Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

LÁRIONAD NÁISIÚNTA CÓIREÁLA DRUGAÍ

NATIONAL DRUG TREATMENT CENTRE

DRUG ANALYSIS LABORATORY

HSE National Drug Treatment Centre
Drug Analysis Laboratory

A Guide to Service Users

6th Edition April 2017

Introduction

This toxicology laboratory guide has been written for medical, nursing and support staffs who avail of The HSE Drug Treatment Centre (HSE-NDTC) drug analysis service. It provides general information on how to access this service and details the range of tests available.

The Drug Analysis Laboratory provides a national drug analysis service to the HSE Addiction Services, general practitioners, hospitals (general, psychiatric and maternity), juvenile detention centres, voluntary organizations, the Dublin Drug Court and the Probation Services.

I welcome the 6th publication of this user guide and I commend the hard work of the laboratory team for its compilation and distribution.

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HSE-NDTC Laboratory

April 2017

General Information

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Samples for Drug Analysis

Samples for drug testing include urine, blood, hair and oral fluid.

Table 1: Drug detection times in biological matrices

Sample type	Detection time range	Drug use detected
Oral fluid	0-48 hours	Acute, under the influence
Blood	0-48 hours	Acute, under the influence
Urine	Days - weeks	Recent
Hair	Use over extended time	Chronic/ Forensic

Urine

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 for testing for the presence or absence of drugs. However, urine is unsuitable for determining drug levels due to the many factors which influence the composition and concentration of urine.

Blood

Blood is more suitable than urine for determining drug levels however it is more difficult to collect especially from intravenous drug users and drug levels are low compared to levels found in urine. The time during which the drug can be detected after use is in the order of hours, as opposed to days.

Oral fluid (Saliva)

Sampling may be time consuming and the volume of oral fluid is small. Drug levels in oral fluid are low compared to levels found in urine. Testing of oral fluid is not as well developed as urine testing and it has a short window of detection.

Hair

Hair can demonstrate a historical record of drug use. However, the sampling must be carried out according to a detailed protocol and the analysis is very time consuming and highly specialized. There can be issues such as external contamination of the hair. Hair is not routinely tested by this laboratory.

Consent

The HSE NDTC Drug Analysis 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.

Packaging and Transport

The laboratory will only accept samples packaged according United Nations (UN) regulations. Under these regulations samples are divided into two groups:
1) Diagnostic: a specimen collected for the purpose of diagnosis.
2) Infectious: a specimen containing a viable microorganism that is known, or reasonably believed, to cause disease.

UN approved packaging consists of a **triple packaging** system:

- **Primary receptacle** – the urine bottle. This must be leak-proof, clearly labeled and wrapped in enough absorbent material to absorb all fluid in case of breakage.
- **Secondary receptacle** - used to enclose the primary receptacle. This must be durable and leak-proof. Several primary receptacles may be placed in one secondary receptacle. Sufficient additional absorbent material must be used to cushion multiple primary receptacles.
- **Outer packaging** – the secondary receptacle is placed in an outer package which protects it and the contents from outside influences such as physical damage and / or water while in transit.

Supply

Packaging is available commercially (Please contact the laboratory directly if you require further information).

NOTE: It is the responsibility of the sender to ensure the correct designation, packaging, labeling and documentation of all specimens.

Sample Collection

The procedure for sample collection is detailed in Table 2 below (*Standard precautions and procedures should be followed when sampling).*

Table 2: Sample collection

Sample Type	Collection Details
Urine	• *Use clean plastic container without preservative.* • *20 - 30mls where possible.* • *Supervised to ensure sample is not adulterated.* • *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 place (preferably refrigerated) pending dispatch to the laboratory* • *Sample should be dispatched to Laboratory as soon as possible*
Oral Fluid	• *Use Quantisal collection device.* • *Observe donor 10-15mins without food or drink prior to collection.* • *Supervise collection (approx. 5 mins).*
Blood (Serum Methadone only)	• *Serum Red Cap Tube with 10 mls where possible*
Hair	• *Details on hair collection can be obtained from the Laboratory*

Sample Label Information

The following information must be included on the sample container and any request form when submitting a sample for analysis:

- Patient's full name*
- Date of birth*
- Name of clinic or hospital*
- Date of sample collection*
- Name of Doctor
- DAIS code (where applicable)
- Sample type

*Mandatory

Failure to include the above information hinders the processing of a sample.

