HSE National Drug Treatment Centre

Laboratory Handbook

8th Edition

January 2021

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The HSE National Drug Treatment Centre Laboratory

CONTENTS

1.0 GENERAL INFORMATION

1.1 Laboratory Address & Contact Details

HSE National Drug Treatment Centre Laboratory
McCarthy Centre
30 - 31 Pearse Street
Dublin 2
D02 NY2

e-mail: lab@dtcb.ie for general inquiries only
Healthmail: labndtc@healthmail.ie (for specific patient inquiries use healthmail - the secure clinical email)

1.2 Laboratory Location

The laboratory is located on the third floor and can be accessed from the reception lobby via a lift. Access to the reception lobby can be gained by pressing the intercom buzzer at the front door of the building (Pearse St. entrance).

1.3 Laboratory Opening Hours

Monday - Friday: 9.00am - 5.00pm

1.4 Sample Reception

The sample reception area is accessed via the hatch adjacent to the laboratory door, on the third floor.

1.5 Key Contact information

Figure 1: Contact Details

Contact	Name	Telephone Number
General Enquiries	Laboratory Office	01 6488 645
National Drug Treatment Centre	Main switchboard	01 6488 600

Email/website information	Details
Laboratory email	lab@dtcb.ie
Laboratory Healthmail email	labndtc@healthmail.ie
National Drug Treatment Centre website	www.addictionireland.ie

If you need to contact a member of staff, please call the laboratory office directly at 01-6488645 and your call will be transferred to a staff member who will assist you with your query.

1.6 Customers

The NDTC Laboratory provides a national drug analysis service to the HSE Addiction Services, General Practitioners, Hospitals (general, psychiatric and maternity), Juvenile Detention Centres, Voluntary Organisations and the Dublin Drug Court Probation Service. The customer database service is maintained by the customer services manager and new centres can become registered as customers by contacting

the customer services manager (see Section 1.5). Users must be registered before sending samples to the laboratory for testing. Users of the laboratory service should ensure that their contact details i.e. name, address, telephone number are up to date. Any changes should be notified as soon as possible to the customer services manager or designee.

1.7 Customer Satisfaction, Comments and Complaints

The goal of the NDTC laboratory is to ensure that our users receive accurate, reliable, meaningful and timely laboratory results. If customers encounter any problems with the service or have suggestions for service improvement, please contact the customer services manager, quality manager or any other member of laboratory staff. The Laboratory conducts annual customer satisfaction surveys; however customers may be surveyed at more frequent intervals in response to the implementation of major changes to the service, or identification of non-conformities or complaints.

2 REQUESTING LABORATORY TESTS

2.1 Consent

The HSE NDTC laboratory does not take responsibility for obtaining "consent to test" for samples received for drug testing. Consent should be obtained by the doctor or organisation requesting the test, prior to sending samples to the laboratory. If the client is under 18 years old, consent should be obtained from a parent or guardian. Written consent does not need to accompany samples, except in the case of chain of custody and probation samples, which require signed consent to be obtained on the relevant form

2.2 Sample labelling

The criteria for sample acceptance, as described below, are strictly adhered to in order to comply with accreditation standards and in the interest of patient safety. Failure to provide the required data may lead to rejection of the sample. Laboratory personnel are acting correctly when they take action to ensure that the minimum standards set out in this policy are met at all times.

The following information is mandatory and must be included on each sample container;

- **Patient's full name**
- **Date of Birth** (DD/MM/YYYY format)
- **Clinic or hospital name/code**
- **Date of sample collection** (DD/MM/YYYY format)

In addition, the following information may be required on some samples;

- Name of Doctor
- DAIS Code (DAIS addiction clinics only)

2.3 Request forms

The NDTC laboratory strives to be a paper-free laboratory as much as possible, therefore request cards are not necessary for the majority of samples. If extra testing is required, the extra tests can be requested by writing the test name on the sample label (e.g. 6AM, see the abbreviation list in Figure 7).

2.4 Verbal Requests

Extra tests or re-tests can be requested verbally by contacting the laboratory by phone (see section 1.5 for phone details). When requesting extra tests retrospectively, please be mindful of the relevant storage period for the sample (see Section 6 below) as tests can only be added if the sample is still available in the laboratory and if there is sufficient sample left to carry out the extra tests. All telephone requests/conversations will be logged by the laboratory staff.

2.5 Use of e-mail

Never include patient details in e-mails to the laboratory as it is not secure.
Healthmail is a service that allows health care providers to send and receive clinical patient information in a secure manner. If you have healthmail, you may use it to email the laboratory with patient details on the laboratory healthmail account: labndtc@healthmail.ie

2.6 Urgent Requests

External samples: All maternity hospital samples are treated as urgent. If sending an urgent sample from another location, please telephone the laboratory with the specific details of the urgent sample.

In house samples: Please inform the laboratory that a sample is urgent by either sending a STAT request form with the sample, or by informing the laboratory in person/by phone.

3 SAMPLE COLLECTION

3.1 General Guidelines

The procedure for collecting these sample types is detailed in Figure 2 below. Standard Health & Safety precautions and procedures should be followed when collecting biological samples.

It is the responsibility of the person collecting the sample to ensure that it is;

- Collected from the correct individual
- Correctly labelled with sufficient information to allow analysis (see section 2.2)
- Correctly closed i.e. not leaking
- Correctly packaged for delivery to the laboratory (see section 4 below)

3.2 Specific Guidelines

Please follow the guidelines below when collecting the various sample types. If further specific information is required, please contact the laboratory (see section 1.5).

