

**Drug Early Warning from Re-Testing Biological Samples:
Jefferson/Lincoln/Pulaski/Rockcastle Counties, Kentucky**



Office of National Drug Control Policy
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Abstract

The Community Drug Early Warning System (CDEWS) provides timely information about emerging drug use in criminal justice populations in local communities by obtaining and re-testing urine specimens already collected and tested for a limited panel of drugs by local criminal justice testing programs. CDEWS or local staff sample specimens that are ready to be discarded and send them to an independent laboratory for testing for an expanded panel of more than 160 drugs. By using already collected de-identified urine specimens, CDEWS can produce a relatively quick and inexpensive snapshot of the types of drugs recently used by participating populations and their testing program's ability to detect drugs being used by their population.

The CDEWS methodology has been implemented in 15 sites and the results are contained in six reports already released by the Office of National Drug Control Policy.

This report presents CDEWS findings from the study of a third probation program based on the HOPE (Hawaii's Opportunity Probation with Enforcement) model. The HOPE program was developed by Judge Steven Alm in Hawaii in 2004 and his program was the subject of an earlier CDEWS report. The HOPE program enrolls high risk felony probationers with serious criminal histories and extensive substance abuse histories in a program that includes frequent urine drug monitoring coupled with brief jail sanctions for drug test violations. This program model has since been expanded to other jurisdictions throughout the country. In Kentucky, the HOPE program is the model for the SMART (Supervision, Monitoring, Accountability, Responsibility, Treatment) program. The SMART program is being piloted in seven jurisdictions in Kentucky, of which two, (1) Jefferson County and (2) Lincoln/Pulaski/Rockcastle Counties, are the subject of this report. This report presents findings from adult probationers in both the SMART program and the traditional General Supervision program in these locations. Another previous CDEWS study with HOPE probationers was completed in Indiana.

A sample of 86 specimens was collected from the Kentucky SMART program. Of these, 38 had tested positive for any drug in their local limited CJS screen (CJS+) and 48 had tested negative for all drugs in their screen (CJS-). A sample of 176 specimens (83 CJS+ and 93 CJS-) was collected from General Supervision probationers. The de-identified specimens were sent to the CDEWS laboratory for expanded testing.

The CDEWS laboratory then tested the specimens collected for a large panel of more than 160 licit and illicit drugs, including many new psychoactive substances, such as cathinones and synthetic cannabinoids. The expanded testing showed that between one fifth and one third of the probationer specimens from each program that had tested CJS- for all drugs actually contained a likely illicit drug (drug not likely to have been taken under a doctor's supervision), primarily marijuana or the new psychoactive substance (NPS), β -Methylphenethylamine (BMPEA). BMPEA is a doping agent found in nutritional supplements, with stimulant effects that may mimic the effects of amphetamine (a compound to which it is structurally similar).

Finding drugs in urines that had passed the local limited drug screens was expected because the CDEWS laboratory used tests that were many times more sensitive than the local tests and included substances not screened for by the Kentucky Probation programs. These probation programs may wish to consider the costs and benefits of adopting additional and/or more sensitive urine tests to identify the drug users they are currently missing.

As expected, the CJS+ specimens from both the SMART and General Supervision programs contained a variety of drugs, mostly those that were contained in the local drug screen that caused them to be labeled CJS+. However, while CJS+ probationers from both programs were most likely to test positive for marijuana, the CJS+ General Supervision probationers were significantly more likely to test positive for methamphetamine and an NPS, primarily BMPEA, as compared with the CJS+ SMART program probationers. These findings raise the possibility that the General Supervision probationers studied who used stimulants may have also used BMPEA because of its similar effects. Synthetic cannabinoids were rare and found only in a few CJS- persons, suggesting that few probationers were using synthetic cannabinoids to avoid detection by their routine tests.

The General Supervision program probationers who tested CJS+ were also significantly more likely than the SMART program CJS+ participants (55% vs. 24%, $p < .01$) to test positive for a likely illicit drug other than marijuana. These results could indicate that the SMART program's sanctions for current drug use helped in reducing the variety of illicit drugs that their participants used.

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Introduction

The Community Drug Early Warning System (CDEWS) provides timely information about emerging drug use in criminal justice populations in local communities by obtaining and re-testing urine specimens already collected and tested for a limited panel of drugs by local criminal justice testing programs. CDEWS or local staff sample the specimens that are ready to be discarded and send them de-identified to an independent laboratory for testing for an expanded panel of drugs. By using already collected urine specimens, CDEWS can provide a relatively quick and inexpensive snapshot of the types of drugs recently used by criminal justice populations (see Appendices A and B for details). Thus, the CDEWS methodology has two primary objectives: (1) to identify and describe the use of emerging drugs in populations at high risk for recent drug use; and (2) to specify any important drugs that the current local testing program may be missing. A major innovation in the CDEWS methodology used in the current study is the expansion of the CDEWS testing panel to include testing for more than 160 licit and illicit substances, including opioids, benzodiazepines, antidepressants, and new psychoactive substances (NPS), such as cathinones and synthetic cannabinoids, using more sensitive testing technology than many criminal justice testing programs have available.

