thermo scientific

Thermo Scientific High Performing Drugs of Abuse Assays

Have confidence in your test results

- High concordance with confirmatory methods: Overall, ~95%
- Excellent inter-assay and between-run assay precision: <10% CV
- Minimal retesting optimizes efficiency while minimizing operating costs

ThermoFisher SCIENTIFIC

Thermo Fisher Scientific provides an extensive menu of urine assays for drugs of abuse testing. These assays are used worldwide, in thousands of laboratories, and are valued for their accuracy, precision, and reproducibility. This is reflected in the many peer reviewed publications that detail the performance of the Thermo Scientific Drugs of Abuse assays, in comparison with other manufacturers' technologies.

What follows is an overview of the different automated immunoassay technologies available for urine drugs of abuse testing. Also included are the conclusions drawn from over 30 peer reviewed articles that support the use of the Thermo Scientific Immunoassays as a reliable and accurate method for drugs of abuse screening.

Immunoassay Technologies for Drugs of Abuse Testing

Urine drug testing began in the 1970s to test soldiers arriving back from their service in Vietnam. At that time, radioimmunoassays (RIA) and enzyme linked immunosorbent tests (ELISA) were the only testing methods available. These were not ideal for routine, high throughput testing due to exposure to hazardous radioisotopes (RIA) and the requirement for multiple sample preparation and washing steps (RIA and ELISA).[1]

Easier-to-use technologies have since emerged (EMIT, EIA-DRI, KIMS, CEDIA, SEFRIA) that were adapted for use on routine clinical chemistry analyzers, making drug testing more accessible, faster and affordable.

The Thermo Scientific DRI™ and CEDIA™ assays are the most commonly used methods for drugs of abuse testing. They are similar in that they are both competitive homogeneous enzyme immunoassays. The term competitive is used because the enzyme labeled drug and the drug (analyte) in the urine specimen compete for the fixed amount of analyte-specific antibody available for binding. In the absence of drug in the sample, the antibody binds to the drug on the enzyme inhibiting the enzyme activity. In the presence of drug in the urine specimen, antibody binds to the drug in the sample leaving the enzyme to interact with the substrate and causing the enzyme activity to increase. The enzyme activity is directly proportional to the concentration of the drug in the sample.

1970s **RIA: Radioimmunoassays**[1]

- Principle: determine drug levels by introducing a drug-specific antibody labeled with a radioisotope and measuring the subsequent radioactivity of the antibody bound to drug.
- Exposure to hazardous radioisotopes; extensive sample preparation.

ELISA: Enzyme Linked Immunosorbent Assay[1]

- Principle: Target drug is immobilized on a microplate and incubated with an enzyme labeled antibody to the target drug. After washing, the activity of the microplate well-bound enzyme is measured.
- Requires multiple separation and washing steps.

EMIT®: Enzyme Multiplied Immunoassay Technique[1,2]

- Principle: Competitive Immunoassay based on G6PDH enzymatic reaction.
- First homogeneous immunoassay (no wash steps) for use on clinical chemistry analyzers; first offered as lyophilized, followed later by powder, then liquid format.

1990s **CEDIA: Cloned Enzyme Donor Immunoassay**[2,4]

- Principle: A competitive immunoassay which uses genetically engineered enzyme fragments from the bacterial enzyme, ß-galactosidase, to facilitate the reaction.
- Works with automated clinical chemistry analyzers; lyophilized.

EIA (DRI): Enzyme Immunoassay by Diagnostic Reagents, Inc.[15]

- Principle: Competitive Immunoassay based on G6PDH enzymatic reaction.
- First liquid, ready-to-use homogeneous immunoassay for use on an automated clinical chemistry analyzer.

KIMS®: Kinetic Interaction of Microparticles in Solution[3]

- Principle: drug in the specimen and drug bound to the microparticle compete for limited amount of antibody in solution. The amount of drug present in the urine specimen is directly proportional to the agglutination of the particles.
- Adapted to work with automated clinical chemistry analyzers.

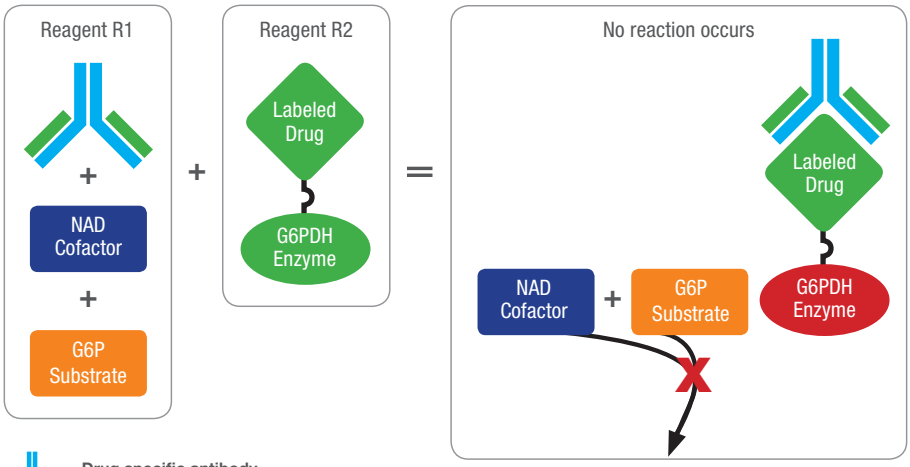
2018 **SEFRIA™: Synthetic Enzyme Fragment Immunoassay**[5]

- Principle: A competitive immunoassay which uses artificial fragments from the bacterial enzyme, ß-galactosidase, to facilitate the reaction.
- Works with automated clinical chemistry analyzers; liquid.

