SmartNotes

Why test for synthetic cannabinoids?

Synthetic cannabinoids are the largest and fastest growing group of new psychoactive substances (NPS) on the market.[1] Sold under the common brand names of "Spice," "K2," and "Kronic", they act upon the cannabinoid receptors in the body, mimicking to varying degrees the main active chemical found in marijuana (Δ9-THC). However, they can have higher potency and higher health risks to users than plant derived THC, causing severe effects such as violent behavior, suicidal thoughts, cognitive impairment, seizures, kidney damage, coma, and even death.[2] Poison Centers across the United States have experienced a significant increase in calls related to synthetic cannabinoids, tripling in number between 2014 and 2015 from 1,085 to 3,572.[3]

Synthetic cannabinoid chemicals are sprayed or soaked on to a mixture of shredded plant material and marketed mostly over the internet or in head shops as incense. Although the packages are labeled "not for human consumption," and marketed as legal and safe, they look like plant material, leaving people to believe that it is a safe alternative to marijuana.[2]

UR-144 and XLR-11 (a fluorinated form of UR-144, also known as 5-F-UR-144), AB-PINACA, AB-CHMINACA, and AB-FUBINACA are among the commonly used synthetic cannabinoid drugs, accounting for at least 60% of synthetic cannabinoids reported in the United States.[2,4] Due to their prevalence and potential for adverse health effects, the Drug Enforcement Administration (DEA) has placed both UR-144 and XLR-11 as Schedule I drugs under the Controlled Substance Act[5], and as of January 2017, the DEA is in the final stages of placing AB-CHMINACA and AB-PINACA as Schedule I substances.[6]

Synthetic Cannabinoids Facts

- **Largest group of New Psychoactive Substances (NPS) on the market**
  - Mind-altering chemicals sprayed on dried, shredded plant materials can be smoked (herbal incense) or solid as liquids to be vaporized and inhaled in e-cigarettes and other devices (liquid incense).
  - Increased disproportionately compared to other NPS groups: doubled in the last few years[1]
- **More toxic than cannabis**
  - Four to one hundred times stronger than marijuana[7]
  - Negative side effects: seizures, hypertension, nausea, vomiting, and even death[2]
  - Shorter duration of action[2]
  - On-set of effects: Peak in minutes versus hours[2]
  - Linked to increased emergency room hospitalizations and fatalities[3]
- **DEA Schedule I Category: The most restrictive category for controlled substances**
  - UR-144, XLR-11, AB-PINACA, AB-CHMINACA, and AB-FUBINACA account for 60% of synthetic canninoids reported in the US.
  - UR-144 and XLR-11 are Schedule I substances[5]
  - AB-PINACA and AB-CHMINACA: in last stages of finalizing as Schedule 1 substances[6]

ThermoFisher SCIENTIFIC

The Thermo Scientific Solution

There are now two Synthetic Cannabinoid Assays which can be used for quick screening for the compounds which are most commonly found. The antibody in each of the assays cross reacts with multiple metabolites and structurally similar compounds, allowing for maximum detection of synthetic cannabinoids.

DEA Schedule I Substance	Synthetic Cannabinoid Assays	Significant Cross-Reactants*	Minor Cross-Reactants†	Cutoff Concentration (ng/mL)
2017 In process	CEDIA AB-PINACA	34	11	20 ng/mL
2016	CEDIA UR-144/ XLR-11	15	23	10 ng/mL

*Tested positive above the cutoff
†Borderline Result: Tested negative but semi-quantitative value is near the cutoff

Maximize Detection

Screen for Presence of Drug

Qualitative Detection (Positive or Negative)

The cutoff concentration is important for qualitative screening, as it gives a result that confirms presence or absence of drug in the sample. Qualitative detection works especially well for prescription drugs which have validated cutoffs; this is because the pharmacokinetic properties are well understood and therefore, cutoff values are highly indicative of the presence or absence of prescription drugs. While qualitative detection works well for prescription drugs, it may not always be the most informative approach for "street drugs" such as synthetic cannabinoids.

