Drugs of Abuse Testing Immunoassays

Thermo Fisher Scientific is a leading provider of Immunoassays for Drugs of Abuse Testing

Thermo Fisher Scientific continues to forge the way in testing for drugs of abuse with an extensive menu of immunoassays for drugs of abuse screening that provide platform-agnostic solutions for large reference and hospital-based laboratories as well as a growing list of non-traditional testing venues such as the workplace, government institutions, insurance companies, drug detection and treatment programs, and physician offices and clinics.

These immunoassays are used worldwide on different analyzer platforms and are the preferred choice in drug testing for their accuracy, precision and reproducibility[1,2]. In addition to routine drug screening, these assays are used widely in the medical research community to answer questions related to cross-reactivity of current and emerging drugs, assess concordance with confirmation methods like mass spectrometry, and correlate pharmacogenomics/behavioral parameters in population studies, to name a few.

1. Evaluation of CEDIA and DRI Drugs of Abuse Immunoassays for Urine Screening on a Thermo Indiko Plus Analyzer; KÖhler KM, Hammer R, Riedy K, Auwärter V, and Neukamm MA. Journal of Clinical Laboratory Analysis. 2017, 31:1

2. Comparison of the Microgenics CEDIA heroin metabolite (6-AM) and the Roche Abuscreen ONLINE opiate immunoassays for the detection of heroin use in forensic urine samples. Holler JM1, Bosy TZ, Klette KL, Wiegand R, Jemionek J, Jacobs A. J Anal Toxicol. 2004, 28(6):489-93.

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Drug Abuse is a global health problem

Illicit use of known drugs or their chemical analogs is a global public health problem with 275 million people (~5% of the world's adult population) affected[3] 29.5 million (11% of users) of those drug users, or 0.6 % of the global adult population, suffers from a drug use disorder that results in dependence (2017 World Drug Report, UNODC). Public health authorities (law enforcement, medical professionals and rehabilitation clinics) are facing the constantly challenging burden of detecting, treating and/or prosecuting these drug abusers.

Drug abuse and its downstream ramifications on a person's overall health and life expectancy contribute to the global disease burden, which includes disability and mortality[4]. Changes in life expectancy, affects gender and age demographics across the world. According to the 2017 World drug report published by the United Nations Office on Drugs and Crime (UNODC), younger men and women are living shorter, less healthy lives which can have a significant impact on the socio- economic state of the world[5]. In addition, people who inject drugs have a higher chance of premature death, high rates of potentially life-threatening infectious diseases, e.g. HIV, hepatitis and tuberculosis, and increased risk of both fatal and non-fatal drug overdoses. This exacerbates the global health crisis even more due to the increased potential for harboring and spreading infectious diseases.

Demand, supply and treatment cases shape global trends of drug abuse

The global average number of people in treatment shows that cannabis is by far the most commonly abused drug with 39% of the treatment seekers having fallen prey to it. This is closely followed by opioids (33% of the population in treatment) and the third position is jointly held by cocaine and amphetamine-type stimulant users each constituting 10% of the population seeking treatment. Drug abuse is closely related to drug availability in different regions of the world.[6]

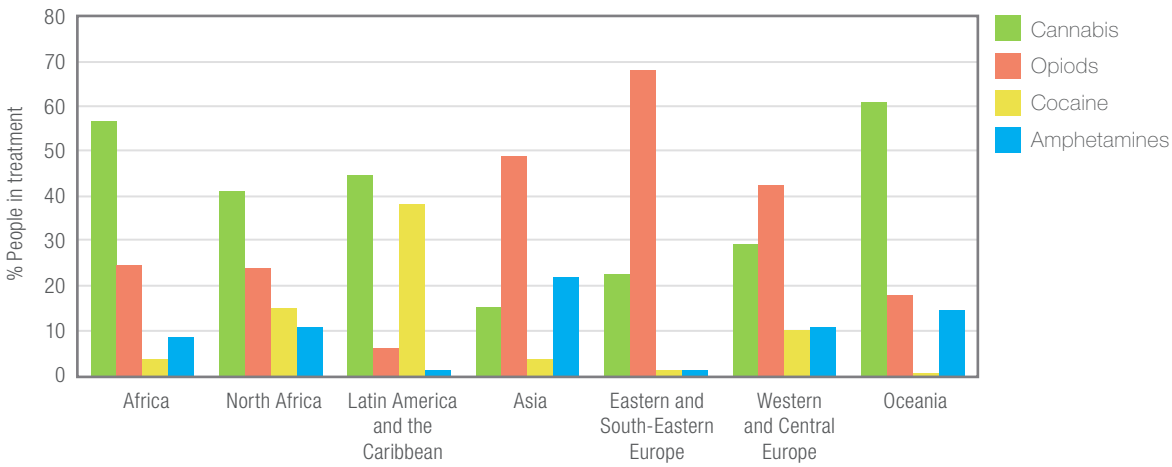
3. World Drug Report, 2018, http://www.who.int/substance_abuse/facts/psychoactives/en

4. Substance abuse and rehabilitation: responding to the global burden of diseases attributable to substance abuse. Wu LT. Subst Abuse Rehabil. 2010, 1:5-11.

5. INCB Report, 2013, Chapter 1, www.incb.org/documents/Publications/AnnualReports/Thematic_chapters/English/AR_2013_E_Chapter_I.pdf

6. GLOBAL OVERVIEW OF DRUG DEMAND AND SUPPLY, 2017 World Drug Report, UNODC

Fig. 4 | Primary Drug of Concern Among People in Drug Treatment, by Region 2015



Source: UNODC, responses to annual report questionaire.