The CDEWS results are especially important for detecting emerging drugs because prior epidemics in the use of illegal drugs have often shown up in urinalysis results from criminal justice populations before they became evident in the larger community (DuPont & Wish, 1992; Wish, 1997). In addition, local testing programs typically can test for only a small number (often 6-12) of different drugs and the CDEWS results for more than 160 substances can be used by the local testing programs to gain some insight into whether their standard limited test panel is adequate to identify most of the drugs being used by their test population.

The CDEWS methodology has now been piloted in 15 sites and the results are provided in six reports already released by the Office of National Drug Control Policy (ONDCP) (Billing et al., 2017; Wish et al., 2013, 2015, 2016, 2016b, 2017). This report presents CDEWS findings from the study of a third probation program based on the HOPE (Hawaii's Opportunity Probation with Enforcement) model. The HOPE program was developed by Judge Steven Alm in Hawaii in 2004 and his program was the subject of an earlier CDEWS report. The HOPE program enrolls high risk felony probationers with serious criminal histories and extensive substance abuse histories in a program that includes frequent urine drug monitoring coupled with brief jail sanctions for drug test violations. This program model has since been expanded to other jurisdictions throughout the country. In Kentucky, the HOPE program is the model for the SMART (Supervision, Monitoring, Accountability, Responsibility, Treatment) program. The SMART program is being piloted in seven jurisdictions in Kentucky, of which two, (1) Jefferson County and (2) Lincoln/Pulaski/Rockcastle Counties, are the subject of this report. These jurisdictions were selected due to their participation in the SMART pilot program and also given their proximity to the cities of Louisville and Lexington. This report presents findings from adult

probationers in both the SMART probation program and the traditional General Supervision probation program in these locations. Another previous CDEWS study with HOPE probationers was completed in Indiana.

Methodology

Site Selection Procedures

We sought adult participants from the Kentucky General Supervision and SMART probation programs. Circuit Court Judge David Tapp was interested in implementing CDEWS in Kentucky and helped us to obtain approval for the study. We recruited the participation of five district offices representing four counties supervising adult probationers in both the General Supervision and SMART probation programs. For each of the probation programs, Districts 16-19 agreed to provide urine specimens for probationers in Jefferson County and District 20 for probationers in Pulaski, Lincoln, and Rockcastle Counties. Logistics for collecting urines from these district offices were discussed with staff over the phone to establish the study protocols. Prior to data collection, the Center for Substance Abuse Research (CESAR) at the University of Maryland, College Park, which carried out this study, submitted an application for the necessary approvals and obtained approval for the study from University of Maryland's Institutional Review Board (IRB). The specific steps taken to recruit and work with these Kentucky probation offices are described in Appendix A, along with more details about the specimen collection in Appendix B. Table 1 provides an overview of the key characteristics of the participating programs.

General Supervision Probationers

The Kentucky General Supervision program collects about 48,000 urine specimens annually from parolees and probationers, with an average number of approximately 32,500 General Supervision probationers tested. An onsite test cup that detects 12 drugs (amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, MDMA, methadone, methamphetamine, opiates, oxycodone, and PCP) is the standard screen used by this program. Other drugs, including synthetic cannabinoids, synthetic cathinones, and heroin (6-MAM) may be tested upon request. Contested positive specimens are sent to an offsite lab, Sterling Laboratories, for confirmation.

SMART Probationers

The Kentucky SMART probation program collects about 1,400 urine specimens annually, from an average number of approximately 275 SMART probationers. An onsite test cup that detects 12 drugs is used as the standard screen for this population too, but, tramadol is tested for instead of MDMA. Some specimens are sent to LabCorp for both general screening and the confirmation of contested positive specimens.

Table 1: Description of the Participating Study Sites

Site	Populations Covered	Type of CJS Laboratory	Drugs in Standard CJS Screen	Targeted Number of Specimens
Kentucky : General Supervision Probationers	Adult General Supervision probationers (est. 48,000 specimens per year from 32,500 General Supervision probationers)	Onsite cup screening; Offsite laboratory confirmation for contested positives	<u>12-panel screen</u> : amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, MDMA, methadone, methamphetamine, opiates, oxycodone, and PCP. Synthetic cannabinoids, synthetic cathinones, and 6-MAM by request.	200 – 10 uncontested positives, 10 contested positives and 20 negatives from each of five participating district offices (40 per office)
Kentucky: SMART Probationers	Adult SMART probationers (est. 1,400 specimens per year from 275 HOPE probationers)	Onsite cup screening; Offsite laboratory confirmation for contested positives	<u>12-panel screen</u> : amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, methadone, methamphetamine, opiates, oxycodone, PCP, and tramadol.	100 – 5 uncontested positives, 5 contested positives and 10 negatives from each of five participating district offices (20 per office)

