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European guidelines for workplace drug testing in urine

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(Article begins on next page)



**EUROPEAN GUIDELINES FOR WORKPLACE DRUG TESTING
IN URINE**

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Abstract:	These European Guidelines for Workplace Drug Testing in Urine have been prepared and updated by the European Workplace Drug Testing Society (EWDTs). The first version of these urine guidelines was published in 2002. During these years the guidelines have been followed by many laboratories in different European countries and their role has been essential particularly in countries lacking legislation for workplace drug testing. In 2014 EWDTs started a guidelines updating project and published new version of the urine guidelines in 2015. Here we represent this new updated version of the urine guidelines. The European Guidelines are designed to establish best practice procedures whilst allowing individual countries to operate within the requirements of national customs and legislation. The EWDTs recommends that all European laboratories that undertake legally defensible workplace drug testing should use these guidelines as a template for accreditation.

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INTRODUCTION

The European drug situation has been in constant change during last years. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has published current information about drug situation in Europe in European Drug Report 2015 [1]. The availability of new psychoactive substances has increased on drug market. These drugs mimic the effects of established controlled drugs and include substances that are not controlled under drug laws. EU countries have been forced to find ways to quickly adapt or update their legislation in front of this situation. The majority of these new psychoactive substances are synthetic cathinones and synthetic cannabinoids. Also established drugs have been increased according to the seizures. The most commonly used drug in Europe is cannabis, followed by cocaine, amphetamines and MDMA. [1] [2]. According to EU Drug strategy 2013-2020, there is also an increasing trend towards poly substance use like combination of alcohol, prescribed controlled medication and illicit drugs. [3]

It is estimated that over 80 million adults in the European Union have tried illicit drugs at some point in their lives [1]. Drugs are involved in all areas of life, also in workplaces where they cause a serious problem for a significant proportion of the working population. Drug use ranges from single experimental use to habitual and dependent use. [4] European Agency for Safety and Health at Work has published a report of performance enhancing drugs, which are used by workers and students under the increasing pressure of demands and efficiency at workplaces and during studies [5].

The main reasons for testing employers according to the employees are to avoid health problems and reduced performance of employees, increased sick leaves and work accidents, possible damage to equipment and products and risk for company reputation [4]. Nowadays also data security of a company is a high priority.

However, there are still European countries where workplace drug testing is not allowed. Also legislation for drug testing is still lacking in many countries. Testing becomes topical and rises to headlines especially after bigger accidents. The tragedy of German Wings contributed European aviation safety agency (EASA) to publish rapidly an action plan for the implementation of the Germanwings Task Force recommendations, which included also drug and alcohol testing program [6].

There are mainly three different types of testing at workplaces. In pre-employment testing an employer is tested for drugs before starting working or signing a contract of employment. In random testing any employer may be forced to be tested anytime and it is

not informed beforehand. In principle, in pre-employment testing and in random testing the employer is not suspected for using drugs. Third kind of situation for drug testing is when an employer is suspected of being under the influence of drugs at the workplace. During a possible rehabilitation program follow up testing is usual. The practices and legislation dealing with all these kind of testing types differ a lot between different countries in Europe. In addition, all types of testing are not allowed in all countries. For different types of testing also different sample matrixes are appropriate, which are mainly urine, oral fluid, hair and blood. Most of the European countries are still lacking legislation for workplace drug testing. There has been a strong demand for a common guideline to unify e.g. the practices of sample taking, test analyses, quality and interpretation of the results. The first guideline of European workplace drug testing society (EWDTS) was published in 2002 for urine. In 2014 EWDTS started a guideline updating project, which was completed in autumn 2015.

Main changes in the new version of the guideline comparing to the former version were:

- New index and structure, which is now similar to the EWDTS guidelines for oral fluid [7] and hair [8]
- In accreditation requirements also the standard EN ISO 15189 in addition to EN ISO/IEC 17025 is accepted. However, method validation should be performed according to the requirements of EN ISO/IEC 17025.
- The guideline is relevant to laboratory based testing only. It is recommended that point of collection testing (POCT) devices used should come with national or international approvals.
- Urine collection procedure is described more in detail.
- Descriptions of key functions and degrees of laboratory personnel is shortened, while it is covered by accreditation. Specimen collectors do not have to be health care professionals.
- Requirements for identification of analytes and confirmation of results more in detail.
- New substances were added to the list of recommended substances to be tested taking into account current drug situation in Europe. It was not reasonable to give a certain minimum list of substances to be tested because of different drug situation in different countries. Laboratories should be aware of current drug situation in their country and advise the customers to choose an appropriate drug panel.

- ~~• Cut-off values for established drugs remained mainly the same. However, they are recommended maximum cut-off values and laboratories can also use lower ones. Cut-off values for new added substances are still under discussion.~~

~~One of the aims of EWDTS is to ensure that workplace drug testing in Europe is performed to a defined quality standard and in a legally secured way. The European Guidelines are designed to establish best practice procedures whilst allowing individual countries to operate within the requirements of national customs and legislation. In addition to these guidelines for urine, EWDTS has published also updated versions for oral fluid and hair. The EWDTS recommends that all European laboratories that undertake legally defensible workplace drug testing should use these guidelines as a template for accreditation.~~

1 General

1.1 Introduction

These guidelines represent an overview of the best practice for European laboratories providing urine workplace drug testing services to maintain the legal defensibility of a drug test when tested by either an employment tribunal or a court of law. They are designed to ensure that the entire drug testing process is conducted to give accurate and reliable information about a donor's drug use.

1.2 Objectives

- To provide a common framework for European providers of urine workplace drug testing services.
- To promote standards by providing guidelines which are accepted at a European level.
- To ensure that the processes undertaken are capable of legal scrutiny.
- To provide safeguards to protect the dignity of the specimen donors and the validity of the specimen.
- To define common quality assurance and quality control criteria for laboratories that are capable of being accredited by an external body.
- To ensure that the entire drug testing process is conducted to give accurate and reliable information about drug use of the donor.

1.3 Scope

These guidelines consider the three key stages of the workplace drug testing process.

- Specimen collection: Obtaining the urine specimen from the donor
- Laboratory analysis: Analysis of the sample for the presence of drugs
- Interpretation: Review and interpretation of the analytical results

1.4 Service Provision

Where a service provider is contracted to deliver all the stages, they must ensure that the minimum criteria in this document are met in all the key areas. In those instances where a customer may undertake some stages of the process within their own organisation (e.g. specimen collection or interpretation), the service provider has a 'duty of care' to ensure that the customer understands the full implications of the drug testing process.

The service provider does not have the authority to make decisions regarding the fitness for work of any individual being tested. It is recommended that any issues related to fitness for work be referred to the company's medical representative.

1.5 Drug testing in Context

It should be explained to any purchaser of a laboratory drug testing service that drug testing should form part of an overall drug policy, which the purchaser has agreed with his employees and should have in place before testing is initiated.

The service provider should have an effective company drugs policy in place. The policy may include drug testing of the staff involved in the analysis and reporting of workplace drug testing results.

1.6 Outline of drug testing process

Specimen collection

Urine specimens for legally defensible drug testing need to be collected under circumstances which respect the dignity of the individual whilst ensuring that the specimen is freshly voided.