Monitor for Borderline Samples

Semi-quantitative (SQ) Detection (ng/mL)

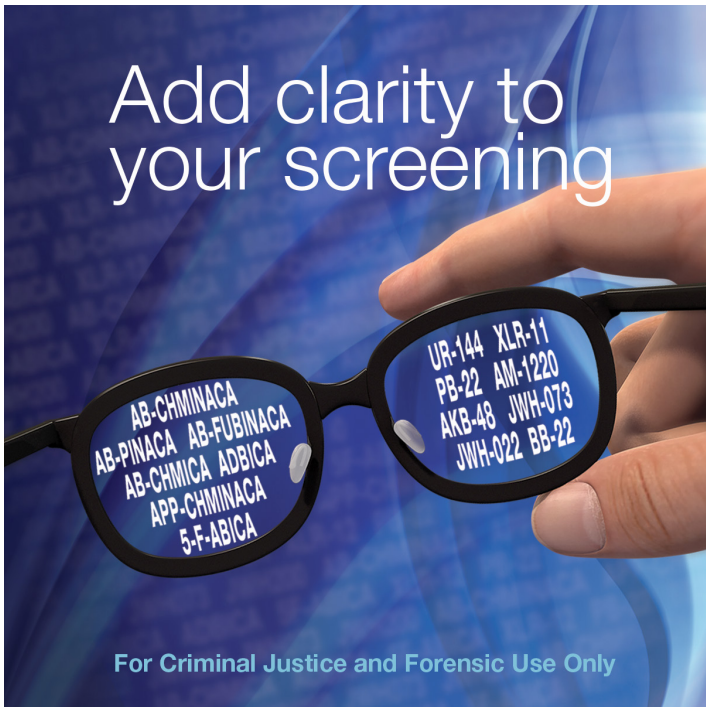
Toxicologists state that "there are no established cutoffs for synthetic cannabinoids as little to nothing is known about dose effect relationship or detection windows and there are no established regulatory limits."[8] The semi-quantitative option in the immunoassay lets you determine if borderline samples, which screen just below the cutoff, contain some level of synthetic cannabinoids. Detection using the semi-quantitative mode is especially important, as the type of synthetic cannabinoid offered in the market can change rapidly. These structurally similar compounds might be missed otherwise in the qualitative detection mode.

Semi-quantitative detection may identify suspect samples, especially from clients that demonstrate behaviors associated with having taken synthetic cannabinoids, as it is possible they might show drugs in the urine which may be below the cut-off. The semi-quantitative mode of detection also provides guidance to the LC-MS/MS lab for confirming if any structurally similar compounds may be present.

Detect Compounds with Low Cross-Reactivity

The Cumulative Response

Structurally similar compounds may not be detected by themselves due to their low cross-reactivity (% cross-reactivity); however, they may give a positive result when multiple drugs are present simultaneously in the urine specimen. This is because the antibody cross-reacts with metabolites and multiple synthetic cannabinoid compounds. This leads to a cumulative response whereby multiple compounds may collectively contribute to a positive test result.[9]



Benefits of Using the Thermo Scientific Synthetic Cannabinoid Assays

CEDIA AB-PINACA Assay

- Specifically detects AB-PINACA , its fluorinated form (5-F-AB-PINACA), and their major metabolites
- Detects a broad spectrum of metabolites and structurally similar compounds commonly abused: AB-CHMINACA, AB-FUBINACA, AB-CHMICA, ADBICA, 5-F-ABICA, APP-CHMINACA and more
- Good correlation to LC-MS/MS
- For Criminal Justice and Forensic Use Only

CEDIA UR-144/XLR-11 Assay

- Specifically detects UR-144 and its fluorinated form XLR-11 (5-F-UR-144) and their major metabolites
- Detects other structurally similar compounds commonly abused: UR-144 pentanoic acid, XLR-12, AM-2201, AM-1220, JWH-250 and metabolites, JWH-018 and metabolites, JWH-200, JWH-020, PB-22 pentanoic acid, AKB-48 metabolite, BB-22 and related metabolites
- Good correlation to LC-MS/MS
- For Criminal Justice and Forensic Use Only