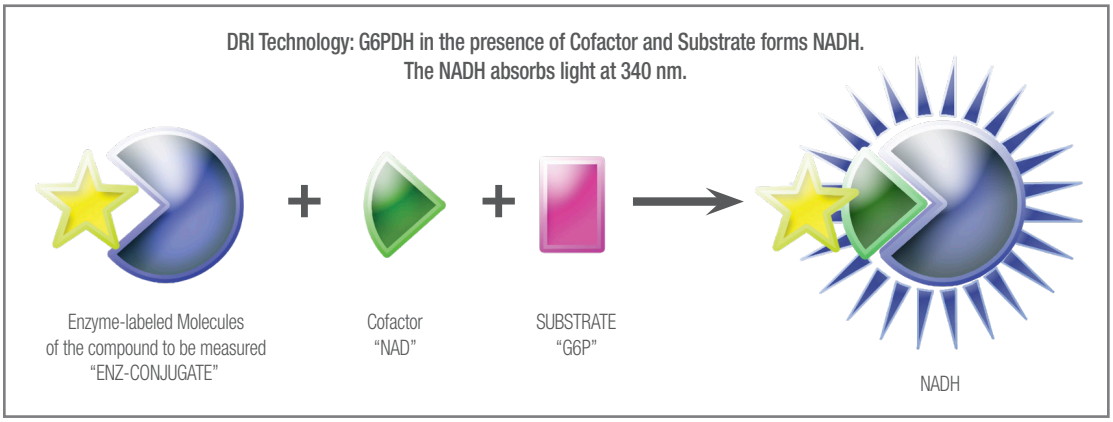
Based on the Global Drug Report, 2017 from UNODC, opioids cause the most negative health impact and treatment burden, but cannabis remains the world's most widely used drug, with an annual prevalence of 3.8 per cent of the adult population, or an estimated 183 million having used cannabis in 2017. With the looming global opioid crisis, opioids appear as a major point of concern for health authorities in North America, South-West and Central Asia and in Eastern and South-Eastern Europe. Treatment for cocaine use is more common in North America, Latin America and the Caribbean but this is not so prevalent in Western and Central Europe. Amphetamines are a problem primarily in East and South-East Asia and to some extent in North America. Globally, drug abuse remains a major health issue that drives the need for treatment and rehabilitation.

The need for treatment of drug abuse, in turn, is directly proportional to the increase in government funding for treatment programs and the increase in demand for faster, more sensitive and accurate detection methods such as automated immunoassays for each of the drug classes. There is a constant arms race to find better, more reliable ways to detect the presence of a drug especially as new synthetic drugs make it to the market.

Automated Immunoassays: ideal to screen for a class of drugs reliably with fast time-to-results

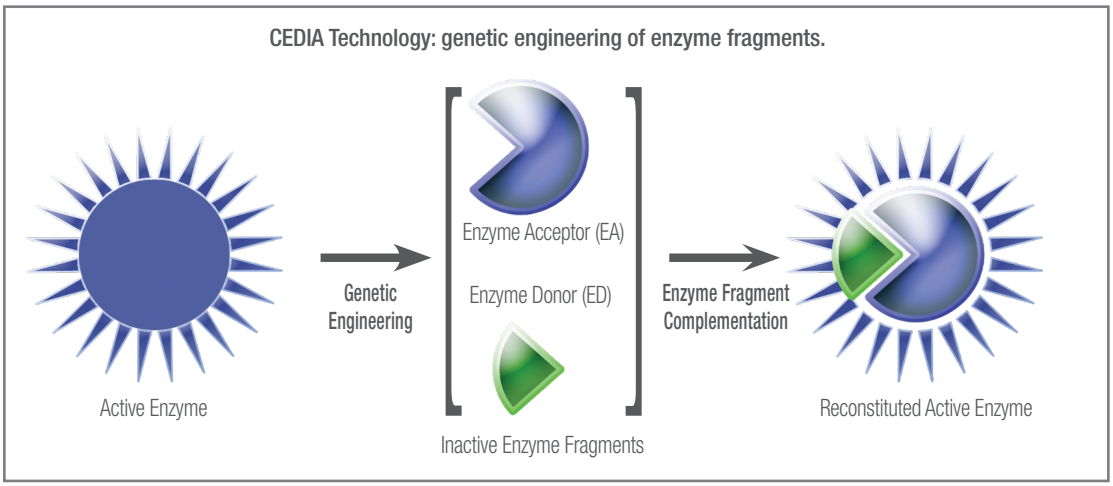
The most practical and accurate way to screen for the presence of a drug class is by testing urine samples using automated Immunoassays that rely on the ability of an antibody to selectively bind to the drug/drug analog/ drug metabolite. Immunoassays have been used for over 40 years for drug screening – the two most common types being, 1) the Homogeneous Enzyme Immunoassay (Thermo Scientific™ DRI™ assays from Thermo Fisher Scientific) which use Enzyme Multiplied Immunoassay Technique, and 2) the Cloned Enzyme Donor Immunoassay also known as Thermo Scientific CEDIA™ (offered by Thermo Fisher Scientific, Microgenics). Typically, Immunoassays can detect a class of drugs that are structurally similar since the antibody recognizes similar compounds. Immunoassays are calibrated based on specific cut-off concentrations of the analyte. Specimens yielding results greater than the cut-off are considered positive and those that fall below the cut-off threshold are considered negative. Cut-off values are not the same as Limit of Detection (LOD) or Limit of Quantitation (LOQ). Cut-off values are higher than detection limits for reliable measurement and low enough to make sure the drug can be detected within a reasonable time-frame after use. This is a key concept that defines assay parameters for the different types of immunoassay technologies.

