass spectra; experience and critical judgement are essential.

Interpretation, at a minimum, should be based on the following principles:

- For a match to be considered “positive”, all of the major and diagnostic ions present in the known (reference) spectrum must be present in the “unknown”. Occasionally, ions that are in the reference spectra may be missing from the “unknown” due to the low overall abundance of the mass spectrum.
- If additional major ions are present in the “unknown” it is good practice to try to determine if the “extra” ions are from a co-eluting substance or “background” such as column bleed or diffusion pump oil (GC/MS).
- Examination of reconstructed ion chromatograms of the suspected co-eluting substance relative to major ions from the reference spectrum will help to determine this.
- If there is any doubt in identification, reference material should be analysed using the same analytical conditions to compare retention time and mass spectral features.

GC/MS chemical ionisation and LC/MS mass spectra are often simpler than GC/MS EI spectra and therefore afford fewer options for the choice of qualifier ions. However, it is often possible to adjust the ionisation energy (e.g. cone or fragmentor voltage with a single quadrupole LC/MS) in order to produce additional or stronger secondary ions. Running the sample under conditions of both low voltage (to maximise the quantification ion signal) and higher ionisation voltage (to promote fragmentation and facilitate confirmation of identity) is an option. Monitoring of a single ion in single stage MS is not considered acceptable, especially for positive identification, in a forensic setting.

When using accurate (high resolution) mass-spectrometry, it is important to consider compounds with the same molecular mass (isobaric) including those with the same empirical formula. This is especially important for positional isomers of new psychoactive substances (e.g. 4-methylmethcathinone and 3-methylmethcathinone) and will result in the same accurate mass regardless of instrument resolution. Consequently, it is necessary to obtain fragmentation mass spectral data (e.g. through collision induced dissociation) for confirmation and/or utilise any differences in retention time.

The level of accuracy required for unique determination of elemental composition will vary depending on the molecular mass (Da) of the compound, but invariably a mass accuracy of  $< 5$  ppm will be appropriate.

The use of isotope (e.g. chloride) or adduct ions (e.g. ammonium) as qualifier ions for identification may be appropriate for certain analytes, when there is limited other mass spectral information and robustness of such ions has been assessed.

In practice, the extent and nature of methods used to “confirm” the presence of a particular analyte will depend in part on the type of case and nature of the analyte. Wherever possible the guidelines outlined above will be observed but it is recognised that there will be situations where the use of a second technique is impractical.

## 8.3. Method calibration and validation

The principal elements of validation are

- Specificity
- Range
- Linearity
- Precision
- Accuracy
- Recovery
- Stability
- Method Uncertainty

The following section is intended to give a broad overview of some of the elements of validation. Detailed guidelines on this topic are already in circulation and the following should be considered alongside these; [4];165(2–3):216–24, the Scientific Working Group for Forensic

Toxicology Validation guidelines [12] and the UK Forensic Regulator Codes of Conduct [7].

In forensic toxicology it is generally accepted that, due to the wide range of analytes and the infrequency with which some are encountered, it may not be viable to conduct a full validation for each method offered by a laboratory. For such methods the ‘fitness for purpose’ should be demonstrated and consideration of validation should be made at such time that the method becomes routine procedure but there should be the same level of confidence in the results obtained.

When conducting casework analyses, laboratories may group specimens into batches. Each batch should contain a sufficient number of calibrators, blanks (with and without internal standards where appropriate) and controls, the total number of which will depend on the size of the batch and the nature of the tests.

For quantitative casework analysis in particular, replicate analysis (e.g. duplicate) should be performed to identify or reduce any errors in mis-sampling. Replication is analysis (including extraction and/or sample preparation) of at least two fresh aliquots of the same sample performed at the same time. The % concentration difference between the two findings should be < 20% to demonstrate accuracy and confidence in the measured result. The calculated mean value of the results should be reported.

When casework analyses are being carried out, wherever possible matrix matched calibrators and quality controls should be used. The use of unextracted calibrators (non-matrix matched) using deuterated standards may be appropriate provided the validity of the approach has been established.