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 free drug from the sample, the specific antibody binds the drug labeled with G6PDH and causes a decrease in enzyme activity. In the presence of free drug, the free drug occupies the antibody binding sites, by allowing the drug bound G6PDH to interact with the substrate, resulting in enzyme activity. This phenomenon creates a direct relationship between the drug concentration in urine and enzyme activity. The enzyme activity is determined spectrophotometrically at 340 nm by measuring the conversion of nicotinamide adenine dinucleotide (NAD) to NADH.[1]

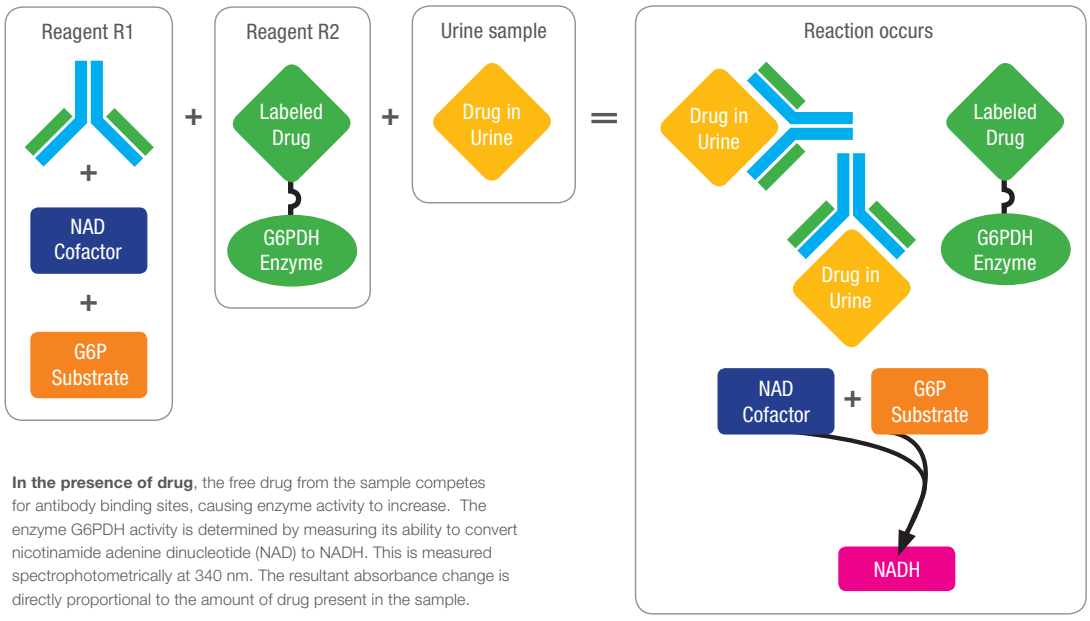
DRI Assay: Absence of Drug



= Drug specific antibody

In the absence of drug, the antibody binds the drug labeled with G6PDH and inhibits enzyme activity.

DRI Assay: Presence of Drug

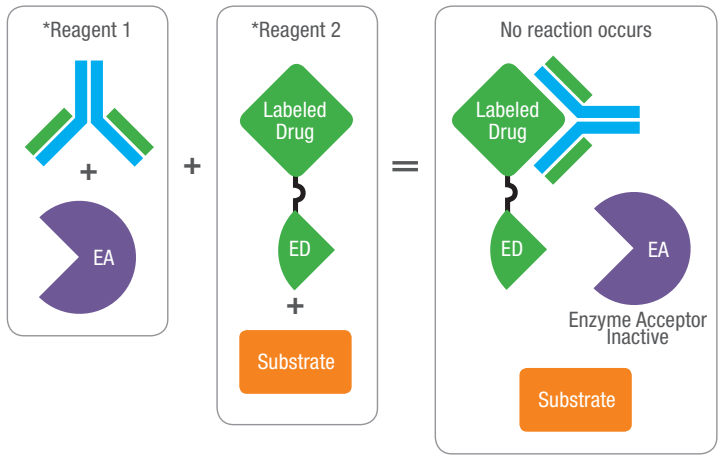


In the presence of drug, the free drug from the sample competes for antibody binding sites, causing enzyme activity to increase. The enzyme G6PDH activity is determined by measuring its ability to convert nicotinamide adenine dinucleotide (NAD) to NADH. This is measured spectrophotometrically at 340 nm. The resultant absorbance change is directly proportional to the amount of drug present in the sample.

CEDIA Technology

The CEDIA technology works similarly to the G6PDH based competitive immunoassays, in that, in the presence of drug in the sample, the limited amount of antibody will bind to the drug in the sample, rather than the enzyme labeled drug, allowing the enzymatic reaction to occur. The CEDIA technology uses two genetically engineered fragments from the bacterial enzyme β-galactosidase as a basis for the enzymatic reaction. When drug is present in the urine sample, the two enzyme fragments (Enzyme Acceptor-EA and Enzyme Donor-ED) re-associate and act on the substrate to form fully active enzyme; this results in a color change that is measured by a chemistry analyzer at 570 nm. In the absence of drug in the sample, the two fragments cannot re-associate to form active enzyme; thus, no colorimetric change occurs. For both technologies, the amount of active enzyme formed and resultant absorbance change is directly proportional to the amount of drug present in the sample.[4]