Figure 2: Sample collection

Sample Type	Collection Details
Urine	Use clean plastic container without preservative. Preferably yellow lidded 70ml urine pots (see figure 3) 20 - 30mls urine where possible. Minimum volume: 3mls Where collection bottle with temperature strip is used, temperature of urine should be between 34-39^{0}C when freshly voided. Sample should be stored in a cool, dry dark place (preferably refrigerated) pending dispatch to the laboratory Sample should be dispatched to Laboratory as soon as possible Point of Care test devices are not suitable for laboratory testing and will not be tested.
Blood (Serum Methadone levels only)	Serum Red Cap Tube with 10 ml blood where possible. Each request must be accompanied by a completed LF8 form. See section 5.5 below for procedure for correct timing etc. of sample collection

3.3 Sample Containers

Figure 3: Recommended Sample containers

Container Type	Details	Tests
Urine container 	Clean, non-preservative added container required. (Sterility not required). Several container brands fulfil these criteria; however the preferred container is displayed in the image. Please ensure that the minimum 4 pieces of info is given on the sample label (see section 2.2).	All routine and non-routine urine tests and confirmatory tests such as; Full drug screen, Zopiclone, Opiate ID etc. See Figure 9 for full list.
Blood container 	Full Red Cap Serum Tube *Several blood tube brands are suitable, provided they do not contain preservative and/or anticoagulant	Blood for Serum Methadone levels only. See Section 5.5.

3.4 Non-Compliant Samples

Non-compliant samples, such as those which do not demonstrate all the mandatory information required in order to unambiguously identify them, i.e. full name, date of birth, clinic location; or samples in unsuitable containers (e.g. Point-of-Care devices) cannot be analysed. If the sample date is not provided, the 'date received' is used as the sample date and a non compliance comment will be included on the sample report.

The laboratory will endeavour to obtain the correct sample identification in order to proceed with analysis, however if this is not possible the sample will be logged as non-compliant and will not be analysed.

Leaking samples are also non-compliant samples. Leaking samples will not be analysed and the sample will be disposed of immediately.

Notification of non-compliances will be sent to the customer by means of a comment on the report, detailing the nature of the non-compliance. Please read these non-compliance comments carefully and contact the laboratory if requested to do so on the report.

4.0 TRANSPORT OF SAMPLES TO THE LABORATORY

The transport of human materials intended for diagnosis/investigation is regulated by ADR (Accord Dangereux Routier), a UN document which defines how such substances should be classified, packaged and transported. UN guidelines specify how substances should be classified, and how these substances should be packaged for transport. Biological diagnostic substances are classified as UN3373 and according to the guidelines, should be packaged and transported in line with Packaging Instruction P650.

Samples are sent to the laboratory from a variety of customers however they can be summarised as 'Internal' and 'External' customers. Irrespective of the source of the sample, it remains the responsibility of the sender to ensure the sample is correctly sealed and packaged to allow it to be transported safely and to arrive intact to the laboratory.

4.1 Internal customers - Packaging requirements

Samples can be delivered by hand, or via the pneumatic chute system. In both cases the sample must be checked to ensure the sample lid is securely closed and the sample is enclosed within an individual biohazard bag. This is particularly important when using the chute, as a leaking sample within a transport canister/pod can affect all other samples within the pod and this may lead to all samples being rejected for analysis if there is a possibility of cross-contamination amongst those samples.

4.2 External customers - Packaging requirements

If a diagnostic substance has been classified as belonging to UN3373, then it must be packed for transport according to the Packing Instruction 650 guidelines. This is a list of requirements covering the quality and construction of the packaging used for transport of liquid substances, which state:-

1. The primary receptacle(s) shall be leak proof
2. The secondary packaging shall be leak proof
3. If multiple fragile primary receptacles are placed in a single secondary packaging, they shall be either individually wrapped or separated to prevent contact between them
4. Absorbent material shall be placed between the primary receptacle(s) and the secondary packaging. The absorbent material shall be in quantity sufficient to absorb the entire contents of the primary receptacle(s) so that any release of the liquid substance will not compromise the integrity of the cushioning material or of the outer packaging
5. The primary receptacle or the secondary packaging shall be capable of withstanding, without leakage, an internal pressure of 95 kPa (0.95 bar)

Packaging which fulfils the above requirements can be purchased from a number of commercial providers and is marked with the symbol below;

Figure 4: UN3373 symbol

5.0 DRUG ANALYSIS

The NDTC laboratory carries out analyses on urine for drug and drug metabolites using the following methodologies: Immunoassay, enzymatic assay, chemical analysis and LC-MS. Further details on the range of assays are given in figures 6, 7 and 9. It should be noted that all analytical results are subject to Uncertainty of Measurement (UoM), see section 8.

5.1 Integrity Testing

Integrity/Adulteration testing refers to tests carried out to determine whether a sample is genuine or if it may have been tampered with. In the NDTC laboratory three types of urine integrity testing may be performed; Creatinine (performed on all urine samples), pH and Specific Gravity testing (only performed on samples taken, and tested by, chain of custody procedures).

- **Creatinine Testing**

Creatinine in urine is tested by an chemical method. Creatinine is a normal constituent of urine. Its concentration in urine varies from day to day and is dependent on hydration status of the individual. Most urine samples have a creatinine level in the 'normal' range, however some urine samples may have a lower level of creatinine i.e. 'dilute' urine. This may reflect recent high intake of fluid, but it could also be caused by addition of fluid to the urine. Dilute urine is valid for drug testing but a comment indicating that the urine is dilute will accompany the drug report. If the level of creatinine falls below 2mg/dl this urine is considered invalid for testing and is reported as 'abnormal'. Figure 5 details the levels of creatinine in 'nomal', 'dilute' and 'abnormal' urine.

Figure 5: Creatinine levels in urine

Urine status after Creatinine testing	Creatinine concentration range	Comment on patient report
Normal	80-200mg/dl	No comment
Dilute	2-20mg/dl	Dilute urine - interpret results with caution
Abnormal	<2mg/dl	Abnormal urine

Please note that these creatinine ranges are adult ranges. We do not use paediatric creatinine ranges when testing neonatal samples – therefore neonatal urine samples are often classed as 'Dilute' by our I.T. system, due to the naturally low creatinine levels in neonates.

- **pH Testing**

pH is measured on a scale of 0 to 14. It is a measure of how acidic or alkaline a liquid is, with more acidic solutions having a lower pH (<7) and more alkaline solutions having a higher pH (>7). Neutral solutions have a pH of 7. The NDTC laboratory defines a pH level of 3 to 11 as 'normal'. pH readings outside this range may indicate tampering of a sample by the addition of, or substitution by, another substance or liquid. When pH values outside the laboratory's normal range are detected in a patient's sample, no toxicology results will be reported and notification of the failed pH test will be given. The pH integrity test is normally only performed on samples taken under chain of custody procedures.