The laboratory may determine the limit of detection (LOD) by determining the mean concentration or response value ( $m$ ) for the blank ( $X$ ) and adding three standard deviations to this value ( $LOD = X_m + 3SD$ ). However, it should be noted that for other assays (e.g. GC, HPLC) the true LOD may be higher than indicated by this formula if significant adsorption or other losses occur. For example, in chromatographic assays, the LOD might be the lowest blood concentration of a drug needed to give a peak height three times the noise level of the background signal from a blank blood sample. Alternatively, for infrequently carried out assays where the analyte measured is always within the calibration range of the assay and well above the LOD, it may be sufficient to indicate that the detection limit is “less than” a certain value. Thus the true LOD may be derived experimentally, but should not be less than the blank plus three standard deviations. The lower limit of quantification (LLOQ) may be derived by adding ten standard deviations (+10SD) to the true value of the blank ( $X_m$ ). However, it is preferable to determine the LOQ experimentally as the lowest concentration for which an acceptable coefficient of variation can be routinely achieved.

For chromatographic assays, the LOD and LLOQ may be defined in terms of the concentration of the lowest calibrator, and therefore may not need to be determined experimentally. However, if results are reported below the value of the lowest calibrator, LOD and LLOQ should be determined. The upper limit of quantification (ULOQ) is usually considered to be the highest calibrator.

The use of a suitable internal standard for all chromatographic assays (e.g. GC, HPLC, GC/MS, LC/MS) is recommended. The internal standard should have chemical and physical properties as similar to the analyte as possible and should be unlikely to be present in the sample population. If a common drug is used as an internal standard, its absence in the sample should be demonstrated by way of an internal standard blank. If the analyte is to be derivatised, an internal standard should be chosen which will form an analogous derivative. Stable isotope (e.g. deuterated) standards are recommended for GC/MS and LC/MS assays, although appropriate non-deuterated internal standards may occasionally give equivalent or better performance. In LC/MS, however, the use of isotopically-labelled internal standards is the most effective way to potentially compensate for ion suppression. The internal standard should be added to the sample at the earliest possible stage in the

method, and in any event before buffering and extraction of the sample. Markers that are added after the initial extraction are regarded as “external standards” and are not acceptable for quantitative analysis.

Linearity of the procedure should be established by typically using at least four calibrators though more are usually run in the assay to permit the removal of outliers. The concentration of the calibrators should be such that they bracket the anticipated concentration of the casework specimen(s). If the concentration of the specimen exceeds the concentration of the highest calibrator (ULOQ), the specimen should be diluted and re-extracted if accurate quantification is required. Otherwise the specimen should be reported as having a concentration greater than the highest calibrator. If the concentration of the specimen should be less than that of the lowest calibrator but greater than the LOD, then the specimen can be reported as containing the analyte at less than the lowest calibrator (LOQ value stated). Use of the term “trace” should be avoided in quantitative analyses. It is acknowledged that some assays are inherently non-linear and that the use of quadratic or other mathematical models may be necessary.

Criteria for acceptance of a chromatographic calibration should be stated in the method procedure. For a multi-point calibration this factor is usually the correlation coefficient. For most applications, an acceptable correlation coefficient is 0.99. However, there may be circumstances where a correlation coefficient of 0.98 is minimally acceptable provided that multi-level quality controls meet the stated criteria. In addition, it is good practice to evaluate the range of the calibration by calculating the value of each calibrator against the curve. Values of  $\pm 20\%$  are generally acceptable for most applications, although  $\pm 10\%$  values are preferred for analytes such as ethanol. Single-point calibrations are discouraged unless quality controls are used at or close to the upper and lower quantitative (LLOQ and ULOQ) reporting limits.

For specimens having concentrations significantly higher than the highest calibrator, the laboratory should exercise precautions so that carry-over of analyte into the next specimen does not occur (8.5.2). Similarly, specimens with very low concentrations should be checked to ensure that carry-over from a previous very high positive has not occurred.

It is recognised that for a variety of reasons occasional analytical results will be outliers; that is, analytical values which deviate significantly and spuriously from the true value. “Outlier” results of quality controls, blanks or calibrators should be obvious. However outlier results of case specimens may not be identified if only run singly, unless that result can be compared with one from a separate analytical determination. For this reason replicate extraction and quantitative analysis, at least in duplicate, is recommended (8.3.5). The laboratory should determine the acceptable criteria for replicate analysis. A maximum deviation of  $\pm 20\%$  of the mean is recommended, or  $\pm 30\%$  if the result is close to the LOQ of the assay.