~~Suitable records must be made when the specimen is collected to document that the specimen collected and the specimen received by the laboratory is one and the same.~~

~~This is the first link in the chain of custody process which, when reconstructed at a later date, can be used to document that the final result belongs to the specimen collected.~~

Analysis

When the specimen is received at the laboratory, checks on the integrity (e.g. colour, odour, etc.) of the sample are carried out. Providing the specimen passes the integrity checks a portion of the specimen is taken and screened for the presence of drugs and sample validity. If the screen results are all negative no further analysis is necessary.

However if the screen tests carried out indicate the possible presence of a drug (above a predefined cut-off level) a confirmation test to prove or disprove the presence of the drug or drug metabolite indicated by the screening test must be carried out on another portion of the specimen.

When a negative result is obtained, either after the screen or confirmation test, it can be reported to the customer. Positive results **may** require interpretation.

Interpretation

A laboratory positive result may be due to other reasons than intake of illicit drugs (i.e. prescribed or over-the-counter medication or dietary causes). It requires interpretation that is best carried out by the laboratory toxicologist in conjunction with a qualified medical practitioner who can consult both with the donor and the donor's medical practitioner.

Record keeping

Suitable records must be made during the analytical process to document that the specimen received by the laboratory and the specimen, about which the final report is written, are one and the same. All samples which prove positive for the presence of drugs and all records of the analytical process, must be kept for an agreed period of time or according to the national legislation to allow for any challenges to be made regarding the findings.

If the customer requires an independent toxicological review, the laboratory must make available, if requested, the analytical data upon which it based its final report.

2 Urine Collection

2.1 Introduction

This is the first link in the chain of custody process which, when reconstructed at a later date, can be used to document that the final result belongs to the specimen collected.

The collection process must be carried out by someone formally assessed as competent and authorised to carry out the collection. Standard Operating Procedures (SOPs) must be written for the collection process, the storage of collection devices, the training of Collecting Officers and the shipping of the collected specimen to the laboratory. These procedures must be followed precisely.

Collection procedures must cover the following aspects:

- Privacy and security of the specimen collection site
- Steps to ensure that the specimen collection is supervised.
- Steps to protect against tampering and adulteration
- Identification of the donor giving the specimen
- Evidence of the written informed consent of the individual to the analysis of the specimen (an example is given in Appendix B).
- Disclosure of recent medication, or evidence that the individual was advised of the significance of recent medication.
- All information is considered as confidential.

~~All specimens for legally defensible drug testing must be collected under circumstances that respect the dignity of the individual whilst ensuring that the sample is freshly voided and has not been tampered with in any way.~~ The collection site must be secure and the absence of potential interfering substances must be guaranteed. The validity of the sample has to be guaranteed.

~~Suitable records must be made when the specimen is collected to document that the specimen collected and the specimen received by the laboratory is one and the same.~~

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7 Where the customer takes responsibility for the collection process, the service provider
8 has a duty of care to ensure that these guidelines are understood.
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10 11 12 **2.2 Personnel**

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14 Specimens must be collected by suitably trained personnel (Collecting Officers). Although
15 no health care professional education is required, a documented training, which includes a
16 demonstration of competence, must be undertaken before collections are performed.
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18 The training must include, at a minimum, instructions on the following:
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- 20 • The collection process
- 21 • The storage and transport conditions of samples
- 22 • The chain-of custody process
- 23 • Troubleshooting (i.e. e.g. how to deal with issues like refusal of the test, insufficient
24 specimen, suspicion of tampering of the specimen)
- 25 • The responsibility of the collecting officer for maintaining donor privacy,
26 confidentiality of information, and specimen integrity.
- 27 • Ethical issues, especially regarding the declaration by the donor of the present use
28 of prescribed and over-the-counter medications.
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33 On successful completion of collector training a person may begin performing collections.
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37 **2.3 Urine Collection Kits**

38 The specimen collection kit should comprise the following components:
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- 40 • Chain of custody form.
- 41 • A unique identifier that links the chain of custody form and specimen bottles.
- 42 • Collection cup, demonstrably clean and unused.
- 43 • Temperature measurement device.
- 44 • At least two specimen bottles (A and B), demonstrably clean and unused.
- 45 • Tamper-evident seal for each bottle.
- 46 • Packaging components that satisfy current postal and courier regulations.
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53 **2.4 Chain of Custody Form**

54 The minimum information required on the Chain of Custody Form is:
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- Unique identification to link the form to the specimen bottles (typically a barcode label or code number assigned to the specimen).
- Information uniquely identifying the donor.
- Evidence that the donor identity has been confirmed.
- Evidence that the donor has given informed consent for the specimen to be tested.
- Date, time and place of collection.
- Names and signatures of all individuals who had custody of the specimen during the collection process.
- Any medication prescribed or non-prescribed that may have been taken in maximum two weeks prior to the specimen being collected.
- Copies for donor, ~~employer~~ MRO and laboratory.

2.5 Urine Collection Procedures

The guidelines give the current best practice for the collection of urine specimens for analysis. A detailed example of urine collection protocol is in appendix A.

The procedures must cover the following aspects:

- Identification of the individual giving the specimen.
- Sufficient information given to the donor about the meaning and content of the drug test to enable informed consent to be given to providing a sample for analysis.
- Privacy and security of the specimen collection site.
- Steps to ensure that the specimen is freshly voided.
- Steps to protect against tampering and adulteration.
- Splitting the specimen into two specimen bottles (A and B).
- Situations to discard a sample and collect a new one (see Appendix A).
- Evidence of the written informed consent of the individual to the analysis of the specimen (see Appendix B).
- Disclosure of recent medication, or evidence that the individual was advised of the significance of recent medication.

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3 Laboratory Organisation

A Quality Management System of the organization / laboratory is required via accreditation according to EN ISO/IEC 17025 and/or EN ISO 15189 in fields of forensic toxicology and/or workplace drug testing analysis.

All personnel must have contracts with the institution (Laboratory Organisation) which they work for and every person must have agreed to the “confidentiality policy” of the institution (in written form).

3.1 Personnel

All personnel should adhere to the requirements of EN ISO/IEC 17025 and/or EN ISO 15189 International Standards and as such, only staff who are suitably qualified and whose competence has been formally assessed can work within the laboratory. The laboratory must maintain accurate job descriptions for managerial, technical and key support personnel involved in the analytical tests.

The laboratory must keep records that establish the individual's qualifications / competency for all functions performed. The individual's file must include an up-to-date *curriculum vitae* listing educational qualifications and previous employment experience, training and competency assessment records for the current tasks performed. Personnel performing specific tasks shall be qualified on the basis of appropriate education, training, experience and/or demonstrated skills, as required.

All laboratory personnel must have received training in Health and Safety issues, the Control of Substances Hazardous to Health (COSHH) Regulations and other relevant legislation.

The key functions outlined below are identified as the minimum requirement for a laboratory to maintain EN ISO/IEC 17025 and/or EN ISO 15189 accreditation for the provision of workplace drug testing services and/or forensic toxicology. It is acceptable for individuals to have responsibility to carry out more than one role. By virtue of the laboratory's accreditation, it can be accepted that the appropriate qualifications for each role are in place.

NOTE: Role titles may vary between organisations, but the responsibilities will remain the same.

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3.2 Laboratory Security

Drug testing laboratories must have a robust security system to ensure that no unauthorised personnel gain access to the laboratory processes or to areas where samples or records are stored as mentioned in EN ISO/IEC 17025 and/or EN ISO 15189.

Unescorted access to these secured areas must be limited to authorised individuals. The laboratory must maintain a record that documents the entry and exit of all visitors to the secured laboratory areas.

The laboratory must maintain a record of all staff who are authorised to enter the secure laboratory areas. This list must be reviewed and updated on a regular basis.