CEDIA Assay: Absence of Drug



***Reagent 1 and Reagent 2 are reconstituted using buffers EARB and EDRB respectively**

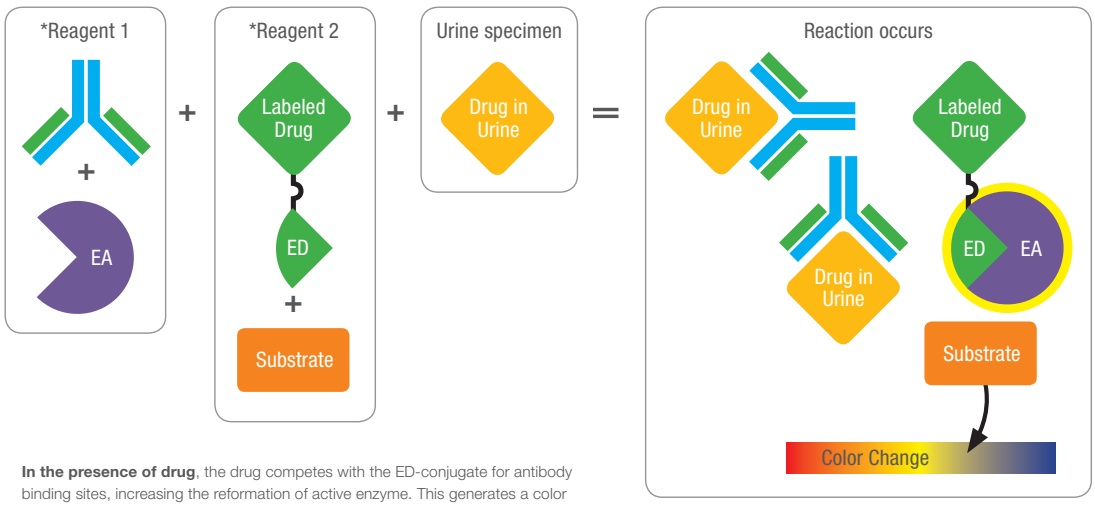
EA = Enzyme Acceptor

ED = Enzyme Doner (conjugated to drug)

= Drug specific antibody

In the absence of drug, the two fragments, EA and ED, cannot re-associate to form fully active enzyme.

CEDIA Assay: Presence of Drug



In the presence of drug, the drug competes with the ED-conjugate for antibody binding sites, increasing the reformation of active enzyme. This generates a color change that can be measured spectrophotometrically at 570 nm. The amount of active enzyme formed and resultant absorbance change are directly proportional to the amount of drug present in the sample.

DRI and CEDIA: The Preferred Assay Methods of Choice

Despite the many technologies available for testing, the DRI and CEDIA technologies have remained in use for over 30 years by laboratories worldwide for their proven assay performance and ease-of-use. Based on the numerous peer reviewed publications that have compared the performance of these immunoassays to other manufacturers' methods, most conclude that the DRI and CEDIA technologies are the preferred choice in drug testing for their accuracy, precision, and reproducibility. [See Table II]. In fact, they are the preferred methods used by more than eighty percent of the labs that are certified by the Substance Abuse Mental Health Services Administration (SAMHSA), an agency that oversees federally regulated employee drug testing in the United States.

Whether a commercial or forensic laboratory, or a laboratory based in a hospital, physicians' office or drug court, each benefits from the superior performance of the DRI and CEDIA immunoassays. These assays are developed to work with a wide range of chemistry analyzers and come with validated parameter applications for the most commonly used instruments. The reliability of the Thermo Scientific drugs of abuse assays provides consistent results within run and between runs, allowing laboratorians to spend less time troubleshooting and more time supporting their patients, doctors, and drug court participants with reliable test results.

Table I: Features and Benefits of the Thermo Scientific Drugs of Abuse Assays

Category	Features	Benefits
Accuracy	Overall ~ 95% concordance with LC-MS/MS, the gold Reference Standard: fewer false positives and false negatives	• Less time & money spent re-screening and performing unnecessary confirmatory tests • More confidence in test results
Specificity	Minimal cross-reactivity to undesired compounds	• Minimizes time, materials and expertise needed for mass spec assessment • More confidence in test results
Precision	< 10% CV; inter-assay and between-run precision	• More confidence in test results, especially around cutoff • Reliable: consistent performance day to day, week to week
Regulatory Status	*FDA Cleared, CE Mark	• Reimbursement opportunities with most healthcare insurance providers
Testing Technologies	DRI and CEDIA performance data presented in over 100 peer reviewed journal articles	• Proven technologies used by thousands of laboratories worldwide for routine testing and clinical research • Confidence in the test results: consistent with results from other laboratories • Automated immunoassay allows for high throughput
Applications	Validated Instrument Parameter Applications, certified for a broad spectrum of chemistry analzyers	• Significantly reduces amount of time required to validate new assays • Supports Regulatory and Laboratory Requirements for Accreditation

* Excluding DRI Fentanyl, DRI EtG, and Synthetic Cannabinoid Assays. These assays are for Criminal Justice and Forensic (CJ&F) use only.