Retention time should be part of the acceptance criteria for chromatographic assays. For GC based assays, deviations of 1–2% from the calibrators or controls may be acceptable. Slightly larger deviations (5%) may be acceptable for HPLC based assays, particularly where the mobile phase is a gradient system.

#### 8.4. Method of standard additions

It is recognised that the matrix of some forensic specimens may be “unique” in some way (e.g. putrefied or embalmed) such that it is difficult or impossible to obtain a similar matrix for the preparation of reliable calibrators and controls. In these circumstances, the use of a “standard addition” procedure may be preferable to a conventionally calibrated assay. In the method of “standard addition” known amounts of analytes are added to specimen aliquots and quantification carried out by comparing the proportional response of the fortified aliquots with that of the unknown specimen. Use of an internal standard and a multiple point calibration is critical to check for potential interferences from unique biological samples.

## 8.5. Contamination

Contamination is a quality concern in all forensic disciplines, however opportunities for this to occur are less so in toxicology. Nevertheless, in forensic toxicology contamination can be avoided by (for example) not using the same sample tip to pipette multiple samples, all biological samples must be in individual labelled containers, examined upon receipt and subsequently for any evidence of contamination and appropriately stored, sterilise or replace all disposable equipment (gloves, scissors, scalpel blades, glassware) that come into contact with biological samples and appropriate cleaning of equipment and surfaces. Witnessing or recording of sample handling and checks may also be of benefit.

It is recommended to segregate the handling and analysis of biological specimens from other exhibits, especially drug material (bulk drug or otherwise), as such material may contaminate biological fluid or other biological specimens (e.g. hair).

The possibility and extent of any carry-over within an analytical system (qualitative and quantitative assays) should be assessed. This can be achieved by analysing a blank (with and without internal standard) after the highest calibrator or high concentration control. It is also good practice for such blanks to be analysed within sample batches and between specimens, especially if analysing matrices of potentially high drug concentration (e.g. liver).

## 9. Quality assurance and quality control

### 9.1. Quality assurance

Quality assurance encompasses all aspects of the analytical process, from specimen collection and receipt through analysis, data review and reporting of results. It includes, but should not be limited to, quality control of each analysis and proficiency testing of the laboratory.

Quality assurance assumes a unique role in the forensic science disciplines because results are subject to challenge in the adversarial justice system. One purpose of a quality assurance program is to detect and prevent error, whether random or systematic, and to initiate appropriate remedial action.

Standards used should be appropriate for the test being carried out, and documentation should be maintained describing their sources and dates of acquisition. Reference material should be stored so as to ensure its stability and integrity. If a standard is prepared in the laboratory, the source(s) of the chemical reagent(s), the method of preparation, and verification of the final product should be recorded and maintained on file.

Where practical, the identity and purity of reference materials should be verified by the laboratory.

Labelling should be uniform for all standards and reagents. Date of acquisition or preparation, and the initials of the preparer, should be included on the label. The expiry date should always appear on the label of liquid reagents as well as any relevant storage conditions. An expiry or re-test date furnished by a vendor/manufacturer determines the useful lifetime of the standard/control unless it can be verified beyond that date.

Initially, a sufficient number of calibrators should be run to determine the characteristics of the calibration curve; a blank and at least four calibration points are recommended for the initial calibration process. The stability of the calibration curve should be tested under laboratory conditions by the addition of controls, both positive and negative.

Controls are not analysed for calibration purposes. As a general rule an adequate set of controls should include, at a minimum, a specimen that does not contain the analyte (defined as a negative/blank control) and a specimen containing the analyte at a concentration that realistically monitors the performance of the assay. Additional controls can be used to test the linearity of the calibration over the desired range.

SOPs should specify corrective action to be taken when control results are outside acceptable limits. Under optimal conditions a laboratory should have a quality control supervisor, but having a staff member dedicated to quality control may be impractical for small laboratories and in such situations these duties may come within the responsibilities of a technical manager or appropriate member of staff.

Forensic toxicology laboratories should participate in an external proficiency testing program which includes appropriate analytes analysed by the laboratory in at least one type of specimen, representative of that typically analysed (e.g. whole blood or serum for a post-mortem toxicology laboratory). The program should realistically monitor the laboratory's analytical capability (qualitative and quantitative). When reviewing proficiency testing scheme results from suppliers, consideration should be given to the novelty of the analysis and number of participants.