CEDIA Synthetic Cannabinoid Assay Benefits

- Qualitative and semi-quantitative detection
- Ability to monitor borderline samples below the cutoff with semi-quantitation: since synthetic cannabinoids are not naturally found in the body, a sample with a concentration close to the cutoff could be suspect, and an indication that the drug was taken (confirmed by LS-MS/MS)
- Ability to detect synthetic cannabinoids with low cross-reactivity
  - – When multiple compounds are present and contribute to the cumulative response
  - – When present in high enough concentrations
- No significant cross reactivity to any other commonly abused drugs (i.e. opioids, over-the-counter drugs)
- Applications available on a wide range of clinical analyzers

CEDIA AB-PINACA Assay Cross-Reactivity

The table below illustrates the numerous variants of AB-PINACA that can be detected using the Thermo Scientific™ CEDIA® AB-PINACA Assay. Some variants have low cross reactivity and may not be detected by themselves; however, they may give a positive result due to cumulative response when multiple drugs are present simultaneously in the urine specimen (to be confirmed by LC-MS/MS). They may also give a positive result if present in the specimen in high enough concentrations.

Significant Cross Reactants Table[10]

AB-PINACA Derivatives and Metabolites	Tested Concentration (ng/mL) ‡	SQ Concentration (ng/mL) §	% Cross-Reactivity
AB-CHMINACA M1A	14	25	179%
5-F-AB-PINACA	14	20.8	149%
AB-CHMINACA M1B	18	22.2	123%
AB-PINACA 5OH pentyl	20	23.7	119%
AB-PINACA 4OH	20	23.7	119%
AB-PINACA N-(4-fluoropentyl) isomer	20	21.6	108%
AB-PINACA pentanoic acid	20	20	100%
AB-FUBINACA	25	23.4	94%
AB-PINACA	25	20.1	80%
5-F-AB-PINACA N-(4-hydroxypentyl) metabolite	28	24.2	86%
AB-PINACA N-(3-fluoropentyl) isomer	32	22.7	71%
AB-FUBINACA 3-fluorobenzyl isomer	40	21.5	54%
AB-CHMINACA	66	25.5	39%
AB-PINACA N-(2-fluoropentyl) isomer	85	23	27%
AB-CHMICA	120	35	29%
5-chloro AB-PINACA	140	21.4	15%
AB-FUBINACA isomer 1	150	23.1	15%
5-F-ABICA	200	24.8	12%
ADB-FUBINACA	310	21.2	6.80%
ADB-PINACA pentanoic acid	450	21	4.70%
APP-CHMINACA	475	21	4.40%
5-F-AMB	510	21	4.10%

Significant Cross Reactants Table[10] continued

AB-PINACA Derivatives and Metabolites	Tested Concentration (ng/mL) ‡	SQ Concentration (ng/mL) §	% Cross-Reactivity
AMB	730	21.4	2.90%
AB-FUBINACA 2-fluorobenzyl isomer	800	20.4	2.60%
ADB-PINACA RM	2,500	32.1	1.30%
ADBICA	2,500	24.8	1.00%
APP-FUBINACA	2,500	22.2	0.90%
EMB-FUBINACA	2,500	20	0.80%
MAB-CHMINACA RM (ADB-CHMINACA)	5,000	33.7	0.70%
AB-FUBINACA 2-fluorobenzyl isomer	5,000	31.9	0.60%
JWH-250 N-(5-carboxypentyl) metabolite	5,000	26.5	0.50%
ADBICA pentanoic acid	10,000	35	0.40%
JWH-250 N-(4-hydroxypentyl) metabolite	10,000	34.1	0.30%
MDMB-CHMINACA	10,000	26.3	0.30%

Minor Cross Reactants Table[10]

AB-PINACA Derivatives and Metabolites	Tested Concentration (ng/mL) ‡	SQ Concentration (ng/mL) §	% Cross-Reactivity
MA-CHMINACA	10,000	19.5	0.20%
AB-CHMINACA M2	10,000	15.9	< 0.2%
AB-FUBINACA isomer 5	10,000	17.7	< 0.2%
AB-CHMINACA M3A	10,000	16.5	< 0.2%
AB-PINACA cabonyl metabolite	10,000	15.1	< 0.2%
STS-135	10,000	10.3	< 0.2%
JWH-018 adamantyl carboxyamide	10,000	9.6	< 0.2%
AB-FUBINACA 2A metabolite	10,000	9.3	< 0.2%
AB-CHMINACA M6	10,000	8.8	< 0.2%
JWH-073 N-(4-hydroxybutyl) metabolite	10,000	8.7	< 0.2%
JWH-250 N-(5-hydroxypentyl) metabolite	10,000	6.7	< 0.2%