- **Specific Gravity Testing**

Urinary specific gravity (SG) is a measure of the concentration of solutes in the urine. It measures the ratio of urine density compared with water density. Specific gravity testing is only carried out in the laboratory on Chain of Custody urine samples, using a reference range of 1.005 - 1.030.

5.2 Routine Drug Screening

Most samples received are routinely tested by immunoassay screening tests, producing a qualitative result i.e. results are reported as 'positive' or 'negative'. Details of the assay types are given on Figure 6

below. The Immunoassays used yield qualitative results which indicate only the presence or absence of a drug/drug class in a sample, based on a defined cut-off level, above which the test is deemed positive, indicating that the presence of a drug/drug class was detected above the cut-off level. If a test result falls below the cut-off level, the result is deemed negative indicating that the drug/drug class was not detected above the cut-off. Cut-off levels are detailed on every test report. The assay for Alcohol, which is a chemical assay, gives information about the concentration of the alcohol level above the cut off value. If the level of alcohol in the sample is below the cut off value, it is reported as negative.

Figure 6: Routine screen assay types

Drug/Drug Metabolite	Assay Type
Amphetamine (class)	Immunoassay
Benzodiazepine (class)	Immunoassay
Cannabis	Immunoassay
Cocaine	Immunoassay
EDDP (Methadone metabolite)	Immunoassay
Opiate (class)	Immunoassay
Alcohol	Chemical

5.3 Non-routine drug screening, Drug metabolite testing & other tests

Most samples received for drug testing are tested only for the routine drug screen detailed in section 5.2. If required, samples may be further tested for the non-routine tests described in Figure 7 below. Non-routine drug screening tests are carried out by request only (e.g. by writing test abbreviation on the label).

Figure 7: Test abbreviations for additional tests

Drug/Drug Metabolite/Analyte	Assay Type	Test abbreviation
Ethylglucuronide	Immunoassay	EtG
6 Acetyl Morphine (Heroin metabolite)	Immunoassay	6AM
Suboxone/Buprenorphine	Immunoassay	BUPN
Pregabalin	Immunoassay	PREGAB
Zopiclone/Zimovane	LC-MS	ZOP
Opiate Identification	LC-MS	OPIA ID
Tramadol	LC-MS	TRAM
New psychoactive substances	LC-MS	Hshop or NPS
Oxycodone	LC-MS	OXY
Benzodiazepine Identification	LC-MS	BENZ ID
Fentanyl	LC-MS	FENT
pH	Chemical assay	n/a
Glucose	Point of Care Test	n/a
hcG (Pregnancy test)	Point of Care Test	hcG

5.4 Confirmatory Analysis

Confirmatory analysis is carried out using liquid chromatography mass spectrometry (LC-MS). Confirmatory testing gives a highly specific and legally defensible result. Confirmatory analysis may be used to confirm a positive result obtained on a screening test. Additionally there are some drugs which are only analysed using this technique; e.g Zopiclone, Tramadol, New Psychoactive Substances, Oxycodone, Fentanyl

High performance liquid chromatography (HPLC) facilitates the rapid separation of compounds from each other and from the other constituents of complex mixtures or matrices. Mass spectrometry (MS) has the capability to separate organic molecules according to their molecular mass and permits their detection with extremely high sensitivity.

Used in tandem, the two techniques, referred to as LC-MS, provide a unique capability for sensitive, selective measurement of molecules such as drugs in urine, and can be used to confirm positive results from immunoassay screening if there are doubts over the validity of the initial screening result.

The categories of confirmatory tests available (with their common abbreviation) are summarised below;

1. Opiate Identification (OPIA ID)
2. Benzodiazepine Identification (BENZ ID)
3. New Psychoactive substances (NPS/Hshop)
4. Zopiclone (ZOP)
5. Cannabis confirmation

Confirmatory analysis should be requested when unambiguous identification of the drug present is required or if the drug can only be identified by confirmatory analysis. Please contact the laboratory with any queries relating to confirmatory analysis.

5.5 Therapeutic drug monitoring of Methadone

Therapeutic drug monitoring of methadone is performed to give information of the serum level of methadone. This information may be used by the clinician to guide methadone prescription dose. It is recommended that a trough methadone level is measured and information on collection of a trough sample is given below.

Therapeutic levels of Methadone

'With chronic administration of 100-200 mg daily oral doses to tolerant subjects, the plasma concentration peaked at 4 hours, with an average value of 830 ng/ml (range, 570 -1060 ng/ml) and declined to 460 ng/ml (range, 280 -790 ng/ml) 24 hours after last dose (average plasma half life of 25 hours). It has been estimated that trough plasma methadone levels should be at least 0.05 - 0.10 mg/L, i.e. 50-100ng/ml, to prevent withdrawal systems in narcotic maintenance patients'.
[Baselt 2004, Disposition of Toxic Drugs and Chemicals in man, 6th edition, p. 642 – 643]

If submitting samples for serum Methadone level testing, all the following criteria must be followed;

- A minimum of 3 days supervised Methadone consumption prior to the day of blood collection.
- The time of dosing on each day should be the same (+/- 30 minutes).
- The blood sample must be taken immediately before the next dose on day 4.
- Samples must be collected into a serum tube.
- The sample must be accompanied by a fully completed request form (LF8).

Failure to adhere to these guidelines will result in unreliable and difficult to interpret results.

5.6 Drug detection windows

After ingestion, drugs are distributed throughout the body and appear in various body tissues in a time dependent manner. The time period which the drug can be reliably detected in any test matrix is called the 'window of detection' .The window of detection of a drug is a function of a combination of many factors including the drug's tendency to be distributed, the matrix/sample type (blood, urine etc), the metabolic pathway of the drug and the individual's response to the drug. Figure 8 gives a general indication of detection times in common test matrices. More specific individual drug information is given in Figure 9.

Figure 8: Drug detection times in biological matrices

Sample type/matrix	Detection time range (window of detection)	Drug use detected
Urine	Days – weeks	Recent
Blood	0-48 hours	Acute, under the influence

Urine is the most commonly used specimen due to its ease of collection and long window of detection (drugs can be detected for a number of days, and in some cases, weeks, after last use). It is the universally preferred sample to screen for the presence/absence of drugs. Urine is however unsuitable for determining drug levels due to the many factors which affect the composition and concentration of urine.