Targeted Number of Specimens

We targeted for collection a total of 200 specimens from Kentucky General Supervision and 100 from SMART probationers from unduplicated persons. As was the case with prior CDEWS studies, we wanted to collect both specimens that had tested positive (CJS+) or negative (CJS-) for anything by the standard local CJS drug screen. We therefore worked with the local staff to collect 200 specimens (10 uncontested positives, 10 contested positives, and 20 negatives, 40 specimens total, from each of five participating district offices (districts 16-20) for a total of 100 CJS+ and 100 CJS- specimens) from the General Supervision probation population. We also collected 100 specimens (5 uncontested positives, 5 contested positives, and 10 negatives, 20 specimens total, from each of these same five participating district offices (districts 16-20) for a total of 50 CJS+ and 50 CJS-) from the SMART probation population.

Collection of Urine Specimens

Prior to collecting the urine specimens, CESAR staff talked with staff from the program by phone to determine their policies regarding required specimen holding periods, testing protocols, detection limits and other relevant site details. Specimens were then accumulated by the program using the specific CDEWS guidelines provided by CESAR as to how specimens were to be handled and stored. Designated probation staff shipped specimens directly to the CDEWS laboratory for expanded drug testing. Additional details of the specimen selection appear in Appendix B. Details about the CDEWS laboratory test panel appear in Appendix C.

Interviews with Toxicologists to Develop the CDEWS Testing Panel

In the prior CDEWS studies, we had learned that both the chemical composition of synthetic drugs available and patterns of use can vary widely even within a brief period of time. It is a recognized challenge for both laboratories and law enforcement to keep up with the rapid changes in the composition of synthetic drugs. The chemists producing these drugs modify the chemical structures of the drugs as existing formulations are scheduled by the DEA and made illegal. To ensure that the drug test panel for this study was as current as possible and included the most relevant drugs/metabolites, CESAR staff reviewed data on emerging drug trends and conducted interviews with toxicologists and other relevant professional contacts to identify substances for inclusion on the panel. Additional information on the data reviewed and persons interviewed appears in Appendix C (see Table C-1 in Appendix C).

Based on the information reviewed, we added 26 new compounds to our previous CDEWS-3 drug screen. Six of these were fentanyl compounds including: 4-ANPP (Despropionyl fentanyl), Betahydroxythiofentanyl, Butyryl Fentanyl, Furanylfentanyl, Parafluorobutyryl fentanyl, and Parafluorofentanyl. In addition, 20 other new psychoactive substances were added: 2C-B-FLY, 2C-T, 4-AAP (Dipyrone metabolite), 4-Fluoroamphetamine (4-FA), 4-Fluoromethamphetamine (4-FMA), 4-MAAP (Dipyrone metabolite), 5-APDB/6-APDB, 5-MEO-MiPT, Bromo-DragonFLY, DHNK (Ketamine metabolite), Dibutylone, Dimethylone, DMT, Ketamine, Loperamide, MT-45, Psilocin, U-47700, W-15, and W-18. Appendix C shows the full test panel. Several additional NPS were identified as relevant to the study but were not included due to reference standard availability and cost.

Testing of Urine Specimens by the CDEWS Laboratory

All specimens were sent to the CDEWS laboratory, the Armed Forces Medical Examiner System (AFMES) Laboratory located in Delaware, for an expanded drug testing panel (see Table C-2 in Appendix C). All specimens were tested for a panel of 26 SC metabolites and 58 other new psychoactive substances, along with 84 other illicit and prescription drugs.

Results

The term *CJS test result* refers to the limited drug screens routinely used by the local criminal justice agency to screen the General Supervision and SMART probationers. *CDEWS test result* refers to the expanded drug tests used by the CDEWS laboratory, which included all of the drugs tested for by the smaller CJS test panels.

We first describe the specimens collected and some basic demographic information about the probationers who provided them. Next, we describe the CDEWS test results for specimens tested with our expanded drug screen. The results for CJS positive (CJS+) and CJS negative (CJS-) specimens are presented separately because we stratified our sample to collect equal numbers of CJS+ and CJS- specimens. Given this stratification, it would be inappropriate for our analyses to simply combine and

average the results from these two groups. After examining the contested and uncontested positive specimens and finding the test results to be quite similar, we combined the contested and uncontested positives in all subsequent analyses.