CEDIA UR-144/XLR-11 Assay Cross-Reactivity

The table below illustrates the numerous variants of UR-144/XLR-11 that can be detected using the Thermo Scientific™ CEDIA® UR-144/XLR-11 Assay. Some variants have low cross reactivity and may not be detected by themselves.

However, they may give a positive result due to the cumulative response when multiple drugs are present simultaneously in the urine specimen (to be confirmed by LC-MS/MS). They may also give a positive result if present in the specimen in high enough concentrations.

Significant Cross Reactants Table[11]

UR-144 Derivatives and Metabolites	Tested Concentration (ng/mL) ‡	SQ Concentration (ng/mL) §	% Cross-Reactivity
UR-144 N-(5-hydroxypentyl) β-D-glucuronide	5	12	240%
UR-144 N-(5-hydroxypentyl)	5	11	220%
UR-144 N-pentanoic acid	10	12	120%
XLR-11	15	15	100%
XLR11 N-(4-pentenyl) analog	15	14	93%
UR-144 N-(4-hydroxypentyl)	15	11	73%
UR-144	20	11	55%
XLR-11 N-(2-fluoropentyl) isomer	20	11	55%
XLR-12	25	11	44%
UR-144 N-(2-hydroxypentyl)	35	11	31%
UR-144 N-(5-chloropentyl) analog	50	14	28%
UR-144 N-(5-bromopentyl) analog	100	17	17%
A-834,735	100	12	12%
UR-144 N-heptyl analog	100	12	12%
A-836,339	100	12	12%

Minor Cross Reactants Table[11]

UR-144 Derivatives and Metabolites	Tested Concentration (ng/mL) ‡	SQ Concentration (ng/mL) §	% Cross-Reactivity
AB-005	100	1	1.00%
AM-2201 N-(4-hydroxypentyl)	250	7	3%
JWH-250 N-(5-hydroxypentyl)	500	9	2%
5-Fluoro SDB-006	500	6	1.20%
JWH-018 N-pentanoic acid	500	6	1.20%
AKB-48 N-pentanoic acid	500	3	0.60%
AKB-48 N-(4-hydroxypentyl)	500	2	0.40%
UR-144 Degradant	500	1	0.20%
AM-1220	1,000	8	0.80%

Minor Cross Reactants Table[11] continued

UR-144 Derivatives and Metabolites	Tested Concentration (ng/mL) ‡	SQ Concentration (ng/mL) §	% Cross-Reactivity
A-796260	1,000	8	0.80%
JWH-073 N-butanoic acid	1,000	7	0.70%
JWH-018 N-(5-hydroxypentyl) ß-D-glucuronide	1,000	7	0.70%
JWH-200	1,000	5	0.50%
JWH-018 N-(5-hydroxypentyl)	1,000	4	0.40%
JWH-018 N-(4-hydroxypentyl)	1,000	4	0.40%
5-Fluoro AKB48 N-(4-hydroxypentyl)	1,000	3	0.30%
JWH-073 N-(5-hydroxybutyl)	1,000	3	0.30%
FUB-144	1,000	2	0.20%
UR-144 Desalkyl	1,000	2	0.20%
PB-22 N-pentanoic acid	10,000	8	0.08%
BB-22	10,000	8	0.08%
PB-22 3- carboxyindole	10,000	2	0.02%
PB-22 N-pentanoic acid 3-carboxyindole	10,000	1	0.01%

‡ = Tested Concentration is the concentration of drug (ng/mL) that was spiked into a drug-free urine matrix (to mimic a sample).

§ = SQ Concentration is the value obtained in the analyzer from the spiked drug-free urine matrix sample (based on a 2 or 5 point calibration curve).