Specimen bottles must be retained within the secure laboratory area until the disposal date.

3.3 Laboratory Head

There must be one person who has overall responsibility for the professional, organisational, educational, and administrative activities of the drug testing facility.

This person is responsible for the day-to-day management of the drug testing laboratory.

Some of the functions may be delegated to other appropriately qualified personnel but the overall responsibility for any delegated functions will remain with the designated Laboratory Head (typically the Laboratory Supervisor).

3.4 Authorising Scientist

A person responsible for the review and certification of pertinent data and quality control results, prior to release of accurate and reliable analytical results.

3.5 Laboratory Analyst

A person responsible for undertaking the day-to-day analytical procedures.

3.6 Toxicologist

A person responsible for interpreting a toxicological analytical result for the customer or the customer's designated Medical Review Officer.

3.7 Expert Witness

A person to present evidence to administrative or disciplinary proceedings that are based on analytical results reported by the laboratory.

3.8 Quality Manager

A person responsible for quality assurance within the laboratory organisation.

3.9 Other Personnel

Other technical or non-technical staff who must have the necessary training and skills for the tasks assigned.

4 Laboratory Analysis Procedures

4.1 Process

When specimens are received at the laboratory, initial checks on the specimen's chain of custody and appearance are carried out. If the specimen passes these checks a portion of the specimen in bottle "A" is taken and goes through initial screening tests for the presence of drugs. Further testing of sample validity may also take place at this point.

If the screening results are all negative (below a pre-defined cut-off level) no further analyses are necessary.

However, if the screening tests carried out indicate the possible presence of a drug (above a pre-defined cut-off level) a confirmation test to prove or disprove the presence of the drug or drug metabolite indicated by the screening test must be carried out on another portion of the specimen.

The screen-only presumptive positive test is not considered to be legally defensible, but may report preliminary presumptive positive results as local legislation allows. In the report it has to be mentioned that preliminary presumptive positive result may be false positive

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7 and requires confirmation.

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9 If the first analysis is performed by a confirmation-level analysis (mass spectrometry), the
10 positive findings have to be retested with another portion of the specimen.
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12 13 14 **4.2 Chain of Custody**

15 Laboratories must use chain of custody procedures to maintain control and accountability
16 of specimens and aliquots from receipt through completion of testing, reporting of results,
17 during storage, and continuing until final disposal of specimens and aliquots.
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19 Chain of custody records must be maintained on paper or in computerised form.
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22 23 24 **4.3 Specimen receipt**

25 The laboratory should receive at least two sealed specimen bottles and a corresponding
26 chain of custody form.
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28 At least one of these (referred to, in this document, as the “B” bottle) must be retained
29 unopened and stored in conditions that reflect the storage of the specimen under test
30 (referred to, in this document, as the “A” bottle).
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35 When a sample is received in the laboratory:
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- 37 • Incoming orders and specimens must be registered by the laboratory.
- 38 • Incoming specimens are immediately checked regarding completeness,
39 intactness and suitability for testing.
- 40 • Its packaging must be examined for evidence of tampering in transit.
- 41 • The information on the specimen bottles within the package must be compared
42 with the information on the accompanying chain of custody form.
- 43 • Any discrepancies must be noted and, where appropriate, reported immediately
44 to the customer. Some minor discrepancies may be tolerated in the
45 documentation without termination of the analysis. These must be agreed with
46 the customer prior to analysis and should be documented.
- 47 • Appendix C lists examples of fatal flaws in the chain of custody and is provided
48 for guidance. Flaws of this nature would normally result in the specimen not
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7 being tested.
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10 4.4 Sample processing

11 Separate representative portions (aliquots) of the specimen in bottle 'A' will be used for the
12 screening and confirmation tests. The sample preparation should follow the standard
13 operating procedure and the manufacturer's instructions for the collection system being
14 used. Aliquots must be taken in such a manner that excludes the possibility of
15 contamination.
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21 **Short term storage:** samples that are not currently undergoing analysis must be
22 refrigerated at 2-8°C. Stability has to be investigated and appropriate measures
23 undertaken to ensure the sample is valid for the analysis.
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26 The A and the B specimens must be stored under identical conditions.
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28 The quality control requirements in section 67 must be satisfied when conducting either
29 screening or confirmation tests, either on single samples or samples grouped in batches.
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32 4.5 Urine Validity Testing

33 The aim of validity testing is to demonstrate that the sample submitted for analysis is urine.
34 The validity of the sample must be checked either before or during the screening process.
35 Creatinine should always be analysed. The laboratory may also test for pH, nitrite, other
36 adulterants or use tests to check the adequate functioning of the antibody in the
37 immunoassay.
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42 *Determination of the creatinine concentration*

- 43 • If the creatinine concentration is less than or equal to 2.0 mmol/L (226 mg/l), the
44 specific gravity must be determined. Acceptable values for specific gravity are
45 1.001 – 1.020.
- 46 • Samples with creatinine results within the range 0.5-2.0 mmol/L (56 -226 mg/l) and
47 specific gravity results within range, should be reported as dilute. Because dilution
48 of urine may cause false negative results, a comment should be added to negative
49 drug testing results. Specimens which screen positive will be confirmed normally
50 and reported if confirmed positive (at or over the pre-defined cut-off value).
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- Specimens with creatinine results less than or equal to 0.5 mmol/L (56 mg/L) and/or specific gravity results out of range may be unsuitable for testing and should be reported as e.g. "specimen validity failed". Samples which screen positive will be confirmed normally and reported if confirmed positive (at or over the pre-defined cut-off value). Negative drug testing results should not be reported.

Measurement of pH

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- Results within the range 4-9 are deemed to be within a normal range. Results less than 4 or greater than 9 should be considered to be adulterated. Samples falling outside this range should be reported as e.g. "Specimen validity failed".
 - Specimens with pH values outside the normal range which screen positive will be confirmed normally and reported if confirmed positive (at or over the pre-defined cut-off value). Negative drug testing results should not be reported.

Nitrite test: if the nitrite concentration is determined

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- A nitrite level equal to or above 500 µg/mL is conclusive proof of an adulterated sample. The result should be reported as e.g. "Specimen validity failed".
 - Specimens with nitrite concentrations above this level which screen positive will be confirmed normally and reported if confirmed positive (at or over the pre-defined cut-off value). Negative drug testing results should not be reported.

Testing for other adulterants

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- If other tests indicate that the sample has been adulterated, or is otherwise unsuitable for analysis then it should be reported as e.g. "Specimen validity failed"
 - This remark is also reported when the specimen does not fall under the criteria of pH, creatinine or nitrite above, yet is still not suitable for testing. This can be due to an unidentified interferent or poor specimen quality such as turbidity.

5 Analytical Methods and Validation

5.1 Acceptable Screening Techniques

~~Following methods are accepted e.g.:~~ These methods only may be used:

- Immunoassays
- Gas Chromatography
- High Performance Liquid Chromatography
- All chromatographic techniques coupled to mass spectrometry.
- Capillary Zone Electrophoresis

5.2 Laboratory Screening Tests

The initial screening test ~~must shall be based on one acceptable use an appropriate~~ technique (see 5.1). The ~~assay test using the selected technique~~ must be validated prior to its use.

Recommended maximum screening cut-off concentrations for workplace drug testing are listed in Table 2. These recommended cut-off concentrations may be subject to change reflecting advances in technology and knowledge.