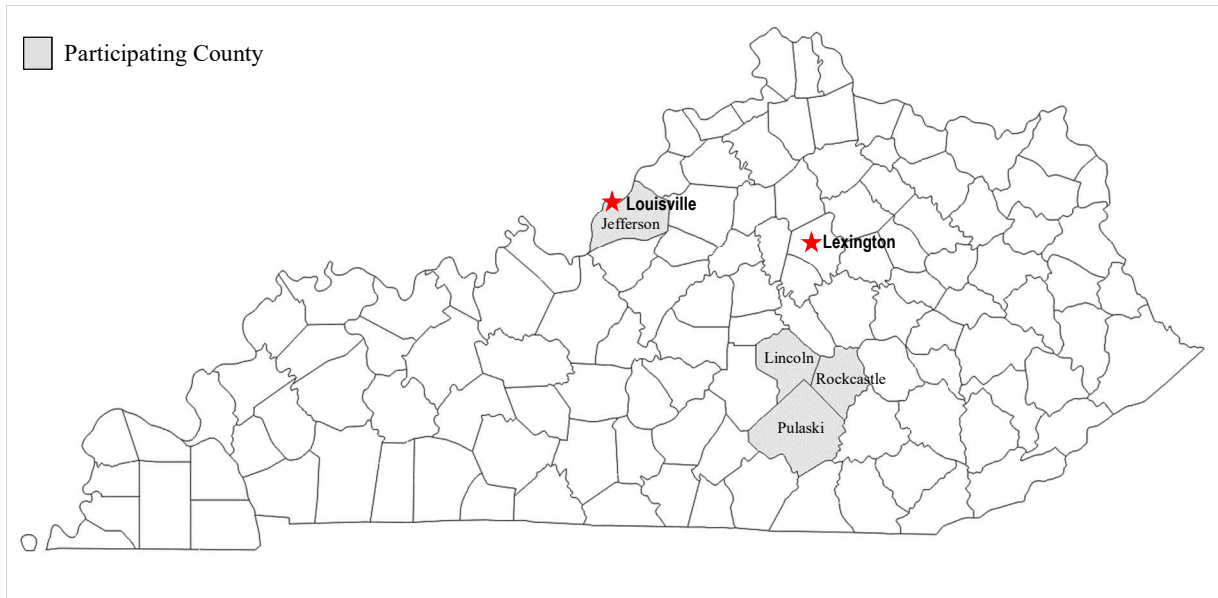
A. Specimens Received

Specimens were collected between July and December 2016. We had targeted 200 specimens (100 CJS+, 100 CJS-) from Kentucky General Supervision and 100 (50 CJS+, 50 CJS-) from SMART probationers and received a total of 262 (121 CJS+; 141 CJS-) specimens. Table 2 shows the specimens received, according to the local CJS testing results and the CJS probation program. We collected specimens from five districts in Kentucky, with Districts 16-19 representing Jefferson County (Louisville area) and District 20 representing Pulaski, Lincoln, and Rockcastle Counties (nearby to the Lexington area) as shown in Figure 1. We received a total of 176 (83 CJS+ and 93 CJS-) specimens from Kentucky General Supervision and 86 (38 CJS+ and 48 CJS-) specimens from Kentucky SMART.

Table 2: Number of CJS Positive and Negative Specimens Sampled From Each Office, by Program

	Kentucky General Supervision		Kentucky SMART	
	CJS+	CJS-	CJS+	CJS-
Office District	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>
16	9	21	1	6
17	20	20	10	11
18	21	19	10	9
19	14	11	7	12
20	19	22	10	10
Total	83	93	38	48

Figure 1: Locations of Participating Probation Programs



B. Demographic Characteristics of Persons Providing Specimens

Table 3 shows that the majority of CJS+ and CJS- specimens from both the General Supervision and SMART probationers came from men who were 21-40 years of age or younger. Most specimens from both probation groups came from persons identified as Caucasian, closely followed by specimens from persons identified as Black/African American. Almost all persons in the sample were of Non-Hispanic descent (not shown).

Table 3: Demographic Characteristics of Adults Providing Specimens from Kentucky General Supervision and Kentucky SMART, by CJS Drug Screen Result

	Kentucky General Supervision		Kentucky SMART	
	CJS+ (N=83)* %	CJS- (N=93)* %	CJS+ (N=38)* %	CJS- (N=48)* %
Gender				
Male	77%	80%	63%	83%
Female	23	20	37	17
Total	100%	100%	100%	100%
Age				
18-20	5%	6%	8%	8%
21-25	20	15	18	25
26-30	23	18	21	21
31-40	35	37	24	29
41-50	13	15	11	11
51 and older	4	9	18	6
Total	100%	100%	100%	100%
Race				
Caucasian	54%	60%	50%	62%
Black/African-American	45	39	47	38
Other	1	1	3	0
Total	100%	100%	100%	100%

Notes:
 *N's vary slightly for some characteristics because of missing information.
 Some percentages have been rounded.

C. Drugs Detected by the CDEWS Laboratory

General Supervision

CJS+ Specimens: Table 4 shows that the most common individual drugs found among CJS+ specimens from General Supervision probationers were marijuana (46%), methamphetamine (29%), amphetamine (23%), cocaine (21%) and buprenorphine/norbuprenorphine (17%). Almost half (45%) of the specimens were positive for a non-fentanyl opioid, mostly morphine (16%), hydrocodone (12%), oxycodone (11%), and/or hydromorphone (10%). These results were expected because most of these drugs were included on the drug testing panel that had identified them as CJS+. A fentanyl compound was detected in two percent of specimens, either fentanyl/norfentanyl or 4-ANPP (Despropionyl fentanyl). A new psychoactive substance (NPS) was found in 22 percent of

specimens, primarily BMPEA (16%). BMPEA is a doping agent found in nutritional supplements, with stimulant effects that may mimic the effects of amphetamine (a compound to which it is structurally similar) (Cholbinski et al., 2014). Benzodiazepines were found in eight percent of specimens and seven percent were found to be positive for an antidepressant. None of the CJS+ specimens in this group tested positive for an SC.