% Cross-Reactivity = SQ Concentration / Tested Concentration x 100

SQ = Semi-quantitation

The higher percent cross-reactivity means the higher the likelihood the compound will be detected. When the SQ Result is just below the cutoff value, it may give an indication that a sample could have drug(s) present. Since synthetic cannabinoids are not naturally found in the body, a sample with a concentration close to the cutoff may indicate that the drug was consumed (to be confirmed by LC-MS/MS). To monitor for these borderline samples, we recommend using the semi-quantitative mode when screening for synthetic cannabinoids.

For more information, please contact your local Thermo Fisher Scientific Sales Representative or call Technical Service at toll free 1-800-232-3342 or 510-979-5000, Option 2, then 3 or techservice.mgc@thermofisher.com

Order Information

Part Number	CEDIA AB-PINACA Assay Description	Size
Reagent		
10022971	CEDIA AB-PINACA Assay	3 x 17 mL
10022977	CEDIA AB-PINACA Assay	1 x 65 mL
Calibrators		
10022930	CEDIA Negative Calibrator III	1 x 7.5 mL
10022931	CEDIA AB-PINACA 5 ng/mL Cal	1 x 5 mL
10022932	CEDIA AB-PINACA 20 ng/mL Cal	1 x 5 mL
10022933	CEDIA AB-PINACA 50 ng/mL Cal	1 x 5 mL
10022934	CEDIA AB-PINACA 100 ng/mL Cal	1 x 5 mL
Controls		
10022935	CEDIA AB-PINACA Control Set Low (10 ng/mL), High (30 ng/mL)	2 x 5 mL each level

Part Number	CEDIA UR-144/XLR-11 Assay Description	Size
Reagent		
10022949	CEDIA UR-144/XLR-11 Assay	3 x 17 mL
10022955	CEDIA UR-144/XLR-11 Assay	1 x 65 mL
Calibrators		
10022753	CEDIA Negative Calibrator II	1 x 10 mL
10022754	CEDIA UR-144 10 ng/mL Cal	1 x 5 mL
10022755	CEDIA UR-144 20 ng/mL Cal	1 x 5 mL
10022756	CEDIA UR-144 40 ng/mL Cal	1 x 5 mL
10022759	CEDIA UR-144 60 ng/mL Cal	1 x 5 mL
Controls		
10022760	CEDIA UR-144 Control Set Low (5ng/mL), High (15 ng/mL)	2 x 5 mL each leve1

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References

1. UNODC United National Office on Drugs and Crime, March 2015, vol 13, pg 4.
2. NIDA, SAMHSA-ATTC Blending Initiative, www.naatc.org (accessed February 27, 2017).
3. NFLIS 2015 annual report, pg 18.
4. NFLIS, Special Report. Synthetic Cannabinoids and Synthetic Cathinones Reported in FLIS, 2013-2015, cover page.
5. U.S Department of Justice, Drug Enforcement Administration, UR-144 (TCMP-018;KM-X1) and XLR11 (5-F-UR-144), May 2013, https://www.deadiversion.usdoj.gov/drug_chem_info/spice/spice_ur144_xlr11.pdf (accessed February 28, 2017).
6. U.S Department of Justice, Drug Enforcement Administration, Schedules of Controlled Substances: Temporary Placement of Three Synthetic Cannabinoids Into Schedule I. https://www.deadiversion.usdoj.gov/fed_regs/rules/2015/fr0130.htm (Accessed February 28, 2017).
7. https://www.redwoodtoxicology.com/services/synthetic_cannabinoid_urine (accessed April 21, 2017).
8. Wohlfarth, A., Scheidweiler, K.B., Chen, X., Liu, H-F, Huestis, M.A. Qualitative Confirmation of 9 Synthetic Cannabinoids and 20 Metabolites in Human Urine Using LC-MS/MS. Anal Chem. 2013 April 2; 85(7).
9. Barnes, A.J, Young, S., Spinelli, E., Martin, T.M., Klette, K.L., Huestis, M.A. Evaluation of a homogeneous enzyme immunoassay for the detection of synthetic cannabinoids in urine. Forensic Sci Int. 2014 August; 241; 27-34.
10. The Thermo Scientific CEDIA AB-PINACA Assay package insert.
11. The Thermo Scientific CEDIA UR-144/XLR-11 Assay package insert.

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