Cut-off concentrations for substances not indicated in Table 2 will need to be agreed with the customer taking into account the performance of the assays to be used and the pharmacokinetics of the drugs involved.

All screening test results must be reviewed with regard to the results of the validity tests performed.

Specimens that test negative on all the initial screening tests and pass the validity tests must be reported as negative and the specimens can be disposed of as agreed with the customer. Specimens that test negative on all the initial screening tests but fail the validity tests may be further investigated to determine the reason why.

The presumptive presence for any drug following the initial preliminary screen must have the presence of the drug or drug metabolite confirmed (refer to section 6.4 Confirmation Tests). If the first analysis is performed by a confirmation-level analysis (mass-spectrometry), the positive findings have to be confirmed and quantified by reanalysis with another portion of the specimen.

5.3 Standardisation of Laboratory Screening Assays

All assays must be calibrated against appropriate standards by following laboratory protocols based on the manufacturer's recommendations or validated alternatives.

The assay must be calibrated against one named compound, and the cross-reactivity to other related compounds must be determined.

The customer must be informed of the limitations of the tests.

5.4 Confirmation Tests

The presence of the drugs indicated by a positive screening result must be confirmed using a chromatographic technique in combination with mass spectrometry (e.g. GC-MS or LC-MS). If the first analysis is performed by a confirmation-level analysis (mass spectrometry), the positive findings have to be confirmed and quantified by reanalysis with another portion of the sample.

All confirmations must be quantitative. The customer must be informed of the compounds detected in the confirmation tests.

Recommended maximum confirmation cut-off concentrations for workplace drug testing are given in Table 3.

Confirmation cut-off concentrations may be subject to change as advances in technology or other considerations warrant identification of substances at other concentrations. When a sample is tested for substances not indicated in Table 3, the

Confirmation cut-off levels for substances not indicated in Table 3 must be agreed with the customer taking into account the performance of the assays to be used (i.e. limit of detection and limit of quantification) -and the pharmacokinetics of the drugs involved (i.e. different metabolites and their detection times).-

Specimens that are below the agreed cut-off concentration must be reported negative. No further testing for drugs will be undertaken and the specimens must be discarded.

Specimens that contain drugs and/or metabolites at concentrations greater than or equal to the agreed cut-off level must be reported as positive.

Laboratories must adhere to national and international guidelines that specify additional criteria for chromatographic and mass spectral acceptability.

5.5 Validation

All methods must be validated and their suitability for intended purpose must be evaluated in accordance with EN ISO/IEC 17025. Laboratories accredited according to EN ISO 15189 should produce evidence of adequate method validation and certificate of participation to Proficiency Test and External Quality Assessment.

The following parameters have to be determined at least for quantitative confirmation analyses and whenever possible, for screening analyses: precision, cut-off verification, selectivity, limit of detection, limit of quantification, sensitivity, specificity, stability, measurement uncertainty and matrix effects.

5.6 Authorisation and Reporting of Results

Before any laboratory test result is released, the results and chain of custody documentation must be reviewed and certified as accurate and complete by a competent member of staff (analytical validation). At a minimum, the report must include the specimen identification number and the test result (positive/negative) for each specimen submitted.

Reporting must be managed in accordance with EN ISO/IEC 17025 and/or EN ISO 15189 requirements. In addition the cut-off used for the test should be included.

Only drugs that have been confirmed by a recognised confirmation test may be reported as positive.

Specimens that fail integrity or validity tests must be identified to the customer on the report. The laboratory must define and agree the meaning of all terms used in the report to the customer. Results must be transmitted to the customer's designated representative in a manner that will ensure confidentiality of the information. Laboratory results should not be provided verbally. Written or electronic results must be transmitted to the customer's designated representative in a manner that will ensure confidentiality of the information.

5.7 Long-Term Storage of Specimens

The laboratory must demonstrate that the long term storage conditions of specimens are adequate to ensure that analytes are stable over the time period required for any re-test

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7 Currently long-term frozen storage (-20°C or below) indicates that most positive specimens
8 will remain suitable for any necessary retest.
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10 Unless otherwise authorised in writing by the customer, drug testing laboratories must
11 retain all specimens confirmed positive in properly secured long-term frozen storage for a
12 minimum of 1 year.
13
14

15 Within this one-year period the customer may request the laboratory to retain the
16 specimen for an additional period of time. If no such request is received, the laboratory
17 may discard the specimen after the end of 1 year. The laboratory shall be required to
18 maintain any specimens known to be under legal challenge for a further agreed period.
19 Specimens must be retained within the secure laboratory area until the disposal date
20 agreed with the customer. Negative specimens (A+B) may be discarded as per the
21 laboratory and customer agreed timetable.
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28 **5.8 Records**

29 The laboratory must maintain and make available for an agreed period, documentation of
30 all aspects of the testing process and chain of custody documentation involved in the
31 generation of a positive result.
32
33

34 The required documentation must include:

- 35
- 36 • Training and competency records for all individuals authorised to have access
37 to specimens and specimen data.
- 38 • Chain of custody forms
- 39 • Quality assessment/quality control records
- 40 • Standard operating procedures
- 41 • All test data (including method validation, calibration curves and calculations for
42 determining test results)
- 43 • Maintenance and instrument calibration records
- 44 • Reports
- 45 • Records of proficiency testing and computer generated data
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52 The laboratory will be required to maintain documents for any specimen under legal
53 challenge for a further agreed period.
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7 Document control must be managed in accordance with EN ISO/IEC 17025 and/or EN ISO
8 15189 requirements and records containing details of individuals should be dealt with in
9 line with European Data Protection Legislation.
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11 12 13 14 **6 Quality Assurance and Quality Control**

15 **6.1 Quality Assurance**

16
17 Drug testing laboratories must have a quality management system which encompasses all
18 aspects of the testing process including but not limited to:
19

- 20 • Specimen receipt
 - 21 • Chain of custody
 - 22 • Security and reporting of results
 - 23 • Screening and confirmation testing
 - 24 • Certification of calibrators and controls
 - 25 • Validation of analytical procedures
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31 Quality assurance procedures shall be designed, implemented and reviewed to monitor
32 the conduct of each step of the testing process.
33

34 The testing laboratory and all screening and confirmation tests used in Workplace Drug
35 Testing must be fully validated and accredited by a recognised external accreditation body.
36 When an unaccredited method is used the customer should be informed accordingly.
37
38
39

40 **6.2 Quality Control**

41 Calibrators and controls shall be prepared using either certified drug reference materials or
42 certified standard solutions obtained from where possible two commercial manufacturers
43 and should be appropriate to the matrix. If two manufacturers are not feasible then the
44 controls should be taken from separate lots from the same manufacturer.
45
46
47

48 The laboratory must retain records to demonstrate that all calibrators and controls are
49 traceable back to primary standards (if available).
50

51 The calibrators and controls shall be properly labelled as to content, concentration, date
52 placed in service and expiry date.
53
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All standards (~~e.g.~~ i.e. pure reference materials, stock standard solutions, purchased standards) shall be labelled with the following:

- Date received (if applicable).
- Date prepared or opened or placed in service.
- Expiration date.
- Lot number of drug reference materials.
- Initials of the technicians who has prepared the (in house) calibrator etc.

All data acquired on control samples as well lot number of drug reference materials must be recorded in such a way as to facilitate interpretation of control results and trends.

6.3 Laboratory Screening Tests

These are the minimum requirements for the suitable control of all laboratory screening tests.

A system suitability check must be carried out prior to the analysis of samples.