Non-Compliant Samples

Non-compliant samples are samples which do not demonstrate the **mandatory information** required to identify a particular sample, i.e. full name, date of birth, sample date and location from which the sample was sent.

Samples missing any of the aforementioned data **cannot be analysed**. The laboratory will make every effort to obtain the correct sample identification in order to proceed with analysis.

Leaking samples are 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 sender by means of a comment on report or a non-compliance form detailing the nature of the non-compliance.

Request Forms

Request forms for routine screening are available on our website www.addictionireland.ie.

Range of Testing

Testing is divided into several categories including:

- Testing for adulteration
- Routine urine screening
- Non-routine urine screening
- Confirmatory analysis
- Oral fluid screening
- Serum Methadone levels.

See details in the Table 3 below. (See page 5)

Testing for adulterants

Adulteration testing refers to tests carried out to determine whether a sample is genuine or if it has been tampered with. Methods of urine adulteration include dilution with, addition of, or substitution by, a drug-free substance or solution.

Dilution is probably the most common method of adulteration used by drug users to evade detection of misuse. Creatinine levels in urine can indicate the extent of this dilution, therefore all samples received for analysis are tested for creatinine.

'**Normal**' urine should have a Creatinine concentration in the range 80-200mg/dL.

'**Dilute**' urine is indicated by a Creatinine reading of less than 20mg/dL.

'**Abnormal**' urine is indicated by a Creatinine reading of <2mg/dL.
No other test results will be reported on these samples

Abnormal **pH** readings will indicate tampering of a sample by the addition of or substitution by, another substance or liquid.

Table 3: Range of Testing

Sample type	Test Type	Method	Test	Window of Detection	Normal Turnaround Times
Urine	Routine Screen	IA	**Opiate Class**	3-10 days	24-48 hours
			6-AM	24 hours	
			Benzodiazepine Class	2-28 days	
			EDDP	Unknown	
			Cannabis class	2-28 days	
			Cocaine	2-4 days	
			Amphetamine Class	1-2 days	
		Enzymatic	**Alcohol**	1-2 days	
		Chemical	**Creatinine**	n/a	
	Non-Routine	Enzymatic	**Pregnancy**	n/a	
		Chemical	**pH**	n/a	
			Glucose	n/a	
		IA	**EtG – Alcohol marker**	1-4 days	
			Buprenorphine	2-4 days	
	Confirm	LC-MS	**Opiate Identification**	3-10 days	5-10 days
			Zopiclone	Unknown	
			'Headshop' products (psychoactive substances)	Unknown	
			THC-COOH (Cannabis metabolite)	2-28 days	
		LC-MS	**Benzodiazepine identification**	2-28 days	
Oral Fluid	Screen	IA	**Opiate Class**		3-5 days
			6-AM		
			Benzodiazepine Class		
			Methadone		
			Cannabis class		
			Cocaine		
			Amphetamine		
			Methamphetamine		
Blood	Screen	IA	**Methadone levels**	n/a	Contact Lab

Please Note: Turnaround time is measured from time of receipt of sample at the laboratory

Abbreviations:
6-AM: 6-acetylmorphine, primary metabolite of heroin; EtG – Ethyl Glucuronide (Alcohol biomarker)
EDDP: 2-ethylidine-1,5-dimethyl-3,3-diphenylpyrrolidine, primary metabolite of methadone
LC-MS: Liquid Chromatography Mass Spectrometry; IA: Immunoassay; Screen: Screening Test

Routine Screening Analysis

The majority of drug testing performed by the laboratory falls into this category. Routine screening is carried out by immunoassay, enzyme assay or chemical assay. These are rapid methods used for screening drugs of misuse. Tests included in routine screen are detailed in table 3 above.

Immunoassay is a **qualitative method** which indicates only the presence or absence of a drug/drug class in a sample.

Each test by immunoassay has **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.

With the exception of alcohol, the current format used does not give any information about the level or concentration of the drug present.

It should be noted that all analytical results are subject to **Uncertainty of Measurement (UoM),** *see section on Uncertainty of Measurement (page 11). The performance of qualitative test results around the cut-off concentration is routinely monitored by the use of quality controls which are run with every batch of samples. Clinical consideration and judgment should be applied to all immunoassay test results. Confirmatory analysis may be requested for a positive drug screening result if required. (See page 8)

'True and 'False' Positives

Care should be taken when interpreting immunoassay screening results, as some over the counter drugs will give 'true' positive results. An example of this is Solpadeine® which will give a positive opiate result because it contains codeine, which is also classified as an opiate type drug.
Some drugs and medications can also produce **' false' positive results** when tested using immunoassay, due to cross reactivity and further confirmatory analysis may be necessary. This cross reactivity occurs most **commonly** with **opiate** and **amphetamine** drug classes.