DRI Technology



The DRI technology is based on competitive binding of a drug labeled with glucose-6-phosphate dehydrogenase (G6PDH), and free drug in the urine sample. In the absence of drug in the sample, the specific antibody binds the drug labeled with G6PDH and inhibits enzyme activity. In the presence of drug in the sample, the drug labeled with the enzyme is free to initiate enzyme activity, converting nicotinamide adenine dinucleotide (NAD) to NADH, which is read at 340nm by the chemistry analyzer.

CEDIA (Cloned Enzyme Donor Immunoassay) Technology



The CEDIA technology uses two inactive genetically engineered fragments from the bacterial enzyme b-galactosidase as a basis for the enzymatic reaction. Drug bound to the enzyme donor (ED) fragment competes with the drug in the sample for the antibody binding site. If the drug bound to ED binds to the antibody, it is prevented from reassembling with the enzyme acceptor (EA) fragment and activating the enzyme. In the presence of drug in the sample, the enzyme donor fragment reassembles with the enzyme acceptor fragment, creating the active enzyme, which then reacts

with the substrate to produce a colored product. Formation of this colored product is directly proportional to the change in absorbance at 570 nm. This is measured by a chemistry analyzer. CEDIA assays have some unique inherent advantages: a linear calibration curve with high precision over the whole assay range, lack of endogeneous enzyme activity, minimal serum interference, chemically defined conjugates and flexibility in assay design.[7]

DRI, and CEDIA, depend on the amount of active enzyme formed and resultant absorbance change is directly proportional to the amount of drug present in the sample.

Immunoassays based on DRI and/or CEDIA technologies have been evaluated extensively by various laboratories worldwide, resulting in over a hundred peer reviewed publications. This analysis includes a detailed review of 15 peer reviewed articles showcasing the capabilities and performance of the CEDIA and DRI assays in testing for drugs of abuse in different clinical laboratories (reference or commercial testing), hospitals and independent academic research laboratories.

7. CEDIA in vitro diagnostics with a novel homogeneous immunoassay technique. Current status and future prospects. Engel WD, Khanna PL. J Immunol Methods. 1992, 150(1-2):99-102.

"The EtG immunoassay showed a strong correlation with the LC-MS/MS reference method (r=0.94, p<0.001) and there was 100% agreement in the frequency of marker positive and negative findings between the immunoassay EtG results and the LC-MS/MS analysis of EtG and EtS."

Immunoassay for ethyl glucuronide in vitreous humor: A new tool for postmortem diagnostics of alcohol use. Rainio J, Kultti J, Kangastupa P, Tuomi H, Ahola S, Karhunen PJ, Helander Z, Niemelä O. Forensic Science International, 2013. 226, 261-265.

"The Microgenics CEDIA high sensitivity assay demonstrated the highest positive screening rate as well as the highest confirmation rate of the four assays [CEDIA, CEDIA high sensitivity, DRI, and Roche KIMS assay]."

Evaluation of Four Immunoassay Screening Kits for the Detection of Benzodiazepines in Urine; Rebecca T. DeRienz, Justin M. Holler, Megan E. Manos, John Jemionek, and Marilyn R. Past, Journal of Analytical Toxicology Vol. 32, July/August 2008

"...the CEDIA assay detected 12 of 13 compounds and the EMIT II Plus and HEIA assays 10 of 13 at the highest concentration (1000 ng/mL)."

Detectability of designer benzodiazepines in CEDIA, EMIT II Plus, HEIA, and KIMS II immunochemical screening assays. Bergstrand MP, Helander A, Hansson T and Beck O. Drug Testing and Analysis, 2017. 9: 640-645.

Multiple Drugs of Abuse Assays

Background

In the European Union, at least one quarter of the adult population has tried illicit drugs – both those that have been around for a long time and are well characterized, as well as the newer psychoactive substances (NPS) which are not so well understood. For those individuals presenting to the emergency department for acute drug toxicity, it is important to understand what drugs they are taking to better manage their care. Doctors rely on the test results obtained from rapid urine immunoassays as well as what individuals self-report.

Publication

Title: Acute Recreational Drug Toxicity: Comparison of self-reports and results of immunoassay and additional analytical methods in a multicenter European case series.

Authors: Liakoni E, Yates C, Dines AM, Dargan PI, Heyerdahl F, Hovda KE, Wood DM, Eyer F.

Journal: Medicine (2018) 97:5

Purpose of Study

Compare self-reported drug use against test results from immunoassays and chromatographic-MS methods.

Thermo Scientific Assays

CEDIA/DRI THC
CEDIA/DRI Cocaine Metabolite
DRI Amphetamines
CEDIA Amphetamines/Ecstasy
CEDIA Heroin Metabolite
CEDIA/DRI Opiates
CEDIA/DRI Methadone
CEDIA Buprenorphine
DRI Tricyclics Antidepressant
CEDIA LSD
CEDIA/DRI PCP

Analyzer Used for Testing

Abbott™ Architect™ c4000 - Immunoassays
Mass Spec: LC-MS/MS or GC-MS Confirmation

Specimens – Urine specimens from 10,956 cases of acute recreational drug toxicity, that presented to the emergency rooms within the European Drug Emergencies Network Plus project, were tested. Euro-DEN Plus Project Center locations include: Basel, Drogheda, Dublin, London (2 centers), Mallorca, Oslo, Paris.