Assays must be calibrated weekly or when quality control samples indicate poor performance.

Control samples at concentrations of approximately 25% below and above the cut-off concentration for each drug group must be included in every batch of samples. These must be sourced independently from calibrators.

Quality control samples must comprise at least 5% of the total number of samples in each batch being analysed.

6.4 Confirmation tests

These are the minimum requirements for identification of analytes and confirmation of results [91]

6.4.1 Identification

Mass spectrometry coupled to chromatography

a) Mass spectrometry coupled to a chromatographic separation method is a very powerful combination for identification of an analyte in the sample extract. It simultaneously provides retention time, ion/charge ratios and relative abundance (intensity) data.

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7 *Requirements for chromatography*

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9 b) The minimum acceptable retention time for the analyte(s) under examination should be
10 at least twice the retention time corresponding to the void volume of the column. The
11 retention time of the analyte in the extract should correspond to that of the calibration
12 standard (may need to be matrix-matched) with a tolerance of $\pm 1\%$, for both gas
13 chromatography and liquid chromatography (Figure 1).
14
15

16
17 *Requirements for mass spectrometry (MS)*

18
19 c) Reference spectra for the analyte should be generated using the same instruments and
20 techniques used for analysis of the samples. If major differences are evident between a
21 published spectrum and the spectrum generated within the laboratory, the latter must be
22 shown to be valid.
23

24
25 d) Identification relies on proper selection of diagnostic (characteristic) ions. The (quasi)
26 molecular ion is a diagnostic ion that should be included in the measurement and
27 identification procedure whenever possible. In general, and especially in single-stage MS,
28 high m/z ions are more specific than low m/z ions (e.g. i.e. $m/z < 100$).
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30

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32 e) Extracted ion chromatograms of sample extracts should have peaks (exceeding S/N 3:1
33 of similar retention time, peak shape and response ratio to those obtained from a
34 calibration standard analysed at comparable concentration in the same batch. Shift in
35 retention time should not exceed 1% compared to calibration standard.
36

37
38 Chromatographic peaks from different selective ions for the same analyte must overlap
39 with each other. Where an ion chromatogram shows evidence of significant
40 chromatographic interference, it must not be relied upon to quantify or identify residues.
41 The ion that shows the best signal-to-noise ratio and no evidence of significant
42 chromatographic interference should be used for quantification.
43
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45
46 f) In case of full scan measurement, careful subtraction of background spectra, either
47 manual or automatic, by deconvolution or other algorithms, may be required to ensure that
48 the resultant spectrum of the chromatographic peak is representative. Whenever
49 background correction is used, this must be applied uniformly throughout the batch and
50 should be clearly indicated.
51

52
53 g) Different types and modes of mass spectrometric detectors provide different degrees of
54 selectivity and specificity, which relates to the confidence in identification. General
55

requirements for identification by MS-methods have been published [91] and should be regarded as guidance criteria for identification, not as absolute criteria to prove presence or absence of a compound.

h) The relative intensities or ratios of selective ions (full-scan MS or SIM) or product ions (MS/MS), expressed as a ratio relative to the most intense (product) ion, should correspond to those of the calibration standard at comparable concentrations and measured under the same conditions. Matrix-matched calibration solutions may need to be used. Table 4 indicates the maximum tolerances for ion ratios.

i) The variability of ion ratios should preferably be determined from calibration standards during initial method validation and subsequently during routine analysis. Diagnostic ions should have an ion ratio of > 0.05 (least/most intense ion).

j) At higher deviation of the relative abundance of a qualifier ion, analysis needs to be repeated. If tolerances still remain beyond acceptance criteria, further investigation of influences of matrix effects or disturbing compound are recommended –such as standard addition experiments or change of chromatographic system - to verify or to exclude the presence of a compound. In these cases complementary interpretation by an experienced analyst is recommended.

k) For a higher degree of confidence in identification, further evidence may be achieved from additional mass spectrometric information. For example, evaluation of full scan spectra, isotope pattern, adduct ions, additional accurate mass fragment ions, additional product ions (in MS/MS), or accurate mass product ions.

For High resolution (HRMS) the mass resolution shall typically be greater than 10000 for the entire mass range at 10% valley (which equates to resolving power of 20000 FWHM (full width at half maximum).

For accurate mass measurements (AMM) the instrument mass error in routine mass measurements must be less than 2 mDa and resolution shall typically be greater than 5000 FWHM. For combination of LC with HR-QToF-MS/MS or other mass spectrometric technique with HR-MS/MS the following settings are recommended for mass spectral identification based on a mass spectral library (commercial or home-made):

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7 For HR-QToF-MS/MS analysis a mass resolution of > 10000 amu with a mass accuracy of
8 < 5 ppm and an isotope ratio comparability of better than 80% should be used in routine
9 analysis. If comparison to a library is performed with MS/MS spectra, a fit value of > 70 %
10 should be used as a threshold, for identification of compounds. Additionally, 1% tolerance
11 of LC-retention time is required (see above, e).
12
13
14

15
16 l) The chromatographic profile of the isomers of an analyte or any relevant metabolites
17 may also provide evidence. Additional evidence may be sought using a different
18 chromatographic separation system and/or a different MS-ionisation technique.
19
20

21 **6.4.2 Confirmation of results**

22
23 If the initial confirmatory analysis ~~does not provide unambiguous identification or~~ does not
24 meet the requirements for quantitative analysis (e.g., ion ratios not in the suspected range,
25 or chromatographic interference), a ~~confirmatory~~ reanalysis of the A-sample is required.
26 This may involve reanalysis of the extract or the sample. ~~In cases where a detection~~
27 ~~threshold for a drug is exceeded, a confirmatory analysis of a portion of the B-sample may~~
28 ~~be required by the authorities.~~
29
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31

32 For unusual analyte/matrix combinations, a confirmatory reanalysis is also recommended.
33

34 The use of different determination techniques and/or confirmation of qualitative and/or
35 quantitative results by an independent expert laboratory will provide further supporting
36 evidence.
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40 **6.5 External Quality Assessment**

41
42 The laboratory must take part in appropriate external quality assessment schemes. When
43 the scheme is not available, the laboratory has to conduct appropriate inter-laboratory
44 testing to ensure appropriate assay performance.
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48 **6.6 Sub-contracting**

49 Drug testing laboratories should carry out all laboratory work with their own personnel and
50 equipment. If it is necessary to sub-contract, inter-laboratory transfer of samples is
51 performed with strict adherence to chain of custody procedures. The sub-contracted
52 laboratory and its methods used must be accredited by a recognised external accrediting
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body and compliant with these guidelines. Analyses undertaken by sub-contracted laboratories must be identified on the test report to the customer.

7 Interpretation of Results

A confirmed analytical positive result may be due to medication (prescribed or over-the-counter) or due to dietary causes. An essential part of the drug testing process is the final review of analytical results.

The interpretation is best carried out by a qualified medical professional (e.g.i.e. Medical Review Officer) or a Toxicologist (depending on the country-specific situation) (See chapter 43).

7.1 Toxicology Review

It is mandatory that a toxicologist is available to advise the customer and/or Medical Review Officer regarding queries with test results.

7.2 Medical Review

The Medical Review Officer (MRO) is a medical physician with responsibility for interpreting laboratory results together with a toxicologist. Depending on the country-specific situation a medical physician usually has greater access to medical records than a toxicologist and may therefore be in a better position to provide interpretation of positive analytical results.