Blood samples are only accepted in the NDTC laboratory for the therapeutic monitoring of blood methadone levels (see section 5.5 for further information).

Figure 9: Summary of the windows of detection, turnaround times and accreditation status for all our tests.

Sample type/ Matrix	Test Type	Method	Test	Window of Detection	Normal Turnaround Times	Accredited to ISO/IEC 17025-2017
Urine	Routine Screen	Immuno-assay	Opiate class	2-4 days[1]	24 - 48 hours	Yes
			Benzodiazepine class	3-30 days[1]		Yes
			EDDP	Unknown		Yes
			Cannabis class	1-30 days[1]		Yes
			Cocaine	2-4 days[1]		Yes
			Amphetamine class	1-2 days[1]		Yes
		Enzymatic	Alcohol	7-12 hours[1]		Yes
		Chemical	Creatinine	n/a		Yes
	Non-Routine	Enzymatic	Pregnancy (POCT)	n/a		No
		Chemical	pH	n/a		Yes
			Glucose (POCT)	n/a		No
		Immuno-assay	6-AM	24 hours[2]		
			EtG: Alcohol marker	Up to 48 hours[3]		Yes
			Buprenorphine	4-24 hours[4]		Yes
			Pregabalin	Up-to-6 days[5]		No
	Confirmatory	LC-MS	Opiate Identification		5-10 days	No
			Zopiclone			No
			'Headshop' products (psychoactive substances) Bath salts only, no synthetic cannabinoids (Spice)			No
			THC-COOH (Cannabis metabolite)			No
			Benzodiazepine identification			No
Blood	Screen	(ELISA)	Methadone levels	n/a	5-10 days	Yes

* Please note: Turnaround time is measured from time of receipt of sample at the laboratory and is measured in working days. See Section 5.8 for more detail on Accreditation.

Abbreviations

6-AM: 6-acetylmorphine, primary metabolite of heroin EtG: Ethyl Glucuronide (Alcohol biomarker)
LC-MS: Liquid Chromatography Mass Spectrometry POCT: Point of Care Testing
EDDP: 2-ethylidine-1,5-dimethyl-3,3-diphenylpyrrolidine (primary metabolite of methadone)

References

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3. Hadland, SE. & Levy S.Objective testing - Urine & other drug tests. Child Adolesc Psychiat Clin N Am 2016 25(3) 549- 565
4 Kronstrand R., Nyström, I., Andersson, M. , Gunnarsson, L., Hägg,S., Josefsson M., Ahlner, J., Journal of Analytical Toxicology, Vol. 32, October 2008
5. Spigset O, & Westin, AA. Detection times of pregabalin in urine after illicit use: when should a positive specimen be considered a new intake? Ther Drug Monitoring 2013 Feb; 35(1) 137-40

5.7 Result interpretation on screening assays

'True and 'False' Positives

A positive result indicates that there is a detectable level of drug in the patient's urine that is above the established cut off for the assay. Appendix 1 details the compounds detected by the screening assays.

Care should be taken when interpreting immunoassay screening results. The assays for opiates, amphetamines and benzodiazepines are class assays i.e. there is more than one type of each drug in that class detectable whereas the assays for cannabis, cocaine, 6-AM and EDDP are highly specific for one drug or drug metabolite. Some commonly used medications can cause positive results on the opiate or amphetamine assay e.g. Solpadeine® (contains the opiate codeine) will cause a positive opiate result and lisdexamfetamine (an ADHD medication) gives an Amphetamine positive result.

Some drugs and medications can also produce 'false' positive results when tested using immunoassay, due to cross reactivity with a similar compound in the patient urine e.g. over-the-counter decongestant medications can cause a false positive result on the amphetamine assay assay due to the presence of pseudoephedrine. Because of the possibility of cross-reactivity, screening results by immunoassay alone are not legally defensible and further confirmation of the test result may be required depending on the purpose of the testing.

If you have any queries about a positive result, or if the result is unexpected, please contact the laboratory. Confirmatory analysis can be carried out on request.

'True' and 'False' Negatives

'True Negative' results occur when the drug of interest is either not present in the sample, or is present at levels lower than the assay's cut-off level.

'False Negative' results can occur due to a range of factors including; limited assay sensitivity, sample adulteration and laboratory error.

If you have any queries about a negative result, or any unexpected result, please contact the laboratory.

5.8 Accreditation

Accreditation is the formal recognition of a body's competence to conduct a specific activity such as testing, inspection or certification. This recognition is based on compliance with international and European standards. Compliance with these standards requires organisations to demonstrate competence, impartiality and integrity (www.inab.ie). Accreditation is provided by the national accreditation body for each Member State; in Ireland this is the Irish National Accreditation Board (INAB).

ISO/IEC 17025 is the standard used by testing and calibration laboratories globally. The laboratory is annually assessed for compliance with International standard ISO/IEC 17025 by a team of Irish and

international external auditors. This includes assessment of the organisation's quality management system and the technical competence of the laboratory to perform the tests within its accreditation scope.

The HSE NDTC Laboratory is accredited by the Irish National Accreditation Board (INAB) to undertake testing in conformity with ISO/IEC 17025:2017 as detailed in Figure 9 above and in the Schedule bearing the Registration number 169T which is available at: http://www.inab.ie/Directory-of-Accredited-Bodies/Laboratory-Accreditation/Testing/HSE-National-Drug-Treatment-Centre.html

5.9 Subcontracted testing

When a request is received from a customer for a test which is not performed in NDTC, the laboratory may, as a service to the customer, subcontract the testing. In this instance, the laboratory will endeavour to subcontract the testing request to a competent external laboratory which complies with ISO/IEC 17025 or equivalent. The Laboratory does not subcontract tests within the scope of its accreditation.