CJS- Specimens: The most frequently detected drug found among CJS- specimens from General Supervision probationers was marijuana (14%), with smaller percentages positive for methamphetamine (5%), cocaine (3%), and morphine (3%). We detected a non-fentanyl opioid in eight percent of specimens and 13 percent were found to be positive for an antidepressant. A fentanyl compound was detected in two percent of specimens; fentanyl/norfentanyl and 4-ANPP. Of the 12 percent of specimens found to be positive for an NPS, the most common NPS found was BMPEA (9%). Synthetic cannabinoids were detected in two percent of the CJS- group.

SMART Probation

CJS+ Specimens: Table 4 shows that the most common individual drugs found among CJS+ specimens from SMART program probationers were marijuana (47%), cocaine (13%), methamphetamine (11%), oxycodone (11%), and hydromorphone (11%). These results were expected because most of these drugs were included on the SMART program's testing panel that identified them to be CJS+. Citalopram, an antidepressant, found in 11 percent of specimens was significantly more likely to be detected in the CJS+ specimens than those that were CJS-. None of the CJS- specimens contained this drug. A non-fentanyl opioid was found in 32 percent of specimens, and 16 percent were found to be positive for an antidepressant. None of the CJS+ specimens tested positive for a NPS, fentanyl, or SCs.

CJS- Specimens: The most frequently detected drugs found among CJS- specimens were marijuana (6%), buprenorphine/norbuprenorphine (6%), and morphine (6%). We detected a non-fentanyl opioid in 13 percent of specimens. Also, 4-ANPP (Despropionyl fentanyl), a fentanyl compound was detected in 2 percent of specimens. An NPS was found in 10 percent of specimens, most commonly BMPEA (6%). Synthetic cannabinoids were found in 4 percent of specimens.

Table 4: CDEWS Laboratory Test Results by Probation Population and CJS Drug Screen Result

(N=262 specimens collected between July 2016-December 2016)

Percent Positive by CDEWS Lab for:	General Supervision - Kentucky [§] (N=176)		SMART Probation – Kentucky [^] (N=86)	
	CJS+ (N=83) %	CJS- (N=93) %	CJS+ (N=38) %	CJS- (N=48) %
Marijuana	46	14	47	6
Methamphetamine	29	5	11	0
Cocaine	21	3	13	2
Amphetamine	23	1	5	0
Any Non-Fentanyl Opioid	45	8	32	13
Morphine	16	3	8	6
Buprenorphine/Norbuprenorphine	17	2	0	6
Oxymorphone	11	2	11	0
Hydrocodone	12	0	8	0
Hydromorphone	10	0	11	0
Oxycodone	6	2	11	0
Codeine	5	1	0	0
Tramadol	2	1	0	0
Methadone/EDDP	0	0	3	0
Any Fentanyl	2	2	0	2
4-ANPP (Despropionyl fentanyl)	2	1	0	2
Fentanyl/Norfentanyl	2	2	0	0
Any New Psychoactive Substance (NPS)	22	12	0	10
β-Methylphenethylamine	16	9	0	6
mCPP†	2	3	0	4
Methcathinone/Ephedrone	2	0	0	0
Mitragynine	0	0	3	0
Pentylone	1	0	0	0
Cathinone	1	0	0	0
Eutylone	1	0	0	0
Methylone	1	0	0	0
Butylone	1	0	0	0
Any Antidepressant	7	13	16*	2*
Citalopram	0	5	11*	0*
Sertraline	2	3	3	0
Trazodone†	1	3	0	2
Desvenlafaxine	4	0	0	0
Venlafaxine	4	0	0	0

Table 4 (Cont'd): CDEWS Laboratory Test Results by Probation Population and CJS Drug Screen Result

Fluoxetine	0	2	0	0
Bupropion	1	1	0	0
Paroxetine	0	0	3	0
Doxepin	0	1	0	0
Amitriptyline	1	0	0	0
Nortriptyline	1	0	0	0
Any Benzodiazepine	8	1	3	0
Alprazolam/α-Hydroxyalprazolam	5*	0*	0	0
Clonazepam/7-Aminoclonazepam	2	1	0	0
Diazepam/Nordiazepam	1	0	3	0
Oxazepam	1	0	3	0
Temazepam	0	0	3	0
Any Synthetic Cannabinoid (SC)	0	2	0	4
UR-144	0	0	0	4
AB-FUBINACA (Parent)	0	1	0	0
AB-CHMINACA (Parent)	0	1	0	0
AB-CHMINACA (metab 4)	0	1	0	0
AB-CHMINACA (metab 6)	0	1	0	0
Other Drugs				
Naloxone	11*	2*	0	2
Cetirizine	4	4	8	2
Cyclobenzaprine	1	2	3	2
Dextromethorphan	1	3	3	0
Ephedrine/Pseudoephedrine	2	1	0	2
Hydroxyzine	1	0	5	0
Ketamine/DHMK	0	0	3	0
Promethazine	0	0	3	0
Zolpidem	0	1	0	0
Loperamide	1	0	0	0

Notes: No PCP or MDMA were detected. The CDEWS Laboratory does not test for barbiturates so the presence of this drug is unknown.