Authors' Conclusions

Self-reporting and analytical tests were in high agreement, especially for cocaine and heroin. Where analytical methods were not available, such as for inhalants, poppers, magic mushrooms, Gamma-HydroxyButyrate (GHB), Lysergic acid diethylamide (LSD), Novel Psychoactive Substances (NPS), and methylphenidate, clinicians relied on self-reports. The immunoassays accurately detected methadone, cocaine and heroin use. The mass-spec methods were best at detecting NPS and differentiating amphetamine –type substances.

> "…the present study found high agreement between self-reported and analytically detected cocaine and heroin use."

Multiple Drugs of Abuse Assays:
Novel Psychoactive Substances (NPS)

Background

Novel psychoactive substances (NPS, “designer drugs”, “legal highs”) are synthetically designed to mimic existing established recreational drugs. They can be grouped into four main categories: stimulants, cannabinoids, hallucinogens, and depressants. The novel substances are typically not detectable with the usual immunoassays for screening for drugs of abuse. It is therefore possible that they can contribute to acute toxicities and medical complications, or even deaths and escape detection. Over 560 substances are currently monitored by the European Monitoring Centre for Drugs and Drug Addiction, with 100 new agents identified in 2015 alone. The UK National Drug Treatment Monitoring System (NDTMS) report in 2015 described 3048 and 1370 adults with documented problematic use of mephedrone and “other” NPS respectively[8].

8. Novel psychoactive substances: types, mechanisms of action, and effects; Tracy DK, Wood DM and Baumeister D. BMJ 2017; 356.

1. Publication

Title: Presentations due to acute toxicity of psychoactive substances in an urban emergency department in Switzerland: a case series
Authors: Liakoni E, Dolder PC, Rentsch KM, and Liechti ME
Journal: BMC Pharmacology and Toxicology 2016, 17:25

Purpose of Study

To systematically collect and analyze data (demographics, clinical findings, substances used, and short-term outcome of patients) related to cases of acute recreational drug toxicity resulting in hospitalizations at the emergency department, University Hospital of Basel, Switzerland, between October 2014 and September 2015. LC-MS/MS analysis with a method covering over 770 substances was applied for confirmation and to detect additional substances like γ-hydroxybutyrate (GHB).

Thermo Scientific Assays

CEDIA Amphetamine/Ecstasy Assay
CEDIA Benzodiazepine assay
CEDIA Barbiturate assay,
CEDIA Cocaine assay
CEDIA Opiate (methadone) assay
CEDIA Heroin metabolite (6-AM) assay
DRI Tricyclics (TCA) Assay
DRI Opiate Assay

Analyzers Used for Testing

Drug screen data not shown

Specimens – Various: Urine.

Authors’ Conclusions

Out of the 50,624 cases admitted to the emergency department, 210 were directly related to acute toxicity of recreational drugs. Most cases were related to illicit use of cocaine and cannabis. In spite of the alarming increase in various NPS being detected in the last years, these substances were infrequently associated with emergency room hospitalizations compared to classical recreational drugs.

Multiple Drugs of Abuse Assays:
Novel Psychoactive Substances (NPS) continued

2. Publication

Title: Detectability of new psychoactive substances, 'legal highs', in CEDIA, EMIT, and KIMS immunochemical screening assays for drugs of abuse
Authors: Beck O, Rausberg L, Al-Saffar Y, Villen T, Karlsson L, Hanssonc T and Helandera A
Journal: Drug Test. Analysis 2014, 6:492–499

Purpose of Study

To evaluate and confirm cross-reactivity of NPS with classic narcotics using established immunochemical tests. In addition to spiked urine, samples from authentic cases of intoxication were studied in order to verify that cross-reactivity to a given substance occurs also for the parent compound and metabolite pattern excreted in urine.

Thermo Scientific Assays	Analyzers Used for Testing
CEDIA Amphetamine/Ecstasy Assay	Beckman-Coulter Olympus AU640
CEDIA Buprenorphine Assay	
CEDIA Phencyclidine (PCP) Assay	
CEDIA Cocaine Assay	

Specimens – Urine specimens sent to the Karolinska University Laboratory for routine testing of Internet drugs

Authors' Conclusions

This study looked at 45 substances considered as NPS and confirmed that a substantial number of these, in addition to mimicking the psychoactive effects of classic abused drugs, possess chemical similarities leading to cross-reactivity in the immunochemical screening tests routinely used for urine drug testing.

Buprenorphine (BUP)

Background

Buprenorphine is a semi-synthetic opioid derived from thebaine, an alkaloid of the poppy Papaver somniferum. It acts as an opioid partial agonist producing typical opioid effects and side effects but is less potent than heroin and methadone. At low doses buprenorphine allows opioid-addicted individuals to discontinue the misuse of opioids without experiencing withdrawal symptoms.

Publication

Title: False-Positive Buprenorphine by CEDIA in Patients Prescribed Amisulpride or Sulpiride

Authors: Birch MA, Couchman L, Pietromartire S, Karna T, Paton C, McAllister R, Marsh A and Flanagan RJ

Journal: Journal of Analytical Toxicology 2013, 37:233–236

Purpose of Study

To evaluate the cross-reactivity of amisulpride and sulpiride in the CEDIA buprenorphine assay.

Thermo Scientific Assays	Analyzers Used for Testing
CEDIA Buprenorphine assay	Beckman-Coulter Olympus AU640

Specimens — Random urine samples from 2 patients prescribed amisulpride, but not buprenorphine.