5.10 Chain of Custody

In order for test results to be defensible in a court of law or professional hearing, chain of custody procedures must be followed. There are two chain of custody procedures employed in the laboratory. One type is specifically designed for the Probation services (single sample). The second chain of custody procedure is for all other purposes requiring chain of custody sampling (A&B samples). The laboratory supplies the necessary kits and forms for both processes. Both chain of custody procedures involve fully documenting who donated, collected and handled the sample thereafter. The HSE NDTC laboratory can provide information on chain of custody procedures. All positive immunoassay screening test results are confirmed using an LC-MS confirmatory analytical method. Please contact Laboratory Customer Services for further information.

Note that accurate completion of the forms at point of sample collection is critical. Incomplete or absent information on the form will be noted as a non-compliance comment on the sample report and is likely affect the validity of the report if used in court.

5.11 Quality Control and Quality Assurance

To ensure the highest confidence in test results, the laboratory adheres to strict quality control (QC) and quality assurance (QA) standards. In order to achieve this, approximately 3% of all samples run are quality control samples.

In order to assess performance of all our accredited tests, the laboratory is involved in four external Quality Assurance schemes from three EQA providers;

LGC – Drugs of abuse in urine, Ethanol in urine
IEQAS – Drugs of abuse in urine.
Arvecon – Ethylglucuronide (EtG) in urine, Replacement Drugs in Serum and Urine

Viewing of quality control data, proficiency testing data and testing procedures will be accommodated on request by arrangement with the laboratory.

6.0 STORAGE AND RETENTION OF SAMPLES

Samples should be sent to the laboratory at the earliest opportunity. If there is any delay, it is recommended that samples are stored in a refrigerator at 4ºC, or if refrigeration is not available, in a cool dark place.

- **Routine Sample Retention**

Post analysis, the laboratory will retain samples for 14 days in refrigerated conditions, after which they will be safely disposed. Should further testing be required outside of this period (e.g. for Zopiclone analysis) samples will be stored in refrigerated conditions until testing is complete.

- **Probation/COC Sample Retention**

Unless otherwise agreed, all Chain of Custody samples and Probation samples will be frozen and retained for 12 months post analysis, after which they will be safely disposed.

6.1 GDPR

As a part of the HSE, the NDTC laboratory must comply with the Data Protection Acts 1988-2018 and the General Data Protection Regulations (GDPR). We endeavour to protect the patient's right to privacy in all our activities. To maintain this privacy and protection of personal information, laboratory staff follow strict guidelines and procedures when accepting, logging, processing and reporting of patient samples to ensure the correct patient receives the correct result. To help protect the privacy of patients, the laboratory request only the minimum of information on each patient sample (see sections 2.2 and 3.4 above) and ask that request cards and other extra information/notes are not sent with the patient sample (see section 2.3). Any breaches of GDPR in relation to laboratory activities are reported to and investigated by the local HSE data protection officer.

6.2 Retention of Records

We will only retain patient information and laboratory records based on the Record Retention Periods, Health Service policy 2013;
https://www.hse.ie/eng/services/list/3/acutehospitals/hospitals/ulh/staff/resources/pppgs/rm/recret2013.pdf

7.0 REPORTING OF RESULTS

Samples are analysed and reported in order of receipt, except for STAT samples which are prioritised.

7.1 Report Format

The front page of each report details the customer name and address, the date on which each report is generated and the scope of INAB accreditation (for accredited tests only). Page 1 also includes useful information with regards to uncertainty of measurement, abbreviations used, integrity tests etc.

Page 2 (and onwards) contain the toxicology results for each patient. Each patient is identified by name, date of birth, clinic code and chart number.

Each sample is identified by a unique barcode (an 8 digit number, starting with the year e.g. 21123456) and sample date.

If a drug/drug class is detected in a sample, the result will appear as a "+" (positive), indicating the presence of the drug. The only exception to this is Alcohol, which is reported numerically if present at a level above 30mg/dL.

When no drug/drug class has been detected, it will be reported as a "-" (negative), indicating that the drug/drug class has not been detected above the cut-off level or concentration.

A blank space indicates that no test was carried out. Screening results will usually be available within 24-48 hours of receipt of samples in the laboratory. Confirmatory testing usually takes longer to perform due to the complexity of the methodology.

Each report contains a unique ID number in the footer section of the page – please quote this ID number, e.g. 25/08/2020-075(1) if querying a particular report with the laboratory.

7.2 Mode of reporting

The method of report transmission used must be agreed in advance with Laboratory Customer Services. The main methods of reporting are via post and electronic systems, with most customers encouraged to use electronic reporting.

Paper Based reporting

- POST: Reports sent by post will be dispatched as soon as possible after completion of analysis.
- FAX: The laboratory no longer faxes reports as per HSE Electronic Communications policy.

Electronic Reporting

- LER (Laboratory Electronic Reporting): The LER is a web-based system developed for NDTC customers which allows authorised users to access results electronically. Results are available once the laboratory authorises the samples.
- DAIS (Drugs Aids Information System): HSE Addiction Services access laboratory results via DAIS. Results are available once the laboratory authorises the samples.

Verbal reporting

Verbal reporting can only be accommodated in the case of an emergency. All verbal discussions are logged into the laboratory's quality management system using form LR04

8. UNCERTAINTY OF MEASUREMENT

When interpreting laboratory reports, consideration should always be given to the Uncertainty of Measurement (UoM) associated with the test result, because no measurement is absolutely exact. When a quantity is measured, the outcome depends on the measuring system, e.g. test procedure, environmental conditions, volumetric effects, reference values, sampling matrix, operator etc. Therefore all measurements are subject to uncertainty and this should be taken into account in the interpretation of laboratory results. This can have a bearing on immunoassay test results which are close to their cut-off point and therefore within the range of measurement uncertainty for the test cut-off.

Clinical consideration and judgment should be applied to any immunoassay test result. Repeat testing or confirmatory analysis may be requested if required. The tests reported are qualitative with the exception of Alcohol which is quantitative when present above the cut-off.