A suitably qualified person should review regularly results of quality control and proficiency testing. Signing and dating the record constitutes appropriate evidence of review. It is important that bench personnel be informed of quality control and proficiency test results and their training records be updated as part of their on-going competency. Attention should be given to procedures for monitoring potential sources of error. Proficiency test materials should be retained until the summary report is received and any corrective action satisfactorily completed.

In the event of proficiency test errors during monitoring of performance a thorough investigation into the source must be instigated resulting in appropriate and timely corrective actions. In this instance the Head of Toxicology Service or suitably qualified person should decide whether the analytical procedures need revising. All corrective actions should be documented.

It is necessary to monitor the performance of assays by calculating the coefficient of variation (e.g. % C.V. of controls). For chromatography, coefficients of variation > 20% require action, although action may be required at lower %CV depending on the specific analysis. Quality control charts should also be used to assess variation in an assay.

Routine maintenance of equipment is an important part of any quality assurance program. It is good practice to document all routine and non-routine maintenance, including tasks such as changing septa and liners on GCs. Documentation may be in a logbook (electronic or otherwise) and if printed can be kept by larger equipment, or as check-sheets filed in a ring binder. Multiple items of similar equipment (e.g. pipettes) should be labelled in order to differentiate them readily.

### 9.2. Quality control

#### 9.2.1. Control materials

In the true sense, a control is a test sample, identical to the unknown, but containing the analyte at a known concentration. Controls can be positive and negative in nature. With each batch of specimens, whether a single specimen or multiple ones, controls would be carried through the procedure in parallel with the unknowns. Casework specimens should be bracketed in the analytical run by passing QCs for results to be accepted. In qualitative assays, acceptable results for positive and negative controls, may simply be positive or negative, respectively. For quantitative assays, negative controls should give results that indicate the analyte is absent, or below the LOD for the assay. An acceptable positive control result of  $\pm 20\%$  is recommended for most drugs, except for controls that are at or close to the LLOQ of the assay, when  $\pm 30\%$  may be more realistic. The control must give a result within a predetermined deviation from its mean value, or the test is deemed "out of control" and therefore, the result generated from the unknown specimen is unacceptable.

It is a common and accepted practice in clinical laboratory work to obtain or prepare material and then establish the target range by replicate analysis of the control in parallel with existing QC material. For

example, control material may be prepared by pooling specimens from multiple cases (subject to adherence to HTA regulations and consent, as appropriate). While that approach is still accepted in forensic toxicology, it is scientifically less desirable than preparing or purchasing control material with a specific weighed-in target concentration, which will allow independent verification of calibration accuracy. If control target ranges are experimentally determined, it is important for that range to be verified against control material, prepared commercially or independently in-house, prior to it being put into routine use.

For some forensic toxicology procedures, providing a true control is no more difficult than any other test. For others, however, in which the matrix may be unique (e.g. decomposed tissues, bone, hair or nails), providing a control is not only difficult, but can never approach the ideal of being identical to the unknown specimen. Controls should be prepared from standard material from a different source or lot/batch number than that used in calibration of the assay. Where this is not practical, the control should at least be prepared using a different weighing or dilution than that used to prepare the calibrators. Control material prepared from the same solution used to prepare the calibrators is unacceptable, since any errors made in preparation of the standard solution will not be detected.

### 9.2.2. Open controls

Open controls are declared and expected results that are known to the analyst. They can be purchased from commercial vendors, prepared in the laboratory, distributed by professional organisations or saved and pooled from former cases (subject to HTA regulations). Regardless of the source, the concentration of the analyte in the control must be validated. For tissue specimens or other unusual matrices, more innovative approaches may be necessary. Fortifying drug-free matrices, such as tissue homogenates, out-dated blood bank blood or plasma to simulate the unknown specimen is acceptable. A “blank” or negative control may, of course, be the unfortified matrix.

Results from quantitative quality control material should be recorded in a manner that readily permits the detection of trends such as the deterioration of reagents, calibrators or controls. For frequently run controls, results may be plotted in a graphical manner such as a Levy-Jennings plot. For less frequently run material, tabulation is acceptable. Determination of the coefficient of variation for the controls may give useful information about the precision of the assay, and may indicate which assays need further development.