§Specimens from the General Supervision probation program in Kentucky are routinely tested for a 12-drug panel screen, including: amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, MDMA, methadone, methamphetamine, opiates, oxycodone, and PCP. Synthetic cannabinoids, synthetic cathinones, and 6-MAM are tested upon request.

^Specimens from the Kentucky SMART probation program are routinely tested for a 12-drug panel screen, including: amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, methadone, methamphetamine, opiates, oxycodone, PCP, and tramadol.

†Trazodone is an antidepressant whose major active metabolite is mCPP. It is not possible to definitively determine whether the presence of mCPP was due to Trazodone use or whether mCPP was taken on its own. Five out of the seven specimens positive for mCPP were also positive for Trazodone.

*p<.05 by Fisher's Exact Test or Chi Square.

Table 5 presents a summary of the likely illicit drugs (drug not likely to have been taken under a doctor’s supervision) detected in the two populations. One would expect to find these drugs in the CJS+ specimens because many of them were included in the routine CJS screen that caused them to be labeled CJS+. About one half (46%) of the General Supervision Program CJS+ specimens contained marijuana, as did 47 percent of the CJS+ specimens from the SMART program. However, there are some significant differences in the drugs identified in the CJS+ specimens from the two programs. The CJS+ specimens from General Supervision probationers contained more NPS (22% vs 0%, $p<.01$), primarily BMPEA, and methamphetamine (29% vs. 11%, $p<.05$). If one excludes marijuana, General Supervision probationers’ CJS+ specimens were twice as likely than the SMART program probationers to test positive for another likely illicit drug in Table 5 (55% vs. 24%, $p<.01$).

The CJS- specimens from the two programs presented a different pattern. While containing fewer drugs, almost one-fifth to one-third of the CJS- specimens from both programs tested positive for at least one of the six drugs in Table 5. Excluding marijuana, 21 percent of the CJS- specimens from the General Supervision program and 17 percent of the CJS- specimens from the SMART program tested positive for one of the other five classes of likely illicit drugs in Table 5, primarily an NPS.

Drug use in these groups was likely even higher than shown in Table 5. Table 5 excludes results for non-fentanyl opioids, many of which could have been misused.

Table 5: Percentage Positive for Selected Likely Illicit Drugs, by Probation Population and CJS Drug Screen Result

(N=262 specimens collected between July 2016-December 2016)

Percent Positive by CDEWS Lab for:	General Supervision Kentucky (N=176)		SMART Probation Kentucky (N=86)	
	CJS+ (N=83) %	CJS- (N=93) %	CJS+ (N=38) %	CJS- (N=48) %
1.) Marijuana	46	14	47	6
2.) Any New Psychoactive Substance (NPS)	22**	12	0**	10
3.) Methamphetamine	29*	5	11*	0
4.) Cocaine	21	3	13	2
5.) Any Fentanyl	2	2	0	2
6.) Any Synthetic Cannabinoid (SC)	0	2	0	4
Positive for Any of 6	82*	32	61*	21
Positive for Any of 5 (excluding marijuana)	55**	21	24**	17

* $p<.05$ by Fisher’s Exact Test or Chi Square.

** $p<.01$ by Chi Square.

Given the number of drugs found in the CJS- specimens from these two programs, we compared the limits of detection (LODs) of the urine tests used by the two probation programs with those used by the CDEWS laboratory. Table 6 shows that, as expected, the CDEWS laboratory tests (LC/MS/MS) had LODs that were much lower (and thus more sensitive) than those used by the Kentucky General Supervision and SMART Probation programs (which mostly used enzyme immunoassay tests). For example, the CDEWS laboratory's test for THC (marijuana) could detect a concentration as low as 5ng/mL while the CJS tests could only detect a concentration of 40-50ng/mL or higher. The greater sensitivity of the tests used by the CDEWS Laboratory provides a possible explanation for why so many drugs were found in the CJS- negative specimens. A full list of the LODs used by the CDEWS laboratory can be found in Table C-2 of Appendix C.