A study carried out in our laboratory showed that for the **CEDIA® Amphetamine/Ecstasy assay**, cross reaction was occurring with other compounds particularly new psychoactive substances such as cathinones **('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. Benzodiazepines, cannabis, cocaine and EDDP immunoassay tests are relatively specific and rarely produce false positive results. *See **Appendix 1 for table of urine kits cross-reactivities.***
Because of cross-reactivity, screening results by immunoassay alone are not legally defensible and further confirmation of the test result is required depending on the purpose of the testing.

Therapeutic drug monitoring of Methadone

Therapeutic drug monitoring of methadone is performed to identify rapid Methadone metabolisers and can **help with titrating Methadone dosages**, provided other factors are considered when interpreting the result, e.g. sex, weight, time of dose, time of sampling etc. (It is always important to treat the patient, not the level).

Blood samples should only be submitted for serum Methadone level testing if the following criteria have been adhered to:

CRITERIA

- 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**.
- The **time** must be the **same** as the previous 3 days +/- 30 minutes.
- Samples must be collected into a **serum tube**.
- The sample must be accompanied by a **request form**/ letter which includes time of dose on previous day, time of dose on day of sampling and time of blood collection.

Failure to adhere to these guidelines will result in **unreliable data** and defeat the purpose of carrying out the procedure.

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 0.83ug/ml (range, 0.57 -1.06) and declined to 0.46mg/L (range, 0.28-0.79) 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 to prevent withdrawal systems in narcotic maintenance patients (i.e. 50-100ng/ml)'.
[Baselt 2004, Disposition of Toxic Drugs and Chemicals in man, 6th edition, p. 642 – 643]

Non-Routine testing

Non-routine tests include 6-Acetylmorphine (6-AM) the primary metabolite of Heroin, Zopiclone, Buprenorphine, 'Headshop' drug analysis (New Psychoactive substances, see *Appendix 4),* pregnancy testing, pH, glucose and Ethyl Glucuronide (EtG).

These tests are carried out on request only.
The full range of analyses available is indicated in Table 3 (page 5).

New Tests

Ethyl Glucuronide (EtG)

EtG is a direct metabolite of ethanol and can be detected several days after the elimination of alcohol from the body thus increasing the window of detection of alcohol use.

Confirmatory Analysis

Confirmatory analysis is carried out using gas chromatography mass spectrometry (GC-MS) and liquid chromatography mass spectrometry (LC-MS).

Confirmatory test results are **legally defensible** provided the sample integrity can be proven (see Sample Collection and Chain of Custody information).

All confirmatory testing (with the exception of chain of custody samples) should be specifically **requested in writing** by a doctor.
See Table 3 (page 5) and Appendices 2 & 3 for further details.

Oral Fluid testing

Oral Fluid tests include Opiates, Benzodiazepines, Methadone, Amphetamine, Methamphetamine, Cocaine, Cannabis and 6-Acetylmorphine (the primary metabolite of heroin). These tests are carried out on request only. Currently the laboratory recommends using **Quantisal® collection devices** (product code QS-0025) available from Alere Toxicology PLC (Concateno) 0044-1235861483.

Depending on the drug used, dose, and route of administration, a drug may be detected in oral fluid in less than one hour after use and remain detectable up to 48 hours after last use.
Substances such as **food, beverages**, over-the-counter **medication**, and mouthwash can affect the oral fluid drug test results. For this reason, before collection of saliva or oral fluid, the collector should observe the donor for a **10-15 min period** in which **the donor should not smoke, consume food or drink**.

The full range of analyses available is indicated in Table 3 (page 5) above.

Subcontracted testing

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

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.

Chain of custody involves **fully documenting** who donated, collected and handled the sample thereafter. The HSE-NDTC laboratory can provide information on chain of custody collection kits and sampling procedures. All **positive immunoassay** screening test results **must be confirmed** by a second analysis using a confirmatory analytical method.

For further information please contact Laboratory Customer Services.