### 9.2.3. Blind controls

As the name implies, these are identical to open controls except their identity is unknown to the analyst. It is generally recognised that this is the ideal way to maintain quality control. A blind control should test the entire laboratory process including receiving, accessioning, analysis and reporting. This can be accomplished by setting up a “dummy account” or by co-operation with the submitting agency. Such blind controls are sometimes called “double blinds”. A more practical approach is to have the accessioning section insert blind controls into each batch of specimens. However, either of these processes can be difficult to accomplish in a small laboratory; they are both costly and time consuming.

## 9.3. Reference materials

The National Institute of Standards and Technology (NIST; [9]), refers to these as Standard Reference Material (SRM). For example, a specific RM may have a melting point of such sharpness and reproducibility that it can be offered as an RM for the calibration of a thermometer in a melting point apparatus. However, it may not be appropriate for preparing a calibration curve. A certified reference material (CRM), or SRM, suitable for the preparation of a standard to which calibration material can be compared, must be certified by a method generally recognised by the scientific community as one that validates

the CRM for this purpose. The nature of the procedure depends, of course, on the properties of the analyte.

It is important to remember that most RMs are not 100% pure. The label or package insert should indicate the purity or the nature of the contaminants or the degree of water of hydration. Further instructions may provide guidance as to how the RM is to be used. For example, perhaps it must be protected from light, or stored at a low temperature or protected from moisture. These instructions must be carefully followed in order to use the RM according to its specifications.

Many toxicants, including drugs, may have limited shelf-lives. Degradation due to photo-reactions, oxidation in the air or by other means, requires periodic assessment of these changes. Methods for detecting such changes are varied but even RMs may not retain their original purity. RMs supplied in solution may have more limited stability than those supplied as pure, dry, solids.

The importance of acquiring pure chemicals used as standards and periodically monitoring their purity, requires the development and implementation of procedures that are part of the laboratory SOPs. The steps that can be used are summarised as follows:

- (1) maintain instruments and all measuring devices at optimal performance with regular calibration checks.
- (2) acquire chemicals to be used as standards from reliable sources who validate the stated purity, preferably by a certifiable trace to a CRM or SRM, or.
- (3) acquire chemicals as RM, carefully following any instructions accompanying the RM for maintaining anhydrous conditions or to avoid deterioration, or.
- (4) acquire chemicals from other sources but always assess the purity of the material by appropriate measurement of physical constants and/or instrumental methods.
- (5) regardless of the source of the chemical for preparation of the standard, devise a means by which the standard can be monitored periodically in order to detect any deviation from its original purity and stability (re-test through in-house experimentation or updated certificate of analysis following re-test by supplier) to avoid using expired standards.
- (6) before using a newly prepared standard, compare its properties with a previously validated standard or with a CRM or SRM.

## 10. Review of data

For each case, before results are reported, all analytical data should be reviewed by scientific personnel who are experienced with the analytical protocols used in the laboratory. At a minimum this review should include

- sample identity
- validity of analytical data and calculations
- quality control data
- data transcription/transfer

These checks may be undertaken by different people and at different stages.

Where possible, the results should be reviewed in the context of the case history, post-mortem findings and any relevant clinical data. The review should be documented within the case record.

Discussion at this stage may suggest that further work or assay repeat is necessary, this should be undertaken as appropriate.

Before the report is submitted the case file should be checked by one or more suitably trained and competent person(s).



## 11. Reporting of results

### 11.1. General recommendations

The report should be in a suitable format for the particular case type. Thus, while it is neither possible nor desirable to suggest a uniform format for reports, they should include all information necessary to identify the case and its source, and should bear test results and the signature of the individual(s) responsible for its contents.

The following recommendations are made:

- (1) name and/or identification number.
- (2) laboratory identification number.
- (3) name of submitting agency and/or individual.
- (4) date submitted.
- (5) date of specimen collection.
- (6) details transcribed from any ante-mortem sample(s).
- (7) date of report.
- (8) specimens tested.
- (9) test results.
- (10) signature of approving individual.
- (11) a phrase such as ‘Unless the laboratory is informed otherwise in writing, samples will be disposed of according to the Human Tissue Act’.

Results are confidential, every precaution should be exercised to ensure that a properly authorised person receives the information when it is transmitted by telephone, secure e-mail, fax, or any other method different from conventional delivery of a written report. If results are communicated by telephone it should be by a suitably trained/competent person. All communication should be documented.

If the results are unverified this should be made clear.