The MRO must have specialist knowledge of and training in

- specimen collection procedures,
- analytical procedures,
- chain of custody and
- alternative explanations for positive analytical results.

The MRO can issue a negative report for a positive analytical result if the test result is likely to be due to the use of declared medication, or a valid alternative medical explanation has been found.

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7 The service provider may provide access to an independent medical review service.
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10 **8 Challenges to Drug Test Results**

11 In situations where there is a challenge to the results of a confirmed positive drug test
12 result, the following guidelines must be used.
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14

15
16 The B specimen should be released for analysis to a drug testing laboratory accredited by
17 a recognised external accrediting body and working to these guidelines. This release
18 requires authorisation from both the customer/MRO and the donor.
19

20
21 The release must be supported by chain of custody procedures that can withstand legal
22 scrutiny and include information about the findings of the original test (corresponding A
23 specimen) and the cut-offs used for the test.
24

25
26 The original laboratory must retain the residue of the original A specimen and its
27 containers so that they can be compared with the B specimen at a later date if required.
28

29 All laboratories that undertake B specimen testing must be able to demonstrate that they
30 can accurately determine the concentration of a drug or metabolite at 50% of the
31 recommended confirmation cut-off concentration listed in Table 3 (or the cut-off used for
32 the original test, whichever is the lower).
33
34

35 On receipt in the testing laboratory, the B sample should follow chain of custody
36 procedures as outlined. It is recommended that the laboratory should carry out validity
37 checks outlined prior to carrying out the confirmation analysis. Only those
38 drugs/metabolites identified for confirmation testing should be looked for.
39
40

41 The final report on the B specimen must say either that the result was reconfirmed or failed
42 to reconfirm. Confirmation cut-off levels are not to be used as the determinant. There must
43 be no comment on the final report that states whether the sample is positive or negative.
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9 Appendix A

Urine Collection Procedure

(Note: Only formally competence tested and authorised persons may act as collecting officers. Medical qualification is NOT required for collecting officers.)

I. Collection Site

Procedures shall provide for a designated collection site to be secure. During the collection process the collection site must be dedicated solely to sample collection and comply with all local health and safety requirements.

The circumstances of the collection site should be arranged so that adulteration of the specimen is prevented as well as possible. To deter the dilution of specimens at the collection site, toilet water colouring agents should be placed in toilet tanks wherever accessible or in the toilet bowl, so the reservoir of water in the toilet bowl always remains coloured. Any other sources of water in the enclosure where urination occurs (e.g. taps, shower) will be secured prior to collection. At the collection site access must be controlled to soap dispenser, cleaning agent, or any other materials that could be used to adulterate the specimen. Also paper towel dispensers, ceiling tiles, or other spaces that could be used to hide adulterants, must be secured during the specimen collection.

II. Access to Authorised Personnel Only

Only authorised personnel shall be permitted in any part of the designated collection site when urine specimens are being collected or stored. The donor has the right to be accompanied with a silent witness, but that should not interfere or delay the collection process, nor is the witness permitted to accompany the donor into the enclosure where the urination occurs.

III. Chain of Custody

During the collection process chain of custody forms will be completed fully by the collecting officer and donor.

IV. Identification of the donor

When a donor arrives at the collection site, the collecting officer will request that the donor presents photographic identification and a signature for comparison. If the donor does not have acceptable photographic identification, the collecting officer will obtain a positive identification of the donor by an authorised supervisor or manager within the parent organisation. If the donor's identity cannot be established, the collecting officer will not proceed with the collection.

V. Informing the donor about the test

The donor has to be informed about the purpose and the content of the test.

VI. Consent of the donor

The donor gives his/her consent for urine collection and analysis of drugs by signature. If the donor refuses to give a sample, a note to this effect should be recorded on the form designated for that purpose. Appendix B gives an example of a Donor's Statement of Informed Consent.

VII. Privacy

Procedures for collecting urine specimens shall allow individual privacy during urination and no observed collection is appropriate in normal cases. Donors have to be treated equally regardless of gender, ethnicity, or any physical impairment. The process should avoid embarrassment but should also be stringent enough to satisfy challenge of the specimen integrity and collection process.

If there is a strong suspicion of specimen adulteration due to not passed specimen validity checks and/or the previous specimen, collected from the donor, was-has been adulterated, the-new specimen can be collected under the direct observation of the collecting officer.

VIII. Integrity of the Specimen

The collecting officer must adopt procedures to minimise the risk of adulteration of the specimen during the collection procedure. The following minimum precautions shall be

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7 taken to ensure that unadulterated specimens are obtained and correctly identified:
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- 9 a. The collecting officer will ask the donor to show that their pockets are empty and
10 remove any unnecessary outer garments such as a coat or jacket that might
11 conceal items or substances that could be used to tamper with or adulterate the
12 donor's urine specimen. The collecting officer will ensure that all personal
13 belongings such as a purse or briefcase remain with the outer garments.
14
15 b. The donor must wash his/her hands with water only prior to urination with inspection
16 of the hands afterwards by the collecting officer.
17
18 c. After washing hands, the donor will remain in the presence of the collecting officer
19 and will not have access to any unregulated source of water, soap dispenser,
20 cleaning agent, or any other materials that could be used to adulterate the
21 specimen.
22
23 d. The donor will choose a clean specimen container. The donor may provide his/her
24 specimen in the privacy of a toilet cubicle or otherwise partitioned area that allows
25 for individual privacy. The collecting officer will remain outside the cubicle until the
26 specimen is collected. The donor will be instructed not to flush the toilet until the
27 specimen is handed to the collecting officer.
28
29 e. The collecting officer will note any unusual behaviour of the donor on the chain of
30 custody form.
31
32 f. Upon receiving the specimen from the donor, the collecting officer will:
33
34 o Check the volume of urine in the specimen container
35
36 - The sufficient volume is approx. 20 millilitres (mL) or more.
37
38 - If the volume is less than 20 mL, the specimen will be discarded and
39 a second specimen will be collected. The donor may be offered a
40 reasonable amount of liquid to drink for this purpose (max 2 times
41 250 mL in 1 hour, not to exceed a maximum of 0.5 litre). In these
42 circumstances a donor should normally be able to provide a 20 mL
43 urine specimen within 2 to 3 hours.
44
45 - The samples must not be combined to provide a sufficient volume.
46
47 - If the donor fails to provide a specimen within this time period the
48 collecting officer will contact the appropriate authority to obtain
49 guidance on the action to be taken.
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51 o Check the temperature of the urine specimen.
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- The temperature-measuring device used must accurately reflect the temperature of the specimen and not contaminate the specimen. The time from urination to temperature measurement is critical and in no case should exceed 4 minutes.
 - The acceptable range of the temperature is 32°C -38°C.
 - A temperature outside the acceptable range is a reason to be suspicious that the donor may have altered or substituted the specimen. Another specimen will be obtained as soon as possible and both specimens will be forwarded to the laboratory for testing.
 - ~~- If there is a strong suspicion of adulteration and/or the previous sample was adulterated the specimen can be collected under the direct observation of a collecting officer.~~
 - o Inspect the specimen to determine its colour and appearance for any signs of contaminants.
 - Any unusual findings will be noted on the chain of custody form.
 - If there is any reason to believe that a donor may have adulterated, altered or substituted the specimen, another specimen will be obtained as soon as possible and both specimens will be forwarded to the laboratory for testing.
 - ~~- If there is a strong suspicion of adulteration and/or the previous sample was adulterated the sample can be collected under the direct observation of a collecting officer.~~
 - g) Both the donor and the collecting officer will keep the specimen container / specimen bottles in view at all times prior to the urine specimen being sealed and labelled.
 - h) The specimen is split into a minimum of two specimen bottles. When the specimen is transferred from the specimen container to the specimen bottles, it will be poured and the collecting officer will request the donor to observe the transfer of the specimen and the attachment of the tamper-evident seal/tape on the bottles. The tamper-evident seal ensures that any tampering with the specimen will be evident to laboratory personnel during the laboratory receipt.
 - i) Direct contact tests (e.g. pH) can only be carried out on the residue of the specimen after the sample has been split and sealed into specimen bottles.