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 in a cool dark place, if refrigeration is not available. Post analysis, the laboratory will **retain samples for 14 days in refrigerated conditions**, after which they will be **disposed of safely**. 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.

Unless otherwise agreed, all **Chain of Custody samples will be frozen** and retained for **36 months** and all **Probation samples will be frozen and retained for 12 months** post analysis.

Reporting of Results

The **front page** of each report **details the customer** name and address, date on which each report is generated and **scope of INAB accreditation** (for accredited tests only).

Each **patient** is identified by name, date of birth, clinic code and chart number.

Each **sample** is identified by a unique barcode 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.

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 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.

Mode of reporting
The method of report transmission used must be **agreed in advance** with Laboratory Customer Services. Routine modes of reporting available are post or electronically (LER, DAIS).

Post:
Reports sent by post will be dispatched as soon as possible after completion of analysis.

Fax:
This reporting method **is being phased out**. Where this method is in use sample results will be faxed as soon as possible after completion of analysis.
To ensure the confidentiality of the information transmitted, faxing of reports will only occur if the laboratory has been provided with a written and agreed secure fax number.

Electronic Reporting

Drugs Aids Information System (DAIS): HSE Addiction Service defined user's access laboratory results via DAIS. This is completed once the laboratory authorises the samples.

Laboratory Electronic Reporting (LER): The LER is a web-based system developed for NDTC customers which allows authorised users to access results electronically. Sample results are available in the system as soon as the analysis is complete.

Verbal reporting:
Verbal reporting can only be accommodated in the case of an emergency.

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 judgement 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.

Uncertainty of Measurement for each test (see figures in brackets below).

URINE TESTS

OPIATE(+/-14.71%); 6-AMOR (+/-14.76%); BENZ(+/-12.26%); EDDP(+/-12.40%); CANN (+/-14.46%); AMPH (+/-14.46%);COCA (+/-12.14%); ALCO (+/-17.79%); ETG (+/-12.16%); BUP(+/-15.5%); pH 3.0 (+/-12.0%); pH 11.0 (+/-11.60%) ;CREA 2mg/dL(+/-12.18%); CREA 20mg/dL(+/-13.77%)

ORAL FLUID TESTS

OPIATE(+/-6.8%); 6-AMOR (+/-1.7%); BENZ (+/-2.9%); CANN (+/-1.6%); AMPH (+/-6.0%); COCA (+/-3.0%), METH (+/-9.5%); METHAMPH (+/-10.4%).

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. (Approx. 3% of all samples run are quality controls).

In order to assess performance, the laboratory is involved in five external Quality Assurance schemes:

- **LGC** – Drugs of abuse in urine, Ethanol in urine and Drugs in Oral Fluid
- Irish External Quality Assessment Scheme (**IEQAS**) – Drugs of abuse in urine.
- **Arvecon** – Ethylglucuronide in urine

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

Accreditation

Our laboratory is accredited by the Irish National Accreditation Board (INAB) to **ISO 17025** (Registration number: 169T)**. ISO 17025** is the main standard used by testing and calibration laboratories globally.

The ISO 17025 standard is a quality system aimed at improving the ability to consistently produce valid results. The two main aspects of ISO/IEC 17025 accreditation are Management and Technical requirements. Management requirements are primarily related to the operation and effectiveness of the quality management system within the laboratory, while technical requirements address the competence of staff, methodology and test/calibration equipment.

In order to maintain this high standard, our laboratory **is assessed annually** by a team of Irish and international external auditors.

The scope of our accreditation can be viewed at http://www.inab.ie/Directory-of-Accredited-Bodies/Laboratory-Accreditation/Testing/HSE-National-Drug-Treatment-Centre.html

Membership and Representation

To ensure best practice and to keep up to date with the latest developments and trends in drug misuse, laboratory staff have professional membership and attend meeting of various international societies, these include:-
ACBI – Association of Clinical Biochemists of Ireland
TIAFT - The International Association Forensic Toxicologists
UKIAFT - UK and Ireland Association of Forensic Toxicologist

The laboratory is also represented at the Early Warning and Emerging Trends (EWET) committee of the National Advisory Committee on Drugs (NACD)

Appendix 1

Urine Immunoassay Cross Reactivity Tables

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)

[This list is 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 ('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.