Authors' Conclusions

Cross-reactivity of amisulpride and sulpiride in the CEDIA Buprenorphine assay was very low in two patients evaluated (estimated at 0.003 and 0.002% for amisulpride and sulpiride, respectively). However, cross-reactivity remains a significant consideration, given the likely high concentrations of these compounds in urine from patients prescribed these drugs (~ 1 g/L in some cases) relative to the low cutoff (5 mg/L) of the buprenorphine assay. Weak false-positive buprenorphine results in patients who denied unauthorized buprenorphine use prior to sampling, but who had been prescribed amisulpride can be further confirmed via LC-MS/MS to ensure whether there is true buprenorphine abuse. The ability to detect norbuprenorphine and norbuprenorphine glucuronide via LC-MS/MS is valuable in such circumstances, and also serves to increase the detection window from the time of last use.

Cannabinoids (THC)

Background

Marijuana comes from the dried leaves and flowers of the cannabis plant. Tetrahydrocannabinol (THC) is the active ingredient in marijuana that causes changes in the brain. THC activates specific receptors, known as cannabinoid receptors. In the healthy brain, cannabinoid receptors are activated by a neurotransmitter called anandamide. Anandamide is known to have a pain-relieving effect. Marijuana also boosts the neurotransmitter dopamine in the brain's reward circuits, which reinforces the behavior of taking the drug. Short-term effects of marijuana use include distorted perception, due to the drug's interference with the brain's ability to process sensory information. Long-term use of the drug can also lead to a series of attitude and personality changes.

1. Publication

Title: COMT val158met and 5-HTTLPR Genetic Polymorphisms Moderate Executive Control in Cannabis Users

Authors: Verdejo-García A, Fagundo AB, Cuenca A, Rodriguez J, Cuya´ E, Langohr K, de Sola Llopis S, Civit E, Farre´ M, Pen˜a-Casanova J and de la Torre R

Journal: Neuropsychopharmacology 2013, 38:1598–1606

Purpose of Study

To test if the two common genetic polymorphisms (the catechol-Omethyltransferase (COMT) gene val158met polymorphism and the SLC6A4 gene 5-HTTLPR polymorphism) linked to the neuroadaptive impact of D9-tetrahydrocannabinol (THC) exposure moderates the harmful effects of cannabis use on executive function (decision-making, memory) in young cannabis users.

Thermo Scientific Assays	Analyzers used for Testing
CEDIA THC Assay	No drug screen data shown

Specimens – Urine from 144 European-Caucasian participants: 86 cannabis users and 58 non-drug users (controls)

Authors' Conclusions

Daily cannabis use is not associated with executive function deficits. COMT val158met and SLC6A4 5-HTTLPR polymorphisms moderate the link between cannabis use and executive performance.

Cannabinoids (THC) continued

Background

Pantoprazole is in a group of drugs called proton pump inhibitors. It decreases the amount of acid produced in the stomach and is used to treat erosive esophagitis (damage to the esophagus from stomach acid), and other conditions involving excess stomach acid. A recently published case found that there was a false-positive urine cannabinoid screen in a patient taking pantograzole.

2. Publication

Title: Cross-Reactivity of Pantoprazole with Three Commercial Cannabinoids Immunoassays in Urine.
Authors: Gomila I, Barcelo B, Rosell A, Avella S, Sahuquillo L, and Dastis M.
Journal: Journal of Analytical Toxicology, 2017;41-760-764

Purpose of Study

Determine potential cross-reactivity of pantoprazole in three commercially available cannabinoid immunoassay screens.

Thermo Scientific Assays	Analyzers used for Testing
Thermo Scientific DRI Cannabinoids Assay	Roche Cobas c520 Analyzer
Alere Triage TOX Drug Screen	Triage Meter
Roche KIMS Cannabinoids II Immunoassay	Roche Cobas c520 Analyzer

Specimens – Eight urine specimens from patients taking pantoprazole.

Authors' Conclusions

All eight specimens confirmed negative for cannabinoids by GC-MS. However, both the Alere Triage Tox Drug Screen and the Roche KIMS Cannabioinds II immunoassay produced false-positive results in five and one patient specimen, respectively. The Thermo Scientific Assay did not give any false-positive results in the eight specimens tested.

> "None [of the] patient sample[s] gave a false-positive result when analyzed by the DRI Cannabinoids Assay."

Cannabinoids (THC) continued

Background

A study was conducted to assess whether secondhand cannabis smoke exposure could cause false-positive cannabis results in the urine of drug-free participants. Six non-smokers were seated with smokers in rooms that had ventilation (2 sessions) and rooms without ventilation (1 session).

3. Publication

Title: Non-Smoker Exposure to Secondhand Cannabis Smoke. I. Urine Screening and Confirmation Results.

Authors: Cone EJ, Bigelow GE, Herrmann ES, Mitchell JM, LoDico C, Flegel R, and Vandrey R

Journal: Journal of Analytical Toxicology 2015; 39:1-12

Purpose of Study

Determine if extreme cannabis exposure can produce positive urine tests at the cutoff concentrations that are commonly used.

Thermo Scientific Assays	Analyzer used for Testing
Four immunoassays were used at different cutoff concentrations (20, 50, 75 and 100 ng/mL) and results were confirmed by GC-MS (LOQ=0.75 ng/mL). Thermo Scientific CEDIA Multi-Level THC Assay Thermo Scientific DRI Cannabinoid Assay GC-MS: THCCOOH	Not indicated

Specimens – Six non-smoking participants had their specimens collected at 0.25, 1, 2, 3, and 4 hours after exposure.