Table 6: Limits of Detection (LODs) Used for Drugs Tested for by the Kentucky Probation Programs and CDEWS Laboratory

	Kentucky: SMART ng/mL	Kentucky: General Supervision ng/mL	CDEWS Laboratory ng/mL
Test (compound)			
Amphetamine	300	300	25
Barbiturates	200	300	Not Tested For
Benzodiazepines	200	300	25†
Buprenorphine	10	10	1
Cocaine	100	150	25
MDMA	Not Tested For	500	25
Methadone	200	300	25
Methamphetamine	1000	500	25
Opiates	100	300	25*
Oxycodone	100	100	25
PCP	25	25	10
THC	40	50	5
Tramadol	200	Not Tested For	25

†Given that the CDEWS Laboratory tests for specific benzodiazepines using LC/MS/MS, the LOD indicated reflects the LOD of the specific benzodiazepine (Oxazepam) that likely would have been detected by the onsite test cups.

*Given that the CDEWS Laboratory tests for specific opioids using LC/MS/MS, the LOD indicated reflects the LOD of the specific opiates that likely would have been detected by the onsite test cups including morphine, codeine, hydrocodone, and hydromorphone (Cone et al., 1992).

D. SC Metabolites Detected

As shown in Table 4, synthetic cannabinoids were not detected in any of the CJS+ specimens from either the General Supervision or SMART program probationers. SCs were detected in two percent of CJS- specimens from the General Supervision probationers and four percent of CJS- specimens from SMART probationers. Four different SC metabolites were found in the CJS- General Supervision specimens. In contrast, all SMART program CJS- specimens that were positive for SCs were found positive for the same metabolite, UR-144. Given that SCs were rare and found only in a few CJS- specimens, it suggests that few probationers were using SC to avoid detection; most jurisdictions do not test for SC.

Study Limitations

The CDEWS model depends on collecting a small number of specimens from unduplicated persons that have already tested positive or negative by the CJS agency's routine drug screen. Every attempt was made to randomly select from the specimens available that met our selection criteria. We do not know whether this small number of samples is representative of all persons tested in the participating CJS populations. However, CDEWS results have been found to be internally consistent and often agree with other indicators of drug use in the studied populations (Wish et al., 2013, 2015). CDEWS is designed to produce an indication of the relative use and availability of drugs in a community rather than prevalence estimates.

CDEWS obtains samples of urine specimens that have already been collected and tested as part of an existing drug testing program. The persons selected for testing are typically at high risk for drug use because of their prior use or treatment history, suspected drug misuse and/or drug offense history. While a population at high risk for drug use is exactly what we seek in order to achieve the CDEWS mission of discovering the use of emerging drugs, it also means that the CDEWS findings do not necessarily represent all persons in the CJS programs we studied. Nevertheless, drug trends in high risk criminal justice populations often foreshadow trends that appear later in the general population (DuPont & Wish, 1992).

Every effort is made to include in the CDEWS Laboratory test panel most of the currently available drugs likely to be misused. However, given the rapidly changing nature of new psychoactive substances, it is possible that some drugs may have been missed by the CDEWS testing panel. The continuously changing nature of the substances available make it difficult to develop urine tests for all of the new drugs as quickly as they are discovered. So it is possible that our results under detect some drugs that were used.

In addition, while we found that some specimens contained multiple drugs/metabolites, this does not necessarily mean that the user sought all of these drugs or was aware of the composition of the substance ingested. Multiple drugs in a specimen may also simply reflect the byproducts produced from formulating, transporting or taking the drug.

The CDEWS test results can only provide an indication of the recent use of prescription and illicit drugs by the people who submitted the specimens. A more complete understanding of the results would require additional study. For example, we cannot tell whether a person testing positive for a prescribed drug is taking it under medical supervision. Nor can our test results tell us why or how often persons used the drug or where they obtained it.

Decisions regarding modifying CJS drug testing protocols should not be based on CDEWS results alone. Rather, local policymakers should review the CDEWS results and weigh the complex law enforcement, public health, and budgetary considerations involved. CDEWS studies may provide

critical information with which to paint a picture of the age and gender characteristics of likely CJS drug users and, most importantly, the local communities where one might wish to collect more detailed information about a particular emerging drug's availability and use.

Summary and Conclusions

Drugs Detected in CJS- specimens

The fact that the CDEWS laboratory found likely illicit drugs in one fifth to one third of the specimens that the SMART program and General Supervision program's standard tests indicated were negative for all drugs was expected. This detection of more drugs probably resulted from the more sensitive tests used by the CDEWS laboratory. These probation programs may wish to consider the costs and benefits of adopting additional and/or more sensitive urine tests to identify the drug users they are currently missing.

Drugs Detected in CJS+ specimens

By design, the CJS+ specimens were most likely to contain the drugs included in the local test panels that caused them to be labeled CJS+. However, while probationers from both programs were most likely to test positive for marijuana, the General Supervision probationers were significantly more likely than the SMART program probationers to test positive for methamphetamine and an NPS, primarily BMPEA. When we excluded marijuana positives, the General Supervision probationers were significantly more likely to test positive for another likely illicit drug. These results could indicate that the SMART program probationers were less likely to use illicit drugs other than marijuana because of that program's sanctions for current drug use. It is also possible that the SMART program participants were less involved than General Supervision probationers with other drugs to begin with, but this hypothesis runs counter to the SMART program's explicit strategy of recruiting seriously drug involved persons.