Table II: Scientific Comparison of Thermo Scientific Drugs of Abuse Assays and Other Manufacturers' Drugs of Abuse Assays

Technologies Evaluated in Article				
Thermo Scientific DRI and CEDIA	**Other Automated Immunoassay Technologies**	**Data Summary**	**Authors' Comments**	**Performance Assessment**
Amphetamines				
DRI	NA	Concordance with GC/MS, Semi-quantitative: 500 ng/mL cutoff Positive: 100%; Negative: 65.0%; Overall: 92.3%, (N = 182) 1000 ng/mL cutoff Positive: 100%; Negative: 74.1%; Overall: 86.4%, (N = 111)	"Accuracy samples were categorized based upon the d-amphetamine GC/MS concentration only." However: "The assay is capable of detecting the presence of both amphetamine and methamphetamine analytes with 100% cross reactivity to both drugs. Therefore samples tested for one analyte may give false positive results due to the presence of the other analyte." [6]	The assay can accurately screen for d-amphetamine and d-methamphetamine. It is also able to detect MDA and MDMA metabolite cross-reactivity at the 500 ng/mL cutoff (36% & 63% respectively) and 1000 ng/mL cutoff (40% & 77% respectively).
Amphetamines/Ecstasy				
CEDIA	NA	Concordance with GC/MS at the 500 ng/mL cutoff: 95.1%, 158/159 positive N = 184, 159 positive	NA	The assay has good concordance with mass spec.[7]
Barbiturate				
CEDIA	*NA	Concordance with GC/MS: CEDIA Barbiturate: 100% N = 28 positives N = 5,000 total specimens	"CEDIA detected 100%...of the barbiturate positive specimens." [4]	The CEDIA Barbiturate assay has excellent concordance with GC/MS.
Benzodiazepine				
CEDIA CEDIA HS DRI	KIMS	Confirmation rates with GC/MS at 200 ng/mL cutoff: CEDIA HS: 98.4% • CEDIA: 59% DRI: 67.2% • KIMS: 34.4% N ≥ 10,000 samples	"CEDIA high sensitivity (HS) assay demonstrated exceptional response to the conjugated standards…[this] allows for the detection of conjugated metabolites in urine." [8]	CEDIA HS is designed to detect conjugated metabolites and results in higher confirmation rates. DRI and KIMS assays were not designed for detecting the glucuronide-conjugates.
Buprenorphine (I and II)				
CEDIA Bup I	HEIA	CEDIA: sensitivity 99%, selectivity 84% HEIA: sensitivity 97%, selectivity 100% N = 120	"Immunoassay sensitivity and selectivity were 97 and 100% (HEIA) and 99 and 84% (CEDIA), respectively, compared with LC–HR-MS." [9]	The CEDIA assay is more sensitive than HEIA but exhibits lower selectivity to some opiate compounds.
CEDIA Bup I Bup II	NA	Concordance with UPLC-MS/MS: CEDIA Bup II - 99.2%; CEDIA Bup I - 97.7% N = 1119 urine specimens from 921 patients	"CEDIA Bup II has excellent correlation to LC-MS/MS and has advantages over the current Bup assay: reduced false positives (no reaction to codeine, morphine and tiapride) and reduced false negatives due to cross-reactivity to Norbup and Norbup-gluc." [10]	The Bup II assay identifies three metabolites: Bup-glucuronide, Norbup and Norbup-glucuronide offering greater sensitivity and specificity over Bup I.
CEDIA Bup I Bup II	NA	Concordance with GC/MS: CEDIA Bup II - 99.2%; CEDIA Bup I - 82.5% N = 120 opiate maintenance therapy patients	"The CEDIA Buprenorphine II assay detects the presence of free buprenorphine, free norbuprenorphine, conjugated buprenorphine and conjugated norbuprenorphine accumulated… The cut-off of 10 ng mL is therefore comparable to the CEDIA Buprenorphe assay cut-off of 5 ng/mL." [11]	The CEDIA Buprenorphone II assay has excellent correlation to GC/MS.

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Cocaine Metabolite				
DRI	*NA	Within-run Precision: 0.8% Between-run Precision: 8.5% Two laboratorians analyzed a daily average of 25 urine samples.	"Comparison for the 95% confidence range (mean ± 2 SD) for each calibrator showed no overlap, thus indicating there was adequate distinction between calibrators." [12]	The DRI assay demonstrated excellent within-run and between-run precision.
CEDIA	*NA	Concordance with GC/MS at the 150 ng/mL cutoff: Cocaine Metabolite: 97.8% (138 positives) 3 were low positives (111, 101 and 109 µg/L) and tested negative by the immunoassay screen. N = 15,600 total samples, 141 positives by GC/MS	"The CEDIA assays for all the major drugs of abuse are reliable and effective for large-volume urine screening programs." [4]	The CEDIA Cocaine assay has good orrelation with GC/MS.
DRI	NA	Concordance with LC-MS/MS at the 300 ng/mL cutoff: DRI: 100% N = 1,674, 82 positive	"The false-positive rate was lowest for benzoylecgonine at 0% (0/82)…" [13]	The DRI Cocaine Metabolite assay (Benzolecgonine) has excellent correlation with LC-MS/MS.
Cotinine				
DRI	NA	Concordance with LC-MS/MS: 100% (no false-negatives) N = 39 cotinine Specimens	When using semi-quant... there is positive bias for DRI Cotinine compared to LC-MS/MS" [14]	DRI Cotinine is useful for screening purposes.
Ecstasy				
DRI	KIMS: ABUSCREEN® Online Amphetamine and modified Amphetamine	Confirmation rate for MDMA and MDA: DRI Ecstasy: 87.5% DRI Amphetamines: 7.94% KIMS Aphetamines: 7.95% KIMS Amphetamines Modified: 19.66% N > 27,000	"The AMPH/METH-specifc reagents (ONLINE and DRI) both reliably detected AMP/MTH-positive samples. The DRI Ecstasy reagent did provide increased sensitivity for MDMA with a good confirmation rate and few false-positive screening results." [15]	The AMPH/METH assays do not have sufficient cross-reacticity to detect MDA and MDMA. The DRI Ecstasy assay is more specific as it was designed specifically to detect MDMA and MDA.
Ethyl Alcohol				
DRI	*NA	Number of Specimens Testing Positive for Ethanol: DRI: 13 Negative samples: 2; read just below 10 mg/dL	"..the two discrepancies...were close to the assay's sensitivies and not considered clinically important. We found the performance of ...the DRI [Ethanol] reagent ...suitable for our patient population drug of abuse testing needs." [16]	The DRI Ethyl Alcohol assay is an accurate method for screening.
Ethyl Glucuronide (EtG) †				
DRI	NA	Agreement with LC-MS/MS: 500 ng/mL cutoff = sensitivity 98.7%, specificity 98% 1000 ng/mL cutoff = sensitivy 97.9%, specificity 98.4% N = 400	"These results indicate a high level of accuracy and selectivity of the DRI EtG assay for quantification of urinary EtG." [17]	DRI EtG assay is very accurate and has good agreement with LC-MS/MS.