Results

All four immunoassays produced the same results at the 50 ng/mL cutoff and all had an agreement with mass spec of 89.2%. These specimens were also tested using the CEDIA assay at 75 and 100 ng/mL cutoffs and had the same agreement with mass spec of 89.2%. However, at the 20 ng/mL cutoff, the four immunoassays had slightly different results for mass spec concordance: EMIT II, CEDIA, DRI and KIMS had agreement with mass spec of 95.2%, 94%, 94-92%, 91.6, respectively. More true positives and true negatives were identified, but specificity decreased at the 20 ng/mL cutoff.

Authors' Conclusions

If lower cutoff concentrations are used, cannabis smoke exposure, under extreme conditions, can produce positive urine tests. However, this was not found at the higher cutoff concentrations (e.g. 50 ng/mL cutoff concentration as used by SAMHSA). These extreme exposure conditions are likely to be rare and only under conditions where exposure is obvious.

> "…extreme cannabis smoke exposure can produce positive urine tests at commonly utilized cutoff concentrations. However, positive tests are likely to be rare…"

Cotinine

Background

Cotinine is an active metabolite of nicotine and remains in the blood longer than nicotine, with a half-life of 18–20 hours. Nicotine is metabolized in the liver by cytochrome P450 enzymes (mostly CYP2A6, and also by CYP2B6) and FMO3, which selectively metabolizes (S)-nicotine. Many insurance providers want to monitor the health risks of individuals, by monitoring for the use of tobacco smoke. Smokers are more apt to have heart disease, lung cancer, and other vascular diseases than non-smokers and as such, are more likely to have higher health costs. As such, smokers may have higher insurance rates due to these risks.

Publication

Title: Comparison of Semi-Quantitative Cotinine Values Obtained by the DRI Immunoassay and Values Obtained by a Liquid Chromatography-Tandem Mass Spectrometry-Based Method: The DRI Immunoassay is Suitable for Screening Purposes Only because Semi-quantitative Values May Be Unreliable.
Authors: Dixon R. Brent, and Dasqupta A.
Journal: Journal of Clinical Laboratory Analysis 00:1-4(2016)

Purpose of Study

Compare the performance of the DRI Cotinine Assay as both a screen and semi-quantitative assay against LC-MS/MS.

Thermo Scientific Assays	Analyzer used for Testing
Thermo Scientific DRI Cotinine Assay	Olympus 2700 Analyzer

Specimens – Thirty-nine urine specimens containing various amounts of cotinine were used.

Authors' Conclusions

No false-negative results were obtained using the DRI Cotinine Assay at the established 500 ng/mL cutoff and thus, conclude it is suitable as a screen for cotinine in urine specimens. LC-MS/MS technology was used to identify and quantify drug concentrations in this samples. While immunoassays provide semi-quantitative values that reflect the antibody specificity, LC-MS/MS provides quantitative values by specifically identifying and determining the concentration of each metabolite/analog/parent drug present in the sample.

Ethyl glucuronide (EtG)

Background

Ethyl glucuronide (EtG) is a minor but long-lasting (detectable in urine for up to 96 hours) metabolite of ethanol. EtG is formed in the body by glucuronidation following exposure to ethanol, usually from drinking alcoholic beverages. It is often used as a biomarker to test for ethanol use.

Publication

Title: Lessons learned from a case of tert-butyl glucuronide excretion in urine — "New" psychoactive alcohols knocking on the back door?
Authors: Arndta T, Buschmannb HC, Schulzc K, Stemmericha K
Journal: Forensic Science International 2017, 281:9–12

DRI EtG assay

"[Our studies] indicated a high level of accuracy and selectivity of the DRI-EtG EIA for urinary EtG." "The DRI-EtG EIA may be applied for routine screening of recent alcohol exposure in clinical and forensic settings."

Evaluation of a New Immunoassay for Urinary Ethyl Glucuoronide Testing; Michael Böttcher, Olof Beck, and Anders Helander Alcohol & Alcoholism, vol 43, No. 1 pp 46-48, 2008

DRI EtG assay has high agreement with Mass Spec

"EtG immunoassays conducted at low cut-offs levels in point-of-care testing settings have high agreement with lab-based EtG-MS." "Based on our findings and its ease-of-use, EtG appears to be well suited to fulfill the role of rapid and non-invasive alcohol biomarker that can be used in clinical research or outpatient addiction treatment settings."

High levels of agreement between clinic-based ehtyl glucuronide (EtG) immunoassays and laboratory based mass spectrometry; Emily Leickly, Michael G. McDonell, Roger Vilardaga, Frank A. Angelo, Jessica M. Lowe, Sterling McPherson, Debra Srebnik, John M. Roll, and Richard K. Ries Am J Drug Alcohol Abuse, vol. 41, 246-250, 2015

Ethyl glucuronide (EtG) continued

Purpose of Study

To access the cross-reactivity from different alcohol glucuronides (EtG homologs), mainly tert-butyl glucuronide in an EtG immunoassay

Thermo Scientific Assays
DRI EtG enzyme immunoassay

Analyzers used for Testing
Beckman Coulter AU680

Specimens – Three consecutive urine samples from an in-patient with a long history of multiple substance abuse (suspected tert-butanol or isobutane abuse) were tested

Authors' Conclusions

DRI EtG assay cross reacts with EtG homologs, mainly tert-butyl glucuronide in patient samples with suspected substance abuse of tert-butanol or isobutane. The authors propose that future research should address the usefulness of alcohol glucuronides (EtG homologs) in urine as biomarkers to detect a wide range of ethanol replacements or "New" Psychoactive Alcohols.