Each laboratory should formulate its own policy for retention or release of information and for response to requests for its documentation. This includes the report format and mode of transmission which should be agreed with the client with the option that these be varied for specific cases on request.

### 11.2. Terminology in reports

“Positive” indicates that a particular substance has been identified in accordance with the laboratory protocols. “Negative”, “Not Detected”, or “None Detected” has been generally used to indicate the analyte or analytes were not found. “None Detected” is preferable. This indicates that particular substances were absent within the limitations of the test(s) carried out.

Tests may be described in a number of ways, as individual chemical entities, groups or classes of substances or combinations of drugs or substances.

There may be both qualitative and quantitative results on a report. Qualitative results should be indicated by naming the test followed by positive or none detected. The term “trace” or a non-specific numerical designation (e.g. positive but < 0.5 mg/L) may be used, for qualitative purposes only, if a substance was detected in a sample, but the concentration was less than the lowest point on a calibration curve or a designated cut-off.

Quantitative results should be identified using appropriate drug nomenclature and units. No quantitative value should be reported from a non-specific immunological or other initial testing procedure, unless the procedure has been appropriately validated through parallel studies with a reference quantitative method.

Preferred units include mg/L or µg/L (ng/mL) for fluids and mg/kg for tissues. Ethanol should be reported as mg% or mg per 100 mL (mg/dL). Other appropriate units may be used for clinical tests.

### 11.3. Preliminary report/statement

Although generally discouraged, issuing a preliminary report/statement may be required before toxicology testing is complete (e.g. for urgent cases). If that is done, only confirmed results should be released, or a clear disclosure included that the results are unconfirmed and subject to verification. The report should also include a statement that testing is incomplete, and where appropriate, that subsequent results may affect the final report and its interpretation.

### 11.4. Revised or supplemental report

After the final report/statement has been issued, it may be necessary to carry out additional tests, in which case a further report/statement must be issued to be read in conjunction with the original report. Such a report should contain the same identifying information as the original and be identified as an additional (supplementary) report.

### 11.5. Corrected reports/statements

After the final report/statement has been issued it may become necessary to correct an error, typographical or otherwise, in this instance a further report/statement must be issued containing the same identifying information as the original report(s) and be identified as replacing the original report.

### 11.6. Release of reports/statements

There should be an SOP detailing the procedure for sending a report to the submitting agency.

### 11.7. Referred tests (sub-contracting)

When samples are forwarded to another laboratory for analysis, there should be a record on the final report/statement indicating this fact. Results of referred tests may be incorporated into the originating laboratory's final report/statement, but the name of the laboratory that actually carried out the test should be stated. If appropriate the referred results may be forwarded directly, but this should be documented in the originator's report/statement.

### 11.8. Retention of records

Retention of records should be dictated by any relevant guidelines. For example, ACPO guidelines for criminal work, and Coronial and Procurator Fiscal rules as appropriate. ACPO guidelines suggest 7 years for “other” types of cases (including coroner's work). Records should include a copy of the report, request and custody forms, work sheets, laboratory data, quality control and proficiency testing records.

Laboratories are strongly encouraged to archive electronic data files for a similar period as the paper records, by backup to suitable media or off-site backup/storage. This is particularly important for full scan MS screening data, where because of the nature of the data it is impractical to keep a complete paper copy. Where possible any software that is required for accessing data should be stored to make sure it is accessible.

There may be regulations governing the time period over which records must be retained. The Head of Toxicology Services is advised to check with the appropriate agencies in their jurisdictions for information.

### 11.9. Disclosure

The full casefile must be made available to the defence, prosecution and Courts as well as the Criminal Case Review Commission if requested.

## 12. Interpretation of toxicology results

### 12.1. General considerations

Specific comments on the effects of drugs on particular individuals should not be made and effects can only be given in general terms.

A forensic interpretation should only be considered if adequate background information is available to enable a holistic approach, for example circumstances of death or incident, appropriate medical/drug history, where appropriate PM report.

Interpretation should only be undertaken by suitable trained/experienced individuals who must not go out of their area of expertise.

The length and extent of interpretation will always be variable depending on the client requirements. One sentence overviews may be misleading as there is always some additional information or alternative hypothesis that should be mentioned (e.g. acute versus chronic use, post-mortem redistribution, relation of concentrations detected with prescription history and/or dose regime etc).