8.1 Urine Assay UoM Calculations

The UoM figures for each test are given in brackets;

OPIATE (+/-19.5%)[a] , 6-AMOR (+/-21.6%) [a] , BENZ (+/-13.5%) [a] , EDDP (+/-12.2%) [a] , CANN (+/- 20.0%) [b] AMPH (+/- 16.6%) [a] , COCA (+/-9.2%) [a] , ALCO (+/-12.4%) [a] , ETG (+/-17.6%) [a] , BUP (+/-27.6%) [a] , pH (+/- 6.5%) [a], Pregabalin (10.87%)[c]

a = based on all 2017 QC data
b= based on 6 months 2018 QC data
c= based on data from 2020 verification study

9. MEMBERSHIP AND REPRESENTATION

To ensure best practice, to maintain continuous professional development (CPD) and to keep up to date with the latest developments and trends in drug misuse, laboratory staff hold professional membership and attend meeting of various international societies. These societies include:-

ACBI - Association of Clinical Biochemists of Ireland
TIAFT- The International Association Forensic Toxicologists
UKIAFT - UK and Ireland Association of Forensic Toxicologists
EWDTS - European Workplace Drug Testing Society
ACSLM - Academy of Clinical Science and Laboratory Medicine
SOFT - Society of Forensic Toxicologists
AACC - American Association for Clinical Chemistry
EFLM – European Federation of Clinical Chemistry and Laboratory Medicine

Membership and contribution to Early Warning Emerging Trends Committee in Department of Health set up to fulfil the requirements of Regulation (EC) No 1920/2006 (as amended) and Council Framework Decision 2004/757/JHA (as amended) with respect to information exchange and the early warning system, as well as for the initial report, risk assessment, and control measures. (European Union Early Warning System on new psychoactive substances)

Membership and contribution to the Working Group was set up by HSE under action 1.3.11 of the National Drug Strategy 2017-2025.

Appendix 1: Urine Immunoassay Cross Reactivity Tables

CEDIA® Amphetamine/Ecstasy Assay (cut-off 1000ng/ml) Drugs producing positive results		
Amphetamine Methamphetamine	N-Methylbenzodioxazolylbutanamine (MBDB) 3,4-Methylenedioxyamphetamine (MDA)	3,4-Methylenedioxyethylamphetamine (MDEA) 3,4 Methylenedioxymethamphetamine (MDMA)

CEDIA® Opiate Class (cut-off conc.300 ng/ml) Drugs producing positive results		
6-Monoacetylmorphine	Morphine Sulfate	Naltrexone HCl
Diacetylmorphine	Nalorphine HCl	Oxycodone
Hydrocodone	Naloxone	Oxymorphone
Hydromorphone		Pholcodine
Morphine		Thebaine

CEDIA® Benzodiazepine Class (cut-off conc. 300ng/ml) Drugs producing positive results		
Alprazolam	Diazepam	Nimetazepam
Bromazepam	Estazolam	Nitrazepam
Chlordiazepoxide	Flunitrazepam	Nordiazepam
Citalopram	Flurazepam	Oxazepam
Clobazam	Halazepam	Prazepam
Clonazepam	Lormetazepam	Temazepam
Delorazepam	Medazepam	Tetrazepam
Demoxepam	Midazolam	Triazolam

CEDIA® 6-Acetylmorphine (cut-off conc. 10 ng/ml) Drugs producing positive results
6-Acetylmorphine

CEDIA® Cannabis (cut-off conc.50 ng/ml) Drugs producing positive results		
11-Nor-9-carboxy-Δ^9-tetrahydrocannabinol	11-OH- Δ^9-THC	8β,11-di-OH- Δ^9 -THC
	1- Δ^9-THC-Glucuronide	Cannabinol
11-nor- Δ^8-THC-COOH	8β-OH-Δ^9 THC	5-Methyl-7-Methoxy-Isoflavone
Δ 9-THC (Dronabinol)	Efavirenz (Sustiva)	Silymarin

CEDIA® Cocaine (cut-off conc. 300 ng/ml) Drugs producing positive results
Benzoylecgonine
Cocaethylene
Cocaine

DRI® Ethyl Alcohol (cut-off conc. 30mg/dl) Drugs producing positive results
Ethanol

CEDIA® EDDP (cut-off conc. 100ng/ml) Drugs producing positive results
2-Ethylidin-1,5-dimethyl-3,3-diphenylpyrrolidin (EDDP)

Immunanlysis® Buprenorphine (cut-off conc. 5ng/ml) Drugs producing positive results
Norbuprenorphine

DRI® Ethyglucuronide (cut-off conc. 500ng/ml) Drugs producing positive results
Ethyglucuronide

Ref: Thermofisher Scientific CEDIA Drugs of abuse documentation.

NB: Lists are not exhaustive; please contact the laboratory if confirmation of a positive result is required.

We have found that CEDIA® Amphetamine/Ecstasy assay may cross-react with other compounds particularly new psychoactive substances (NPS, 'Headshop' Drugs/Bath Salts/Legal Highs). If you have any queries about an Amphetamine positive result please contact the laboratory. Confirmatory analysis can be carried out on request.

Appendix 2 Benzodiazepine Identifications (Benz ID)

The routine immunoassay screening method for benzodiazepines is unable to distinguish between metabolites, therefore urinary benzodiazepine identifications are carried out where required using LC/MS which can specifically target and unambiguously identify the drug or metabolite present.

Benzodiazepines can be short-acting or long acting and depending on the drug taken they can persist for an extended time in the urine of habitual users, even after use has ceased. A further complication is that the metabolic pathways of benzodiazepines can often result in common metabolites (the most significant being Oxazepam), meaning that in many cases it may not be possible to unambiguously determine the parent drug (see Figure 10 below).