MDMA (Ecstasy)

Background

3,4-Methylenedioxymethamphetamine (MDMA), street name - ecstasy, is a psychoactive drug primarily used for recreational purposes. The desired effects include altered sensations and increased energy, empathy, and pleasure. Impairments in multiple aspects of cognition, including attention, learning, memory, visual processing, and sleep have been found in regular MDMA users.

1. Publication

Title: The Influence of Genetic and Environmental Factors among MDMA Users in Cognitive Performance

Authors: Cuya` E, Verdejo-García A, Fagundo AB, Khymenets O, Rodriguez J, Cuenca A, de Sola Llopis S, Klaus Langohr K, Pen˜a-Casanova J, Torrens M, Martín-Santos R, Farre´ M and de la Torre R

Journal: PLoS ONE 2016, 6(11):e27206

Purpose of Study

To understand the association between MDMA cumulative use and cognitive dysfunction, and the potential role of candidate genetic polymorphisms in 5HTT, 5HTR2A, COMT, CYP2D6, BDNF, and GRIN2B genes in explaining individual differences in the cognitive effects of MDMA

Thermo Scientific Assays

CEDIA Amphetamine/Ecstasy Assay
CEDIA Cocaine Assay
CEDIA Opiates Assay
CEDIA Multi-Level THC Assay

Analyzers used for Testing

Drug screen data not shown, only used to qualify candidates

Specimens – Urine samples from 263 Caucasian participants (60 MDMA polydrug users, 110 cannabis users, 93 non-users)

Authors' Conclusions

MDMA lifetime use and gene-related individual differences influence cognitive dysfunction in ecstasy users. In particular, this study demonstrates dose-related effects of MDMA use on visual attention, organization and memory. There is interaction between MDMA use and different gene polymorphisms in determining poorer performance of MDMA users in tests of visual attention and memory (COMT and SERT genes) and verbal fluency (CYP2D6 ultra-rapid metabolizers).

MDMA (Ecstasy) continued

Background

As part of their routine fitness examinations, French Air Force Military crew underwent urine testing for 3,4 methylenedioxymetamphetamine (MDMA or Ecstasy). Thirteen of the 7,803 patients were known to have been prescribed the dyslipidemic drug, fenofibrate, mainly used to reduce cholesterol levels in people at risk of cardiovascular diseases.

2. Publication

Title: A Cross-Reactivity of Fenofibric Acid with MDMA DRI Assay
Authors: Bugier S, Garcia-Heijl C, Vest P, Plantamura J, Chianea D, Renard C.
Journal: Military Medicine, 181, 9:1013, 2016.

Purpose of Study

Determine if the DRI Ecstasy Assay cross reacts with the dyslipidemic drug, fenofibrate.

Thermo Scientific Assays	Analyzer used for Testing
Thermo Scientific DRI Ecstasy Assay	Beckman Coulter Unicel DXC 600

Specimens – 7,803 patients were tested for MDMA for over 3 years and resulted in a total of 15,169 urine samples. Based on the medical records available, 13 patients were confirmed to have a prescription for fenofibrate with a daily dose range of 160-300 mg.

Authors' Conclusions

Of the tested samples, 22 were positive by the DRI Ecstasy Assay (0.15%) and confirms that the fenofibrate drug does interfere with the MDMA immunoassay results. Both MDMA and fenofibric have a common phenyl ring and this may account for the cross-reactivity. Physicians were made aware that recruits may test positive for MDMA if they are taking the drug fenofibrate.

Since fenofibrate is widely prescribed, physicians were alerted that this treatment could lead to false-positive results.

> "…the only similarity in chemical structure that may account for cross-reactivity is that fenofibric acid and MDMA have in common a phenyl ring."

Methadone Metabolite

Background

For those patients that are on a strict methadone dosage regimen for chronic pain or drug addiction, they must demonstrate compliance – e.g. they are taking the drug, rather than diverting it. Despite observed-collection strategies, participants can fool the test by through substitution (using someone else's urine), or adulteration (by adding methadone to the urine).

Publication

Title: Quantification of a Methadone Metabolite (EDDP) in Urine: Assessment of Compliance
Authors: Larson MEM and Richards TM.
Journal: Clinical Medicine & Research, Vol. 7, Number 4: 134-141, 2009.

Purpose of Study

To determine whether patients are adhering to their drug program, researchers wanted to investigate the possibility of utilizing the ratio of methadone metabolite (EDDP) to urine creatinine. This regression model would hopefully predict drug compliance in patients prescribed methadone for either pain management or drug addiction.

Thermo Scientific Assays
Various drugs of abuse tests used for routine screening (not defined)
Thermo Scientific DRI Creatinine-Detect Test
Hewlett-Packard GC-MS EDDP Assay

Authors' Conclusions

The data in this study suggests that the EDDP to urine creatinine ratio may be predictive of adherence or non-adherence to drug treatment programs. However, the authors suggest a larger study is needed to validate these preliminary results.

Opiates (Morphine and Codeine)

Background

Opioids/opiates are a group of drugs that are used for treating pain. They are derived from opium which comes from the poppy plant. Opiates include morphine and drugs structurally similar to morphine (eg, codeine, hydrocodone, hydromorphone, oxycodone). Currently, there is a public health crisis in the US due to misuse of opioid drugs and alarmingly high number of deaths from overdose. In order to manage this crisis, there is increased funding and support from government bodies aiming to discover new and better ways to prevent opioid misuse, treat opioid use disorders, and manage pain.