Opiate Class (*cut-off conc.300 ng/ml)* Drugs producing positive results		
6-Monoacetylmorphine Diacetylmorphine Hydrocodone Hydromorphone Morphine	Morphine-3-Glucuronide Morphine-6-Glucuronide Morphine Sulfate Nalorphine HCl Naloxone	Naltrexone HCl Oxycodone Oxymorphone Pholcodine Thebaine

[This list is not exhaustive] – Please contact the laboratory if confirmation of a positive result is required

6-Acetylmorphine *(10mg/dL)* Drugs producing positive results
6-Acetylmorphine

[This list is not exhaustive] – Please contact the laboratory if confirmation of a positive result is required.

Cannabis (*cut-off conc.50 ng/ml)* Drugs producing positive results		
11-Nor- Δ -9-THC-COOH 11-Nor Δ 8-THC-COOH Δ 9-THC (Dronabinol)	11-Hydroxy- Δ- 9-THC 1- Δ -9-THC-Glucuronide 8-OH- Δ -9-THC	8・,11-di-OH- Δ -9-THC Cannabinol

[This list is not exhaustive] – Please contact the laboratory if confirmation of a positive result is required

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

[This list is not exhaustive] – Please contact the laboratory if confirmation of a positive result is required

Ethyl Alcohol *(mg/dL)* Drugs producing positive results
Ethanol n-Propanol

[This list is not exhaustive] – Please contact the laboratory if confirmation of a positive result is required

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

Oral Fluid Immunoassay Cross Reactivity

We have limited information on cross-reactivity for Oral Fluid tests. Triazolam (Halcion) causes false positive results for 6-Acetylmorphine (6-AM) oral fluid test in patients who are prescribed this drug. Patients on Halcion are therefore unsuitable for oral fluid testing. Urine testing should be used for these patients.

Appendix 2

Interpretation of Benzodiazepine Identifications

The routine immunoassay screening method for benzodiazepines is unable to distinguish between metabolites, therefore urinary benzodiazepine identifications are carried out where required using more sophisticated techniques (LC-MS and GC-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 all use has ceased. A further complication is that the metabolic pathways of benzodiazepines can often result in common metabolites (the most significant being Oxazepam) and this means that in many cases it may not be possible to determine the parent drug. Therefore it can be difficult to unambiguously identify which parent drug(s) was originally consumed.

See Table 4 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 should be interpreted with extreme caution. There is no direct correlation between urine drug levels and blood drug levels.

Parent Drug	Target Drug/Metabolite(s) Tested	Parent
Alprazolam	α–hydroxyalprazolam, Alprazolam	Present
Bromazepam	Bromazepam	Present
Chlordiazepoxide	Chlordiazepoxide, Nordiazepam, Oxazepam, demoxepam	Trace
Clobazam	Clobazam	Trace
Clonazepam	Clonazepam, 7-aminoclonazepam	Present
Diazepam	Diazepam,Nordiazepam,Oxazepam,Temazepam	Trace
Estazolam	Estazolam	Trace
Flunitrazepam	Flunitrazepam, 7-Aminoflunitrazepam	Not usually detected
Flurazepam	2-Hydroxyethylflurazepam	Trace
Lorazepam	Lorazepam glucuronide	Present after hydrolysis
Midazolam	Midazolam	Trace
Nitrazepam	Nitrazepam	Trace
Oxazepam	Oxazepam, Oxazepam glucuronide	Present after hydrolysis
Prazepam	Oxazepam	Not usually detected
Temazepam	Temazepam, Oxazepam	Present
Triazolam	Triazolam, a-hydroxytriazolam	Trace

Table 4: Benzodiazepine and Metabolites

Appendix 3
Interpretation of Opiate Identifications

Heroin is metabolised in the body, firstly to 6-acetylmorphine (6-AM) and then to Morphine.

HEROIN → 6 Acetyl Morphine (6-AM) → Morphine

The presence of 6-AM proves the use of Heroin. However, 6-AM has a short half-life of approx. 24 hours in urine after last use, and therefore Morphine is the most commonly detected metabolite in Heroin abuse, due to its longer window of detection.

Morphine in urine can also result from the metabolism of Codeine, which is included in many 'over the counter' painkillers.

CODEINE → Morphine

To add to the complexity, Acetylcodeine is an impurity often detected in Heroin. Acetylmorphine also metabolises to Codeine.