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Fentanyl †				
DRI	NA	Concordance with LC-MS/MS: Sensitivity: 100% (no false negatives) Specificity: 86% (7 false positives) a) 5 samples cross reacted with risperidone and 9-hydroxyrisperidone. B) 2 samples close to cutoff of 2 ng/mL N = 1,269 by immunoassay; confirmed 79 samples by LC-MS/MS	"The DRI Fentanyl immunoassay can be used to screen for fentanyl or acetylfentanyl; however, confirmation testing should be performed for all samples that screen positive." [18]	Excellent diagnostic sensitivity of 100%; cross reacts with various analogs of fentanyl.
DRI	SEFRIA, ARK	Cross-reactivity to 11 Fentanyl analogs (spiked into blank urine): DRI: detects 10 out of 11 SEFRIA: detects 11 out of 11 ARK: detects 11 out of 11 N = 58 patient urine samples: presence of fentanyl and 7 analogs DRI: 49/58 • SEFRIA: 53/58 ARK: 56/58	"The present results demonstrated that the urinary fentanyl immunoasays are generally useful also for preliminary screening of fentanyl analogs sold as NPS." [19]	The DRI Fentanyl assay cross-reacts with 10 out of 11 fentanyl analogs tested.
Heroin Metabolite (6-AM)				
CEDIA	NA	Concordance with GC/MS: 98% N = 525 specimens	"The CEDIA heroin metabolite (6-AM) immunoassay produced a high confirmation rate when challenged with urine specimens and therefore should be a useful tool in forensic toxicology." [20]	The CEDIA 6-AM assay accurately identifies individuals taking heroin.
CEDIA (6-AM)	KIMS (Opiate)	87 specimens contain 6-AM, confirmed by GC-MS: CEDIA: all 87 specimens screened positive for 6-AM KIMS: 12 screened positive for morphine	The CEDIA heroin metabolite (6-AM) reagent assay appears well adapted for the rapid and specific detection of heroin abuse as an alternative for, or an adjunct test to, the current opiates (codeine/morphine) IA screening procedure." [21]	CEDIA assay can accurately detect 6-AM. KIMS Opiate assay is not designed to accurately identify 6-AM.
Hydrocodone				
DRI	NA	Concordance with LC-MS/MS: 94.8% (qualitative and semi-quantitative) N = 268 specimens	"The DRI Hydrocodone/Hydromorphone assay demonstrated excellent sensivitiy and specificity to hydrocodone, its major metabolites hydromorphone, hydromorphone 3-ß-D glucuronide." [22]	The assay is an accurate method to screen for the presence of hydrocodone and its major metabolites.
LSD				
CEDIA	EMIT II	N = 221 presumed positive by EMIT II, 11 screened positive by CEDIA. KIMS was used to determine the cross-reactivity of the 221 samples. EMIT was found to cross-react with amphetamine (10), barbiturates (1) and opiates (1), causing false positives. N = 24 (a different set of samples), confirmed positive by GC/MS, 23 were positive by CEDIA and EMIT II Precision at cutoff of 0.5 ng/mL CEDIA: 3.5 % CV • EMIT II: 9.0 % CV	"CEDIA demonstrated better precision than EMIT II….cross-reacted with fewer compounds than EMIT II and produced fewer extraneous positives than EMIT II." [23]	The CEDIA LSD assay exhibited superior precision and specificity when compared to EMIT II for LSD.
Methadone				
DRI	*NA	Number of Specimens Testing positive for Methadone at the 300 ng/mL cutoff: DRI: 12	"We found the performance of ...the DRI [Methadone] reagent ...suitable for our patient population drug of abuse testing needs." [16]	The DRI Methadone assay is a reliable and accurate method for screening.