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- The acceptable range of pH is 4-9. The appropriate pH measuring device covers the whole pH-range (e.g. i.e. 1-14) to be able to measure pH outside the acceptable range.
 - A pH value outside of the acceptable range is a reason to be suspicious that the donor may have altered the specimen. Another specimen will be obtained as soon as possible and both specimens will be forwarded to the laboratory for testing.
 - ~~○ If there is a strong suspicion of adulteration and/or the previous specimen was adulterated the sample can be collected under the direct observation of a collecting officer.~~
 - j) A minimum of two sealed specimens together with the corresponding chain of custody documentation in a tamper evident container must be dispatched to the laboratory. One bottle will be used for the drug test while the second bottle will remain sealed at the analytical laboratory in case the donor wishes to challenge a positive result.
 - k) At an appropriate time after the urine specimen has been collected and sealed into the transport bottles the collecting officer will invite the donor to wash his/her hands.
 - l) The specimen bottle will have an identification label that contains at a minimum the date, the donor's specimen number and the donor's signature/initials. The collecting officer will enter all information on the chain of custody form to identify the origin of the specimen. Both specimen bottles and all pages of the chain of custody will be labelled at the time of collection with a unique identifier.
 - m) The collecting officer will ask the donor questions relating to the drugs and medicines consumed within a maximum of 14 days prior to the provision of the urine specimen. These questions will be specific and wide ranging covering areas such as medications prescribed or dispensed by a doctor, dentist or hospital department and over-the-counter preparations. All information is written down to the chain of custody form.
 - n) The donor will be asked to read and sign a statement on the chain of custody form certifying that the specimen identified on the form was in fact the specimen provided by the donor and giving informed consent for the work to be undertaken. Appendix B gives an example of a Donor's Statement of Informed Consent.

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7 o) The collecting officer will complete the specimen chain of custody form and
8 package with the urine specimen ready for dispatch together to the analytical
9 laboratory as soon as possible. If the specimen is not dispatched at once, the
10 collecting officer during storage prior to dispatch must give appropriate
11 consideration to the temperature and security of the specimens. It is advised that
12 the specimens should be stored at 4°C (do not freeze) whenever possible.
13
14 p) Other pages of the chain of custody form will be given/forwarded to the appropriate
15 persons.
16
17 q) The collecting officer and the donor will be present throughout the procedures
18 outlined in the paragraphs of this section.
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23 IX. Exceptional situations

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25 a. The donor is not able to give a sample
26 The donor may be offered a reasonable amount of liquid to drink for this purpose
27 (max 2 times 250 mL in 1 hour, not to exceed a maximum of 0.5 litre). In these
28 circumstances a donor should normally be able to provide a 20 mL urine specimen
29 within 2 to 3 hours. If the donor fails to provide a specimen within this time period
30 the collecting officer will contact the appropriate authority to obtain guidance on the
31 action to be taken.
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35 b. The donor wants to give the sample later
36 The collecting officer must not allow the donor to leave the collection site and come
37 back later to provide a specimen. The collecting officer will contact the appropriate
38 authority to obtain guidance on the action to be taken.
39
40
41 c. Admission of illegal drug use
42 If the donor admits illegal drug use, this should be noted on the chain of custody
43 form.
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48 X. Transportation to Laboratory

49 Collecting officers will arrange to dispatch the collected specimens to the drug-testing
50 laboratory. The specimens will be placed in containers designed to minimise the possibility
51 of damage during shipment and packed properly to comply with local/international mail
52 and courier regulations for biological specimens. Since specimens and the corresponding
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documents are sealed in packages that would indicate any tampering during transit to the laboratory by couriers, carriers, and postal services, usually there is no requirement for documented chain of custody procedures for the transport of the package.

For Peer Review

10 Appendix B**Example of a Donor's Statement of Informed Consent**

I confirm that I have received information about the meaning and content of the drug test. I confirm that I have provided a freshly voided urine specimen to the specimen collector. I have observed the specimen being placed and sealed in the specimen bottles and I confirm that the information on this form and on the specimen labels is correct. I hereby give permission for a minimum of two sealed specimen containers to be sent to the laboratory and I consent that they be tested for evidence of drug use and for tests to be carried out to confirm the validity of the sample. Furthermore, I understand that the results will be communicated confidentially to the employer or a designated representative.

I consent to the above.

Donor's Name (Block Capitals):

Donor's Signature:

Date:

Donor's identifier on the specimen labels

(if different from above):

11 Appendix C**Some examples of fatal flaws in the Chain of Custody**

1. A unique identifier (e.g. barcode) mismatches or absent
2. No documentation received with the sample
3. No written consent to test from the donor
4. Seals broken or tampered with on any bottle
5. No seals
6. Only 1 sample received
7. Insufficient sample for complete analysis
8. Leaking sample
9. No collecting officer name and signature on the chain of custody form

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9 [402] COMMISSION DECISION of 12 August 2002 implementing Council Directive
10 96/23/EC concerning the performance of analytical methods and the interpretation of
11 results (notified under document number C (2002) 3044) (2002/657/EC) (table 4, page 9).

12 Available at: <http://eur-lex.europa.eu/legal->

13 [content/EN/TXT/PDF/?uri=CELEX:32002D0657&from=EN](http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32002D0657&from=EN), last access 27th January

14 2017 <http://eur-lex.europa.eu/legal->

15 [content/EN/TXT/PDF/?uri=CELEX:32002D0657&from=EN](http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32002D0657&from=EN)

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18 [413] GTFCh (01.06.2009): L. D. Paul, F. Mußhoff, "Richtlinie der GTFCh zur

19 Qualitätssicherung bei forensisch-toxikologischen Untersuchungen". *Toxichem Krimtech*,
20 2009, 76 (3), 142-176.

21 https://www.gtfch.org/cms/images/stories/files/GTFCh_Richtlinie_For-

22 [Tox_Version%201.pdf](https://www.gtfch.org/cms/images/stories/files/GTFCh_Richtlinie_For-Tox_Version%201.pdf), last access 27th January 2017

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Table 1 Definitions

For purposes of these guidelines the following definitions have been adopted:

Adulteration	See Tampering
Aliquot	A fractional part of a specimen used for testing. It is taken as a sample representing the whole specimen.
Authorising Scientist	A person who reviews all pertinent data and quality control results in order to attest to the validity of the laboratory's test reports.
Calibrator	A solution of known concentration used to calibrate a measurement procedure or to compare the response obtained with the response of a test sample/sample. The concentration of the analyte of interest in the calibrator is known within limits ascertained during its preparation. Calibrators may be used to establish a calibration curve over a concentration range of interest.
Chain of Custody	Procedures to account for each specimen by tracking its handling and storage from point of collection to final disposal. These procedures require that the donor identity is confirmed and that a chain of custody form is used from time of collection to receipt by the laboratory. Within the laboratory appropriate chain of custody records must account for the specimens until disposal.
Chain of Custody Form	A form used to document the procedures from time of collection until receipt by the laboratory.
Collecting officer	A person trained to collect specimens from donors.
Collection Site	A place where individuals present themselves for the purpose of providing a specimen for analysis.
Confirmation Test	An analytical procedure to identify and quantify the presence of a specific drug or metabolite which is independent of the initial test and which uses a different aliquot, technique and chemical principle from that of the screen test in order to ensure reliability and accuracy.
Customer	The organisation requesting the drug testing service.
Cut-off	A concentration level set to determine whether the sample is positive or negative for the presence of a drug.
Donor	The individual from whom a urine specimen is collected.
Laboratory	The facility providing the analytical services to detect drugs of abuse.
Negative result	A result reported by the laboratory that indicates that either no drug or drug metabolite is present in the specimen or that any drug or drug metabolite present is below the cut-off.
Observed Collection	A donor gives the specimen under the direct observation of the collecting officer.