Many factors such as how much fluid has been consumed prior to giving the sample, the time since the drug was taken, the physical condition and metabolism of the patient etc. may influence the dilution of a urine sample and therefore the drug level present. Therefore drug levels in urine may be subject to large fluctuations. If urine is dilute, drug levels will be lowered. Consequently urinary levels of benzodiazepines are not performed in the NDTC Laboratory

Figure 10 - Benzodiazepines and their metabolites

Benzodiazepine	Trade name	Metabolites
Flurazepam	Dalmane, Dalmapam	2-hydroxyethylflurazepam
Flunitrazepam	Rohypnol	7-aminoflunitrazepam, nifoxipam
Alprazolam	Xanax, Gerax	α-hydroxyalprazolam
Chlordiazepoxide	Librium	demoxepam, nordiazepam, oxazepam
Clobazam	Frisium	desmethyclobazam
Lorazepam	Ativan	Lorazepam
Midazolam	Buccolam	α-hydroxymidazolam
Prazepam	Centrax	oxazepam
Triazolam	Halcion	α-hydroxytriazolam
Temazepam	Insomniger, Nortem	oxazepam
Diazepam	Valium, Anxicalm	oxazepam, temazepam, nordiazepam
Bromazepam	Lexotan	3-hydroxybromazepam
Clonazepam	Rivotril	7-aminoclonazepam
Oxazepam	Serax	oxazepam
Nitrazepam	Mogadon	7-acetamidonitrazepam, 7-aminonitrazepam
Lormetazepam	Noctamid	Lorazepam
Estazolam		3-hydroxyestazolam
Etizolam		α-hydroxyetizolam
Phenazepam		3-hydroxyphenazepam
Deschloroetizolam		9-OH-methyl-, 2 OH-ethyl, 6-OH-deschloroetizolam
Diclazepam		delorazepam, lorazepam, lormetazepam
Flubromazepam		hydroxy-flubromazepam
Pyrazolam		Pyrazolam
Clonazolam		7-aminoclonazolam
Flunitrazolam		7-acetamidoflunitrazolam, 7-aminoflunitrazolam
Flubromazolam		Flubromazolam
Nifoxipam		3-OH-7-aminodesmethylflunitrazepam, 3-OH-7-acetamidoflunitrazepam
Flualprazolam		Unknown
Ketazolam	Anxon	norketazolam, diazepam, nordiazepam, oxazepam,
Adinazolam	Deracyn	N-desmethyladinazolam, α-hydroxyalprazolam, estazolam
Halazepam	Paxipam	nordiazepam, 3-OH halazepam

Appendix 3 Opiate Identifications (Opia ID)

The routine screen by immunoassay will be positive when certain opiates are present in the urine sample at a concentration above the cut-off concentration of 300ng/ml Heroin. Morphine, Codeine and Dihydrocodeine will cause a positive result in the screening assay when present at levels above the cut-off.

Naloxone (present in Suboxone) can also occasionally cause an opiate positive on the routine screen if present at very high levels.

Oxycodone has also been known to cause an opiate positive at very high levels; at therapeutic levels it should not cause a positive.

Tramadol does NOT cause an opiate positive on the routine screen and so needs to be requested if required.

Fentanyl does NOT cause an opiate positive on the routine screen and so needs to be requested if required.

If the routine test is opiate positive and further analysis is requested in order to determine the source of the opiate positive, a 6-AM screening test will first be performed on the sample. As 6-AM is a unique metabolite of Heroin it is only present in urine after recent ingestion of Heroin, a positive 6-AM result indicates that Heroin has been taken in the recent past (within 24 hours). A 6-AM negative result may indicate either that the ingestion of heroin is not recent or that the individual has not taken Heroin and that the sample is opiate positive due to a non heroin opiate. An 'opiate positive, 6-AM negative' test can be subjected to further testing by LC/MS in order to determine what opiate has been taken.

Metabolism of Opiates

Because of the similar metabolic pathways of some opiates it can be difficult to distinguish between the use of heroin, morphine or codeine. The unique metabolite of heroin (6-acetyl morphine) has a short half life and may no longer be present in urine. Both morphine and codeine may be present after heroin use, morphine use or codeine use. The ratio of codeine to morphine is then used to indicate the drug initially taken. If more codeine than morphine is present in a sample it would indicate that codeine has been ingested. If more or similar levels of morphine and codeine are present in a sample it is not possible to definitively determine which drug was taken.

Figure 11 Opiates and their metabolites

Drug Taken	Metabolites/Drugs found
Heroin	6-AM and Morphine, Codeine (as impurity)
Codeine	Codeine and Morphine
Dihydrocodeine	Dihydrocodeine
Morphine	Morphine
Oxycodone	Oxycodone and Oxymorphone
Naloxone	Naloxone
Tramadol	Tramadol, O-desmethyltramadol
Tapentadol	Tapentadol, N-desmethyltapentadol
Fentanyl	Fentanyl
Naloxone	Naloxone

NB: If Tramadol, Oxycodone, Fentanyl or Tapentadol analysis is required, this must be specifically requested by listing the drug e.g. Fentanyl.

Appendix 4 New Psychoactive substances (NPS)

The terms 'Legal highs', 'Head Shop products' or 'New Psychoactive Substances' refer to a new drugs with stimulant or psychoactive effects which had not been encountered as drugs of abuse or recreational drugs until recent years.

Initially these were sold as 'legal' highs in so-called 'Head Shops' in Ireland and via the internet. Various legislative changes led to these being controlled drugs and the so called 'Head Shops' were closed down.

Unfortunately the controls put in place have not eliminated the use of these substances and they are still in use in the illicit drug market.

The HSE-NDTC laboratory is currently testing in the order of 500 samples annually for New Psychoactive Substances (on request only). The profile of drugs detected over the years has changed over time and the panel of drugs screened is updated periodically to include more recent variants in the compounds tested and as reference standards become available.

The parent drug is looked for in these analyses, as little is known about the metabolism of these drugs and in general, drug standards of the metabolites are not yet commercially available. There may be metabolites of these compounds that are present in higher concentrations than the parent in the urine and present for a longer time than the metabolite. It is not known how long any of these compounds are present in the urine.

The profile of drugs detected over the years has changed over time and the panel of drugs screened is updated periodically to include more recent variants in the compounds tested and as reference standards become available.

The laboratory does not test for the synthetic Cannabinoids (spice compounds) it only tests for the powders or "bath salts". A negative result for the 'Headshop' test does not mean that an individual has not taken a so-called 'Headshop' drug, it just means that they have not taken one of the compounds tested for in our assay.