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Methadone Metabolite (EDDP)				
CEDIA	*NA	Concordance with GC/MS: 99/108 confirmed for EDDP CEDIA: 99/108 were positive for EDDP, 100% concordance with GC/MS 9 samples could not be confirmed due to insufficient specimen	"The CEDIA EDDP assay is a sensitive and reliable technique to determine the compliance of subjects prescribed methadone for opiate detoxification and maintenance in the clinical setting." [24]	The CEDIA EDDP assay is the ideal assay to monitor for patient compliance.
Methaqualone				
DRI	EIA	Concordance with EIA: 98.4% DRI: 67 negative, 63 positive EMIT (EIA): 68 negative, 62 positive, 3 discordant samples were found to contain borderline concentrations of methaqualone and were confirmed positive by GC/MS. N = 139	"There is good correlation between DRI and commerically available EIA assay." [25]	The DRI Methaqualone assay is a highly accurate and reliable screening method.
Opiates				
DRI CEDIA	NA	Concordance with GC/MS at the 300 ng/mL cutoff: DRI = 95.2% CEDIA = 94.9% N = 414 samples	"Data derived from this study indicated DRI and CEDIA adapted by this study generated acceptable preliminary test results for ….morphine/codeine…" [26]	The CEDIA Opiate and DRI Opiate assays have very low false positive and false negative rates.
Oxycodone				
DRI	NA	Concordance with GC/MS: Specificity: 99.8% Sensitivity: 99.1% N = 1523 Specimens	"We have found the DRI-Oxy assay with a cutoff of 100 ng/mL a highly reliable method for the detection of oxycodone and /or oxymorphone in urine specimens." [27]	The DRI Oxycodone assay is a highly specific method for the detection of oxycodone and oxymorphone.
DRI	NA	Concordance with LC-MS/MS at 100 ng/mL cutoff: 93.8% (45/48), no false negatives	"In conclusion, the DRI Oxycodone immunoassay at 100 ng/mL cut-off is a reliable assay to detect oxycodone concentration in urine with no false negative results." [28]	The DRI Oxycodone assay is a reliable immunoassay at the 100 ng/mL cutoff.
DRI	HEIA	Cross-reactivity: DRI: Naloxone and Naloxone glucuronide = no cross-reactivity even at 100,000 ng/mL HEIA: Naloxone = cross-reacts at 2000 ng/mL; Naloxone glucuronide cross-reacts at 5600 ng/mL N = 7 positive samples by GC/MS	"…be aware of the cross-reactivity of naloxone and naloxone glucuronide with the …HEIA assay..to prevent false accusations against patients taking Suboxone" [29]	For patients who are taking Suboxone, the HEIA Oxycodone assay may result in false positive results. The DRI assay will not have this problem.
Phencyclidine (PCP)				
DRI	*NA	DRI PCP: Within-run Precision, %CV: Neg Cal: 1.6%; Cutoff Cal at 25 ng/mL: 1.3%; High Cal: 1.5% DRI PCP: Between-run Precision, %CV: Neg Cal: 4.5%; Cutoff Cal at 25 ng/mL: 4.0%; High Cal: 4.0%	"Comparison of the 95% confidence range (mean ± 2 SD) for each calibrator showed no overlap, thus indicating there was adequate distinction between calibrators." [12]	The DRI PCP assay demonstrated excellent within-run and between-run precision.
CEDIA	*NA	Concordance with GC/MS: DRI: 100% N = 4 positive samples N = 8,800 total samples screened	"The new line of CEDIA tests for drugs of abuse is reliable, convenient, easy to use, and effective and efficient for large-volume workplace drug testing and other applications." [4]	The CEDIA PCP assay has good concordance with GC/MS.

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Propoxyphene (PPX)				
DRI	EMIT II Plus, KIMS (ABUSCREEN Online)	Agreement with GC/MS: DRI: 100% • KIMS: 100% • EMIT II Plus: 80% N = 160 samples of which 100 were positive by GC/MS	"The discordant ...results were due to poor cross-reactivity of EMIT II to norpropoxyphene." [30]	DRI Propoxyphene assay has better sensitivity than EMIT II.
THC (Cannabinoids)				
CEDIA DRI	EMIT II	Sensitivity: (positive as positive) EMIT II: 84% • DRI: 82.5% • CEDIA: 62% Specificity: (negative as negative) EMIT II: 94.7% • DRI: 97.8% CEDIA: 99.3% Efficiency: (sensitivity plus specificity) EMIT II: 92.8% • DRI: 95.2% CEDIA: 92.9%	"All three assays had similar performance efficiencies (at the 50 ng/mL cutoff). CEDIA had highest specificity; EMIT II highest sensitivity; DRI highest overall efficiency." [31]	DRI has the best overall concordance with GS/MS.
CEDIA	KIMS	False-Positive Findings in 8 patients treated with Pantoprazole, with 2 sampling timepoints, each patient N = 16: DRI: no false positives KIMS: one false positive	"Patients with cannabis hyperemesis syndrome suffer persistent vomiting and are frequently prescribed a Pantoprazole… DRI Cannabinoids assay was not interfered by Pantoprazole." [32]	The DRI Cannabinoids assay does not cross-react with Pantoprazole; as such, no false positives were identified. The KIMS assay did have a false positive.
Tricyclics Antidepressants (TCA)				
DRI	*NA	Number of Urine Specimens Tested Positive: DRI TCA: 10 "The 10 samples positive for a tricyclic antidepressant were from patients prescribed either doxepin, nortryptyline, amitriptyline, imipramine or desipramine."	"We found the performance of ...the DRI [TCA] reagent ...suitable for our patient population drug of abuse testing needs." [16]	The DRI TCA assay is a reliable and accurate method for screening patients prescribed tricyclic antidepressant drugs.
Synthetic Cannabinoids: UR-144/XLR-11 ‡				
CEDIA	NA	Concordance with LC-MS/MS: Cutoff 10 ng/mL CEDIA: 96.4% N = 84 urine specimens	"The assay demonstrates reliable detection of UR-144-related synthetic cannabinoids, without significant cross-reactivity to other commonly abused opioids and/or prescribed drugs." [33]	The assay accurately identifies UR-144/XLR-11 and its metabolite and is highly specific.
Synthetic Cannabinoids: AB-PINACA ‡				
CEDIA	NA	Concordance with LC-MS/MS: Cutoff 20 ng/mL CEDIA: 88.9% N = 90 urine specimens	"1) The assay demonstrates ability to detect multiple structurally similar INACA synthetic cannabinoids. 2) A number of other synthetic cannabionids, when in high enough concentration, may also be detected. 3) A portion of the positives samples (4 out of 100) determined by the immunoassay could not be confirmed by the available LC-MS/MS methods." [34]	The assay identifies a broad range of INACA like compounds; however, mass spec standards are not available to confirm for all variants.