Where interpretation is not possible due to the above, the reason(s) for this should be stated.

### 12.2. Interpretive strategy

A case strategy should have been followed and customer requirements considered. A record of discussions and agreement with the customer should be documented.

Consideration should be given to prescription, drug and medical history of the individual tested in addition to scene evidence, suspicions, or other drugs to which they are known to have had access to. In some cases it may be necessary to request this information from the customer (instructing authority). Information regarding specific situations and circumstances (e.g. recently released from prison) can also be relevant.

Where possible, opinions and interpretation should address the question(s) arising from the circumstances of the case.

### 12.3. Interpretive considerations

#### 12.3.1. Specimens

- Sample type (e.g. blood, urine, vitreous humour, stomach contents)
- Anatomical site of collection
- Sample condition
- Sample integrity
- Pre-submission storage conditions or issues (if known)
- Volume of sample (for police casework)
- Container type and preservative used (please refer to section 6 above)
- Timing (date and time of collection in relation to incident)

#### 12.3.2. Analysis

- Analyses have been carried out in accordance with Lab Guidelines (please refer to sections 8 & 9 above)
- The methods used have been demonstrated to be appropriate for the sample type (e.g. method for the analysis of ante-mortem serum may not be appropriate for post-mortem whole blood)

#### 12.3.3. Post-mortem and sample changes

- Post-mortem redistribution
  - Concentrations will vary between anatomical sites
  - Detailed interpretation should not be made on non-femoral blood
  - Direct (e.g. stomach) and indirect (bladder diffusion) contamination is a possibility
- Post-mortem production and loss of substances

- Analyte stability
  - Breakdown of drugs and metabolites – including during the analytical process
  - In-vitro ethanol production/loss

#### 12.3.4. Pharmacokinetics (PMK) and pharmacodynamics (PMD)

- In life PMK parameters do not apply to the post-mortem situation.
- Half-lives and elimination rates
  - these should be considered in relation to the time of the incident
  - published ranges should be referred to
  - may be affected by organ failure/diseased state
- Metabolic profile
  - parent drug:metabolite
  - pharmacogenetics
  - acute and chronic use
  - consider the metabolic pathway
- Drug interactions (possible physiological and metabolic effects)
- Volume of Distribution (Dose calculations)
  - PMK calculations should not be carried out on post-mortem results/data
- Tolerance
- Age
- Gender

#### 12.3.5. Other considerations

- Post-mortem findings (e.g. liver necrosis from paracetamol toxicity)
- Route of administration/ingestion
- Alternative source of positive findings (e.g. endogenous production, drug adulterants and impurities, natural sources, metabolic source)
- References (where appropriate use original articles and state references used, including in-house reference data)

### 12.4. Alternative explanations

Standard statement – should the information supplied change or more information become available, the interpretation may need to be reassessed.

All possible scenarios should be considered.

### 12.5. Peer case review

All aspects of the case (including critical findings) must be reviewed by a forensic toxicologist of appropriate experience before the report is issued.

## 13. Safety

The laboratory must comply with appropriate legislation and adhere to specific regulations for your organisation. Of particular consideration is if the laboratory has cause to handle and/or receive any unidentified substances that may pose an unknown safety risk. Consideration should be given to the potential for harm through direct or indirect exposure that may occur e.g. anthrax or highly potent substances such as fentanyl and its analogues. An appropriate risk assessment should be undertaken and/or procedures put in place to remove or minimise such risk to the individual, the laboratory staff, wider population and the environment. If necessary, specialist advice and assistance should be sought.

### Appendix 1. Organisations contributing to the UKIAFT Forensic Toxicology Laboratory Guidelines 2018

Aberdeen Royal Infirmary  
Alere Forensics (formerly ROAR Forensics)

Analytical Services International (ASI) Ltd  
Cellmark Forensic Services  
Forensic Medicine and Science, University of Glasgow  
Forensic Regulator's Office  
Forensic Science Northern Ireland  
Hampshire Scientific Services  
Imperial College London  
Leicester Royal Infirmary  
LGC Forensics  
Medical Bureau of Road Safety  
Official Analyst's Laboratory, Jersey  
Randox Testing Services  
SPSA Forensic Services (Edinburgh)  
State Laboratory, Ireland  
The Drug Treatment Centre Board, Dublin  
University of Huddersfield  
Independent consultants

## References

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