Routine matrix for opioid testing is the urine. However, in July 2012, SAMHSA's Drug Testing Advisory Board (DTAB), a scientific council which advises SAMHSA's Federal workplace drug-testing program, issued recommendations to evaluate Oral Fluids (OF) as an approved alternative specimen for federally regulated workplace drug testing programs.

Publication

Title: Morphine and Codeine Concentrations in Human Urine following Controlled Poppy Seeds Administration of Known Opiate Content
Authors: Smith ML, Nichols DC, Underwood P, Fuller Z, Moser MA, LoDico C, Gorelick DA, Newmeyer MN, Concheiro M and Huestis MA
Journal: Forensic Sci Int. 2014, 241: 87–90

Purpose of Study

Establish benchmarks for urine morphine pharmacokinetics after ingestion of known amounts of morphine and codeine in poppy seeds for comparison with new alternative matrices like oral fluids being used to detect opiates intake. This study used four commercially available opiate immunoassays for each urine specimen and quantified morphine and codeine concentrations using GC-MS.

Thermo Scientific Assays	Analyzers used for Testing
CEDIA Heroin Metabolite (6-AM) Assay at 10µg/L cutoff	Hitachi P or D Module Immunoanalyzer (Roche Diagnostics)

Specimens – 391 Urine samples collected over 32 h from 22 participants, 15 male, 7 female (18-64 year old) post consumption of 45g of poppy seeds containing 15.7 mg morphine and 3 mg codeine

Authors' Conclusions

Poppy seed consumption can result in urine specimens positive for morphine at the USA federally regulated drug testing cutoff concentration of 2000µg/L. The authors call for continued efforts to distinguish heroin from poppy seed ingestion eliminating the so-called "poppy seed defense" in treatment programs and litigation.

Opiates (Morphine and Codeine) continued

Background

Testing for opiates and establishing a particular opiate drug as the cause of the toxicity is complex because positive opiate results can be caused by multiple potential sources of opiates in biological samples. For identifying heroin or morphine intake by analyzing urine for morphine and codeine, medical review officers must rule out ingestion of poppy seeds as a source for the positive opiate test.

Publication

Title: Laboratory Testing for Prescription Opioids
Authors: Milone MC
Journal: J. Med. Toxicol. 2012, 8:408–416

Purpose of Study

Due to the limited cross-reactivity of antibodies with the diversity of opioid drugs, urine specimens containing many drugs may escape detection by opiate immunoassays. This article reviews metabolic pathways for common opioid drugs of abuse (morphine, codeine, hydrocodone, hydromorphone, fentanyl, oxycodone, oxymorphone, buprenorphine, methadone) and discusses method sensitivity that need to be considered for correct interpretation of screening tests.

Thermo Scientific Assays	Analyzers used for Testing
CEDIA Opiate assays, compared PI (Siemens EMIT, Abbott FPIA)	No screening data shown

Specimens – Review article did not showcase data from any specimen

Authors' Conclusions

The ideal approach to testing depends on the goal for which testing is used. In the clinical setting, unconfirmed immunoassay screening results will continue to be the method of choice to identify cases of drug abuse since it can take 24 hours or more to complete confirmatory testing depending upon the laboratory's testing work flow. For pain management, immunoassays may show its best efficiency when combined with other screening tools such as behavioral assessment tools.

Oxycodone

Background

Oxycodone, prescribed under the brand name of Oxycontin, is the most commonly prescribed narcotic drug used to treat acute pain. Like other opioids, it is known to lead to addiction and ultimately, abuse. As such, it is important to accurately test for compliance and possible diversion of therapy.

Publication

Title: Comparison of Response of DRI Oxycodone Semiquantitative Immunoassay with True Oxycodone Values Determined by Liquid Chromatography Combined with Tandem Mass Spectrometry: Sensitivity of the DRI Assay at 100 ng/mL Cut-Off and Validity of Semiquantitative Value
Authors: Dixon R Brent, Davis B, and Dasgupta A.
Journal: Journal of Clinical Laboratory Analysis 30: 190-195 (2016)

"In our function as a beta site for the new DRI Oxycodone Immunoassay, we determined that the assay has superior sensitivity and specificity when compared to other screening assays." [pg 828]

Can an immunoassay become a standard technique in detecting oxycodone and its metabolites? Jude M. Abadie, Jim H. allison, David A. Black, James Garbin, Andrew J. Saxon, and Daniel D. Bankson Journal of Analytical Toxicology, Vol 29, Nov/Dec 2005

Purpose of Study

This study compared the performance of a commercially available immunoassay, Thermo Scientific DRI Oxycodone Assay, against the reference method, LC-MS/MS.

Thermo Scientific Assays	Analyzer used for Testing
Thermo Scientific DRI Oxycodone Assay	Roche Cobas c501 analyzer

Specimens – Forty-eight urine specimens from patients taking oxycodone.

Authors' Conclusions

The DRI Oxycodone assay successfully identified all oxycodone specimens with oxycodone concentrations over the 100 ng/mL cutoff and is a reliable immunoassay for analysis of oxycodone in urine. LC-MS/MS technology was used to confirm the presence of the drug and quantify drug concentrations in the samples. While immunoassay assays provide semi-quantitative values that reflect the antibody specificity, LC-MS/MS provides quantitative values by specifically identifying and determining the concentration of each metabolite/analog/parent drug present in the sample.

"The DRI Oxycodone assay successfully identified all oxycodone specimens with oxycodone concentrations over the 100 ng/mL [cutoff]."

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