NA=not available; no other technologies were discussed in the publication
*NA=not available; other technologies were discussed in the publication but they are no longer available on the market
† USA: For Criminal Justice and Forensic Use Only (CJ&F)
International: In Vitro Diagnostic (IVD)
‡ USA: For Criminal Justice and Forensic Use Only (CJ&F)

References

1. Edwin F. Ullman, Homogeneous Immunoassays: Historical Perspective and Future Promise. *Journal of Chemical Education*, Vol. 76 No. 6, June 1999.
2. Mark J. Levy, Anna P. Jaklitsch Homogeneous Enzyme Immunoassays: EMIT, Recent advances in clinical biochemistry: Edited by CP Price and KGMM Alberti. Churchill Livingstone, Edinburgh, pages 11 - 20. 1985.
3. Michael Hailer, York Glienke, Inge-Maria Schwab, and Ludwig von Meyer, Modification and Evaluation of Abuscreen OnLine Assays for Drug Metabolites in Urine Performed on a COBAS FARA II in Comparison with EMIT d.a.u.Cannabinoid 20. *Journal of Analytical Toxicology,* Vol. 19, March/April 1995.
4. David A. Armbruster, Edward C. Hubster, Melvin S. Kaufman, and Monica K. Ramon, Cloned Enzyme Donor Immunoassay (CEDIA) for Drugs of Abuse Screening, Clin. Chem. 41/1, 92-98 (1995); Drug Monitoring and Toxicology.
5. https://immunalysis.com/products/sefria (Accessed November 6, 2018)
6. Microgenics, a part of Thermo Fisher Scientific. DRI Amphetamines Assay, Package Insert. Thermo Scientific, PN 0130, August 2017.
7. Microgenics, a part of Thermo Fisher Scientific. CEDIA Amphetamine/Ecstasy Assay, Package Insert. Thermo Scientific, PN 10006576, February 2018.
8. Rebecca T. DeRienz, Justin M. Holler, Megan E. Manos, John Jemionek, Marilyn R. Past, Evaluation of Four Immunoassay Screening Kits for the Detection of Benzodiazepines in Urine, *Journal of Analytical Toxicology*, Vol. 32, July/August 2008.
9. Sarah L. Belsey, Lewis Couchman and Robert J. Flanagan, Burprenorphine Detection in Urine Using Liquid Chromagraphy - High-Resolution Mass Spectrometry: Comparison with Cloned Enzyme Donner Immunoassay (ThermoFisher) and Homgeneous Enzyme Immunoassay (Immunalysis), *Journal of Analytical Toxicology*, 2014:38:438-443.
10. Michael Böttcher, Nicky Günther, Field evaluation of a new homogeneous Buprenorphine Immunoassay, Poster - SOFT 2016, Dallas, TX.
11. Florian Pitterl, Barbara Saxl, Lakshmi Anne, Marion Pavlic, Comparison of CEDIA Buprenorphine II Assay vs on Market CEDIA Buprenorphine Assay in Human Urine, Poster - TIAFT 2016, Brisbane, Queensland, Australia.
12. LA Broussard and L. Hanson, Evaluation of DRI enzyme immunoassays for drugs of abuse screening on the Cobas Mira, *Clin Lab Sci*, March 1, 1997; 10(2): 83-86.
13. R Gencheva, A Petrides, M Kantartjis, M Tanasijevic, J L Dahlin, S Melanson, Clinical Benefits of Direct-to-Definitive Testing for Monitoring Compliance in Pain Management, *Pain Physician*, November/December 2018; 21:E583-ES92.
14. R Brent Dixon and Amitava Dasgupta, Comparison of Semiquantitative 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 Semiquantitative Values May be Unreliable, *Journal of Clinical Laboratory Analysis*, 00:1-4 (2016).
15. Peter R. Stout, Kevin L. Klette, and Russell Wiegand, Comparison and Evaluation of DRI Methamphetamine, DRI Ecstasy, Abuscreen ONLINE Amphetamine, and a Modified Abuscreen ONLINE Amphetamine Screening Immunoassays for the Detection of Amphetamine (AMP), Methamphetamine (MTH), 3,4-Methylenedioxyamphetamine (MDA), and 3,4-Methylenedioxymethamphetamine (MDMA) in Human Urine, *Journal of Analytical Toxicology*, Vol. 27, July/August 2003.
16. V. Haver, D. Black, and J. Garbin, Evaluation of DRI Drug-of-Abuse Reagents on the Hitachi 911, *Journal of Analytical Toxciology*, Vol. 22, September 1998; Letter to the Editor.
17. Michael Böttcher, Olof Beck, and Anders Helander, Evaluation of a New Immunoassay for Urinary Ethyl Glucuoronide Testing, *Alcohol & Alcoholism*, Vol. 43, No. 1, pp. 46-48, 2008.
18. Bei-Tzu Wang, Jennifer M. Colby, Alan H.B. Wu and Kara L. Lynch, Cross-reactivity of Acetylfentanyl and Risperidone with a Fentanyl Immunoassay, *Journal of Analytical Toxicology*, 2014: 38: 672-675.