For the latest information on these products and the legislation relating to them, refer to www.drugs.ie and the Irish Legislation website http://www.irishstatutebook.ie

For the latest information on NPS in Europe see the EMCDDA annual report and other publications on the EMCDDA website http://www.emcdda.europa.eu/

Appendix 5 NDTC Publications

NDTC Laboratory Journal Articles

Publication Year	Article details
2009	"1-Benzylpiperazine (BZP) Abuse Amongst Attendees of The Drug Treatment Centre Board"; S McNamara; The Irish Medical Journal, June 2009; Vol. 102, No. 6.
2010	"Head Shop" Compound abuse amongst attendees of The Drug Treatment Centre Board; S McNamara, S Stokes, N Coleman; The Irish Medical Journal, May 2010 Vol. 103: 5
2011	"Quantitative evidence of a heroin drought" S Stokes; Drug Net Ireland, Issue 40, Winter 2011
2013	"Screening of Stimulants Including Designer Drugs in Urine Using a Liquid Chromatography Tandem Mass Spectrometry System" P O'Byrne; P Kavanagh; S McNamara; S Stokes; Journal of Analytical Toxicology 2013; doi: 10.1093/jat/bks091
2015	Eurosurveillance, Volume 20, Issue 40, 08 October 2015, Rapid communication "Injection of new psychoactive substance snow blow associated with recently acquired HIV infections among homeless people who inject drugs in Dublin, 2015" C Giese, D Igoe, Z Gibbons, C Hurley, S Stokes, S McNamara, O Ennis, K O'Donnell, E Keenan, C De Gascun, F Lyons, M Ward, K Danis, R Glynn, A Waters, M Fitzgerald on behalf of the outbreak control team
2015	"Pregabalin Abuse amongst Opioid Substitution Treatment Patients" S McNamara, S Stokes, R Kilduff, A Shine; The Irish Medical Journal, Nov/Dec 2015 Vol. 108 No. 10
2017	"New Psychoactive Substances in Europe Conference, Poznan" S Stokes, Drug Net Ireland, Issue 60, Winter 2017
2017	"Increase in cocaine use among OST patients". S Stokes, Drugnet Ireland, Issue 63, Autumn 2017
2019	"The Emergence of New Psychoactive Substance (NPS) Benzodiazepines. A Survey of their Prevalence in Opioid Substitution Patients using LC-MS", S Mc Namara, J Nolan, S Stokes, Ir Med J, 2019 Aug 1;112 (7):970.
2020	'Does Opioid Substitution Treatment have a protective effect on the clinical Manifestation of COVID-19? M. Eagleton, S. Stokes, F. Fenton, E. Keenan, Br J, Anaesthesia 2020 125: e382–3

Copies of articles and posters (below) can be forwarded to customers, if requested.

NDTC Poster Submissions

Publication Year	Poster details
2010	Study of "Head Shop" drugs in samples analysed by The Drug Treatment Centre Board Laboratory, Dublin. UKIAFT Glasgow , S Mc Namara, S Stokes, A Shine, J Hannon
2010	Investigation into Oxycodone use in a cohort of Methadone maintenance patients using immunoassay. Association of Clinical Biochemists of Ireland Conference, 2010 M Kehoe, L Lawlor, S Stokes
2010	Drug Analysis Results from the Laboratory of the Drug Treatment Centre Board 2005 -10. Association of Clinical Biochemists of Ireland Conference, 2010 S Stokes, J Burdett, L Lawlor, M Kehoe, S Mc Namara
2011	Ethyl Glucuronide: A marker for alcohol use in methadone maintenance patients. Association of Clinical Biochemists of Ireland Conference 2011 L Lawlor, S Stokes, G Smith
2012	Positive CEDIA Amphetamine/Ecstasy Assay results arising from New Psychoactive Substances, Society of Forensic Toxicologists Annual Meeting 2012. S Mc Namara, S Stokes, P O'Byrne, P Kavanagh
2012	Positive CEDIA Drugs of Abuse Assay results arising from New Psychoactive Substances, Society of Forensic Toxicologists Annual Meeting 2012. S Stokes, S Mc Namara, I Walsh, P Kavanagh
2012	Removing the 'middleman' in a clinical laboratory environment M Kehoe, L Lawlor, P Murray, S Stokes
2012	Benzodiazepines: A survey of prevalence in methadone maintenance patients using LC/MS. S Mc Namara, P O' Byrne, S Stokes, R Kilduff, N Coleman, E Burke, S Conroy, G Smith
2012	"Spice Drug Prevalence in a Methadone Maintenance Treatment Centre" UKIAFT Annual General Meeting Dublin 2012 Louise Lawlor, Grainne Gaynor, Siobhan Stokes
2013	Prevalence of Spice compounds in patients using drug addiction services in Ireland. UKIAFT 2013, L Lawlor, G Gaynor, S Stokes.
2014	Prevalence of Fentanyl Use in patients using drug addiction services in Ireland Association of Clinical Biochemists of Ireland Conference, 2014 E Burke, S McNamara, L Lawlor
2015	New Psychoactive Substances Prevalence in Samples Tested in the NDTC laboratory 2010-2015, S McNamara, S Stokes, Á Shine, R Kilduff, P O'Byrne
2017	Evaluation of a novel immunoassay for urinary Zopiclone testing Association of Clinical Biochemists of Ireland Conference 2017 C Donaghy, S Mc Namara, S Stokes
2017	Interferences in Proficiency Testing Samples Association of Clinical Biochemists of Ireland Conference 2017 M Kehoe, C Donaghy, S Mc Namara, M Eagleton, S Stokes.
2017	Better sample, Better result – An Oral Fluid Sample Quality Improvement Project Association of Clinical Biochemists of Ireland Conference 2017 C Donaghy, J Nolan, J Hannon, A Shine, S Stokes
2017	New Psychoactive Substances Prevalence in Samples Tested in the NDTC laboratory 2010-2016 , Association of Clinical Biochemists of Ireland Conference 2017 S McNamara, S Stokes, Á Shine, R Kilduff, P O'Byrne
2018	Benzodiazepines: "Are there new kids on the block"? A survey of prevalence in opioid substitution patients using LC/MS. UKIAFT Conference 2018, Dublin S Mc Namara, S Stokes, J Nolan, M Eagleton.
2019	A 'pre-analytical' audit of extra-laboratory errors in urine samples sent for toxicology testing to HSE NDTC Laboratory. PALM conference, 2019 C Donaghy, N Mesinovic, M Eagleton, S Stokes.
2020	ISO/IEC17025:2017 Risks & Opportunities A focus on Pre-analytics, Analytics and Post-analytics. PALM conference, 2020. C Donaghy, M Kehoe, S Stokes.