HEROIN containing impurity **Acetylcodeine → Codeine**
and
HEROIN → 6 Acetyl Morphine (6-AM) → **Morphine**

Because of these similar metabolic pathways, it can be difficult to distinguish between the use of Heroin, Morphine or Codeine, or the use of a combination of more than one of these, because both Morphine and Codeine may be present after Heroin use, Morphine use, or after Codeine use.

The routine immunoassay screening method for opiates is targeted to detect Morphine, Codeine and Dihydrocodeine (or their metabolites) but it cannot distinguish between them.

Procedure for Opiate Identification:
A positive opiate result by immunoassay will be obtained if any one, or a combination of the above, is present above the cut-off concentration of 300ng/ml.

In order to identify which opiate is present in a sample, further testing is required.

Firstly, a 6-Acetylmorphine (6-AM) test is carried out and if positive, Heroin use is strongly indicated. If negative, further confirmatory testing must be performed. Because of the common metabolites, it may not always be possible to unambiguously differentiate between Heroin, Morphine and Codeine use (even using sophisticated confirmatory analysis techniques). See Table 5 below.

Table 5: Interpretation of Opiate ID results

Immunoassay Result	Result Confirmatory analysis	Interpretation
6-AM	n/a	Heroin misuse
Opiate	Morphine	Use of Morphine or Heroin or Codeine or a combination of these
Opiate	Codeine	Confirmation of Codeine use
Opiate	Morphine and Codeine	Use of Morphine or Heroin or Codeine or a combination of these
Opiate	Dihydrocodeine	Confirmation of Dihydrocodeine use

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 have been enacted in Ireland since 2009 to deal with the misuse of these substances. These included various orders declaring specified substances to become controlled drugs under the Misuse of Drugs Act 1977 and Misuse of Drugs (Amendment) Regulations which have all combined to greatly extend the range of banned substances.

As a separate measure the Criminal Justice (Psychoactive Substances) Act 2010 which made it an offence, punishable by up to five years imprisonment, to sell or supply for human consumption, substances having psychoactive effects which are not specifically proscribed under the Misuse of Drugs Acts.

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.

There have been over 600 NPS notified to the EMCDDA and of these, circa two thirds have been notified since 2012. Recently synthetic benzodiazepines and synthetic opioids have emerged including extremely potent synthetic fentanyls. There is no sign of a decrease in this flow of new drugs with 98 new psychoactive substances reported last year. While circa 250 drugs are internationally controlled, the rest are not.

The Laboratory of the HSE-NDTC is currently testing in the order of 500 samples annually for New Psychoactive Substances (on request only). The profile of drugs detected over the last 5 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.

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/

NDTC Laboratory Journal Articles

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2. "Head Shop" Compound abuse amongst attendees of The Drug Treatment Centre Board; S McNamara, S Stokes, N Coleman; The Drug Treatment Centre Board, 30-31 Pearse St, Dublin 2., The Irish Medical Journal, May 2010 Vol. 103, No. 5

3. "Quantitative evidence of a heroin drought" Siobhan Stokes, Drug Net Ireland, Issue 40, Winter 2011

4. "Screening of Stimulants Including Designer Drugs in Urine Using a Liquid Chromatography Tandem Mass Spectrometry System" Paul M. O'Byrne; Pierce V. Kavanagh; Sinead M. McNamara; Siobhan M. Stokes, Journal of Analytical Toxicology 2013; doi: 10.1093/jat/bks091

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   Rapid communication "Injection of new psychoactive substance snow blow associated with recently acquired HIV infections among homeless people who inject drugs in Dublin, Ireland, 2015"

   C Giese [1 2], D Igoe [2], Z Gibbons [3], C Hurley [4], S Stokes [3], S McNamara [3], O Ennis [4], K O'Donnell [2], E Keenan [3], C De Gascun [5 6], F Lyons [7], M Ward [4], K Danis [1 8], R Glynn [4], A Waters [5], M Fitzgerald [4], on behalf of the outbreak control team [9]

6. Contributed to EMCDDA–Europol Joint Report on a new psychoactive substance: 1-phenyl-2-(1-pyrrolidinyl)-1-pentanone (α-PVP) EMCDDA, Lisbon, September 2015

7. "Pregabalin Abuse amongst Opioid Substitution Treatment Patients" S McNamara, S Stokes, R Kilduff, A Shine, HSE National Drug Treatment Centre, McCarthy Centre, 30-31 Pearse Street, Dublin 2; The Irish Medical Journal, November December 2015 Vol. 108 No. 10

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