Positive result	A result reported by the laboratory as positive means that there is conclusive evidence that a drug or drug metabolite is present in the specimen tested at a level greater than or equal to the confirmation cut-off concentration.
Quality control sample	A sample used to evaluate whether or not an analytical procedure is operating within pre-defined tolerance limits.
Medical Review Officer (MRO)	A medical physician responsible for receiving laboratory results from the drug-testing laboratory who has knowledge of substance abuse and has appropriate training or experience to interpret and evaluate an individual's positive test result, in light of declared information.
Sample	A representative portion of a specimen submitted used by a laboratory for testing.
Screening Test	A test to eliminate negative specimens from further consideration and to identify the presumptive positive specimens that require confirmation testing.
Service Provider	The organisation contracted to provide the drug testing service. This may be a laboratory, or a third party providing other elements of the service, and sub-contracting the tests to another laboratory.
Specimen	The portion of urine that is collected from a donor.
Standard (1)	A reference material of known purity or a solution containing a reference material at a known concentration.
Standard (2)	An agreed protocol or procedure (EN ISO/IEC 17025 and EN ISO 15189)
Standard Operating Procedure (SOP)	A written document giving the detailed steps to be followed when undertaking a particular task (e.g. the analysis of a given drug or drug metabolite in a urine specimen).
Tampering	Any process by which an individual knowingly interferes with (or attempts to interfere with) the processes of specimen collection, transport or analysis with the intention of avoiding a legitimate test result. The actions undertaken can include (but are not limited to) the addition of water or foreign substances to the specimen, specimen substitution, damaging bottle seals or packaging and the deliberate consumption of interfering substances or copious volumes of water prior to specimen collection.
Toxicologist	A person responsible for interpreting a toxicological analytical result for the customer or the customer's designated Medical Review Officer.

Table 2 Recommended Substances and Maximum Cut-Off Concentrations for Screening Tests in Urine

The purpose of the cut-offs of listed substances is due to a longer detection time/window. It is a recommendation of the upper limit for cut-off concentrations. In the list below, where the value is given, this is the maximum recommended cut-off.

	ng/mL
Amphetamines group	500
Barbiturates	200
Benzodiazepines group	200
Buprenorphine	5
Cannabis metabolites	50
Cocaine metabolites	150
EDDP (or methadone)	100 (300)
LSD or metabolites	1
Opiates (total)	300
Phencyclidine	25
Propoxyphene or metabolites	300

Cut-off under investigation / discussion:	
Gammahydroxybutyrate (GHB)	-
Ketamine	-
Other opioids (e.g. oxycodone, hydromorphone, tramadol, fentanyl, tilidine)	-
Pregabalin	-
Synthetic cannabinoids	-
Synthetic cathinones (MDPV etc.)	-
Z-Drugs (Zopiclone, Zolpidem, Zaleplon)	-

Note:

1. The laboratory has to take into account country-specific differences in the drug-panel they are using.
2. These recommended cut-off values may be subject to change as advances in technology or other considerations warrant identification of these substances at other concentrations.
3. Cut-off levels for substances not indicated in Table 2 will need to be agreed with the customer taking into account the performance of the assays to be used. The toxicologist/ laboratory have to explain the meaning to the customer.
4. When using immunological analyses the differences in cross-reactivity of different substances have to be noted.
5. The laboratory is responsible for remaining aware of local drug trends and has a responsibility to use this knowledge to advise the customer of the most appropriate substances to be included in the drug testing panel.

Table 3 Recommended Substances and Maximum Cut-Off Concentrations for Confirmation Tests in Urine

The purpose of the cut-offs' of listed substances is due to a longer detection time/window. It is a recommendation of the upper limit for cut-off concentrations. In the list below, where the value is given, this is the maximum recommended cut-off.

	ng/mL
Amphetamines	
Amphetamine (d+ l)	200
Methamphetamine	200
MDA	200
MDMA	200
Other members of the amphetamine group	200
Benzodiazepines or their metabolites	
Alprazolam	100
Bromazepam	100
Clonazepam	100
Diazepam	100
Flunitrazepam	100
Flurazepam	100
Lorazepam	100
Lormetazepam	100
Midazolam	100
Nitrazepam	100
Nordiazepam	100
Oxazepam	100
Phenazepam	100
Temazepam	100
Opiates	

Morphine	300
Codeine	300
6-Monoacetylmorphine	10
Dihydrocodeine	300
Cannabis	
Cannabis metabolite (THC-COOH)	15
Cocaine	
Cocaine metabolite (Benzoylecgonine)	100
Methadone	
Methadone (d+l)	250
EDDP	75
Other drugs:	
Barbiturates	150
Buprenorphine or metabolite	2
LSD or metabolites	1
Phencyclidine	25
Propoxyphene or metabolites	300
Cut off under investigation / discussion:	
Gammahydroxybutyrate (GHB)	-
Ketamine	-
Other opioids (at least Oxycodone, Hydromorphone, Tramadol , Fentanyl, Tilidine)	-
Pregabalin	-
Synthetic cannabinoids	-
Synthetic cathinones (MDPV etc.)	-
Zaleplon	-
Zolpidem	-
Zopiclone	-

Note:

1. The laboratory has to take into account country-specific differences in the drug-panel they are using.
2. These recommended cut-off values may be subject to changes as advances in technology or other considerations warrant identification of these substances at other concentrations.
3. Cut-off levels for substances not indicated in Table 3 will need to be agreed with the customer taking into account the performance of the assays to be used. The toxicologist/ laboratory has to explain the relevance of the cut-offs to the customer.
4. The laboratory is responsible for keeping abreast of local drug trends and -advising the customer regarding relevant drugs for inclusion in the drug testing panel
5. The Limit of Quantification (LOQ) for each drug has to be no more than 50 % of the confirmation cut-off level.
6. The laboratory has to be able to determine d- and l-amphetamines, if required.

Table 4 Recommended maximum tolerances for ion ratios using different MS techniques [102, 113]

Ion ratio (least/most intense ion)	Maximum tolerance (relative) for GC-EI-MS	Maximum tolerance (relative) for GC-CI-MS, GC-MS ⁿ , LC-MS, LC-MS ^{n**}
>50 %	20 %	20 %
>20 - 50 %	20 %	25 %
>10 - 20 %	25 %	30 %
≤10 %	50 %	50 %

Figure 1

$$\frac{rt_{\text{analyte in sample}} - rt_{\text{analyte in calibrator}}}{rt_{\text{analyte in calibrator}}} \leq 0.01$$

For Peer Review