19. Anders Helander, Katarina Stojanovic, Tomas Villén, Olof Beck, Detectability of fentanyl and designer fentanyls in urine by three commercial fentanyl immunoassays, *Clin Chem,* 2018, Vol 1, Issue 8, 1297-1304.
20. Amanda J. Jenkins, Eric S. Lavins, and Ann Snyder, Evaluation of the CEDIA Heroin Metaoblite (6-AM) Immunoassay with Urine Specimens from a Criminal Justice Drug-Testing Program, *Journal of Analytical Toxicology*, Vol. 28, April 2005, 201-204.
21. Justin M. Holler, Thomas Z. Bosy, Kevin L. Klette, Russel Wiegand, John Jemionek, and Aaron Jacobs, Comparison of the Microgenics CEDIA Heroin Metabolite (6-AM) and the Roche Abuscreen I ONLINE Opiate Immunoassays for the Detection of Heroin Use in Forensic Urine Samples, *Journal of Analytical Toxicology*, 2004, 28(6):489-93.
22. Tabssum Naqvi, Pong Chua, Dijana Obralic, Maha Rudrabhatla, Liang Xu, Christopher Semko, Rong Zhang, Vani Bodepudi and Lakshmi Anne, Development of Homogeneous Enzyme Immunoassay for the Detection of Hydrocodone and Hydromorphone in Human Urine, Poster/Abstract, SOFT 2014, Grand Rapids, MN.
23. Russell F. Wiegand, Kevin L. Klette, Peter R. Stout, and Jay M. Gehlhausen, Comparison of EMIT II, CEDIA, and DPC RIA Assays for the Detection of Lysergic Acid Diethylamide in Forensic Urine Samples, *Journal of Analytical Toxicology*, Vol. 26, October 2002.
24. S George, S Parmar, C Meadway and RA Braithwaite, Application and validation of a urinary methadone metabolite (EDDP) immunoassay to monitor methadone compliance, *Ann Clin Biochem*, 2000; 37: 350-354.
25. Microgenics, a part of Thermo Fisher Scientific. DRI Methaqualone Assay, Package Insert. Thermo Scientific, PN 0762, Jan. 2018.
26. Min-Kun Huang, Yu-Shan Dai, Chuong-Huei Lee, Chiareiy Liu, Wen-Ing Tsay, and Jih-Heng Li. Performance Characteristics of DRI, CEDIA, and REMEDIi Systems for Preliminary Tests of Amphetamines and Opiates in Human Urine, J*ournal of Analytical Toxicology*, Vol., 30, January/February 2006.
27. Ronald C. Backer, Joseph R. Monforte, and Alphonse Poklis, Evaluation of the DRI Oxycodone Immunoassay for the Detection of Oxycodone in Urine, *Journal of Analytical Toxicology*, Vol. 29, October 2005.
28. R. Brent Dixon, Bonnette Davis, and Amitava Dasgupta, 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, *Journal of Clinical Laboratory Analysis,* 30: 190-195 (2016).
29. Amanda J. Jenkins, Joseph G. Poirier II, and Matthew P. Juhascik. Cross-reactivity of Naloxone with Oxycodone Immunoassays: Implications for Individiuals Taking Suboxone, *Clinical Chemistry,* 55:7 (2009), Letters to the Editor.
30. Alphonse Poklis, Justin L. Poklis, Lisa D. Tarnai, and Ronald C. Backer, Evaluation of the Triage PPY On-Site Testing Device for the Detection of Dextropropoxyphene in Urine, *Journal of Analytical Toxicology*, Vol. 28, September 2004.
31. Richard A. Gustafson, Barry Levine, Peter R. Stout, Kevin L. Klette, M.P. George, Eric T. Moolchan, and Marilyn A. Huestis, Urinary Cannabinoid Detection Times after Controlled Oral Administration of Δ9-Tetrahydrocannabinol to Humans, *Clinical Chemistry,* 49:7 1114-1124 (2003).
32. Isabel Gomila, Bernardino Barceló, Antonio Rosell, Sonia Avella, Laura Sahuquillo, and Macarena Dastis. Cross-Reactivity of Pantoprazole with Three Commercial Cannabinoids Immunoassays in Urine, *Journal of Analytical Toxicology*, 2017; 41: 460-764.
33. Yunfei Chen, Seema Parveen, John Donaldson, Imad Nashashibi, Chandrasekaran Raman, Neha Betawar, Lakshmi Anne, Tony Prestigiacomo, Tabassum Naqvi. Development of Homogeneous Enzyme Immunoassay for the Detection of UR-144/ XLR-11 and Structurally Related Synthetic Cannabinoids in Human Urine. Poster/ Abstract: SOFT/TIAFT 2017, Baton Rouge, FL.
34. Chi-Yun Pai, Seema Parveen, Chandrasekaran Raman, Tabassum Naqvi, Rong Zhang, Tony Prestigiacomo, Lakshmi Anne. Development of Homogeneous Enzyme Immunoassay for the Detection of AB-PINACA, its Metabolites and Structurally Related Synthetic Cannabinoids in Human Urine. Poster/Abstract: SOFT/TIAFT 2017, Baton Rouge, FL.

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