β -Methylphenethylamine (BMPEA)

BMPEA is a doping agent found in nutritional supplements, with stimulant effects that may mimic the effects of amphetamine (a compound to which it is structurally similar) (Cholbinski et al., 2014). BMPEA was found in 16 percent of the CJS+ specimens from the General Supervision program probationers but not in any CJS+ specimens from the SMART program probationers. This finding was unexpected because BMPEA has rarely been detected in specimens from other CDEWS sites. The finding that 29 percent of the CJS+ specimens from the General Supervision probationers contained the stimulant methamphetamine raises the possibility that the General Supervision probationers studied may have also used BMPEA because of its similar effects. Of the 13 CJS+ specimens from the General Supervision probationers that contained BMPEA, 54 percent also contained methamphetamine. Only 25 percent of the eight CJS- specimens from the General Supervision probationers that contained BMPEA, also contained methamphetamine. The fact that BMPEA was found in the CJS- specimens from both programs suggests that those persons might also be using this

drug in order to avoid detection by the standard drug tests. At the moment, BMPEA, is considered a doping agent in a sports context but is not illegal. More research into the use of this drug is warranted.

Other Drugs Detected

Antidepressants were found in probationers from all groups studied and it raises the question whether these persons were being prescribed these drugs for treatment purposes or misusing these drugs. In contrast, synthetic cannabinoids were rare and found only in a few CJS- persons, suggesting that few probationers in these programs were using synthetic cannabinoids to avoid detection.

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Appendices

Appendix A: Site Selection Procedures

The Kentucky General Supervision and SMART probation programs offered a unique opportunity to collect specimens from two additional populations of probationers. Both of these probation programs use on-site test cups, and also utilize offsite testing laboratories for screening and confirmations of contested positive and other specimens. For this study, we sought both positive (contested and uncontested) specimens, as well as negative specimens that could be collected directly from the probation program offices. Contested positive specimens were obtained directly from the probation offices using excess urine volume prior to their shipment to the probation office's external laboratories. Judge David Tapp was interested in implementing CDEWS in Kentucky and helped us to obtain approval for the study. We held telephone conferences with the judge, probation administrators and program staff to share information on the study and learn about the procedures being used by their site. An overview of the proposed methods was then sent to these staff for review. A formal research application was prepared and submitted to the Kentucky Department of Corrections for review and approval was obtained for the study. Negotiations and approval for this site were very quick and took approximately three weeks (see Table A-1). The UM IRB application was then submitted and approved. Using a specified protocol, specimens were prepared by the probation staff and sent to the CDEWS laboratory. Specimen collection took approximately six months, as the accumulation of specimens from unique persons took several months.

Table A-1: Time to Obtain Approval and Collect Specimens

Site	Time to Obtain Approval	Researcher Time On-Site Collecting Specimens
<i>Kentucky General Supervision and SMART Probation Programs</i>	3 weeks	No time spent on site

Appendix B: Collection of Urine Specimens

The Kentucky General Supervision and SMART probation programs offered a unique opportunity to collect specimens from two additional populations of probationers. Kentucky General Supervision tests its specimens using on-site test cups that test for 12 drugs (amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, MDMA, methadone, methamphetamine, opiates, oxycodone, and PCP), and utilizes an offsite testing laboratory (Sterling Laboratories) for confirmations of contested positive specimens. Other drugs including synthetic cannabinoids, synthetic cathinones, and heroin (6-MAM) may be tested upon request. Kentucky SMART tests its specimens using on-site test cups that test for 12 drugs (amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, methadone, methamphetamine, opiates, oxycodone, PCP, and tramadol), and utilizes an offsite testing laboratory (LabCorp) for both general screening and confirmations of contested positive specimens.

Over the period of approximately six months (July to December 2016), staff at the Kentucky General Supervision and SMART probation programs identified specimens for possible inclusion in the study. Kentucky General Supervision and SMART probation staff began by identifying any contested and uncontested positive, and negative specimens from the programs that could be released for the study. This program had no holding period for negative specimens so specimens were identified for the study as they were being collected. Uncontested and contested positive specimens were obtained directly from the probation offices using excess urine volume prior to their shipment to the probation office's external laboratories.

Positive specimens were defined as specimens positive for any drug on the 12-panel screens. Probation staff tracked the names of the persons from whom specimens had been collected for the study using a participant list to ensure that only one specimen per person was included in the study sample. Specimens selected for the study were de-identified and labeled with the following demographic and other elements: probation program (SMART/General Supervision), submitting office district, specimen collection date, specimen type (uncontested positive, contested positive, or negative), gender, year of birth, zip code of residence, race, and ethnicity. Only specimens with a minimum volume of 10mL were included in the study. Selected specimens were packaged and shipped to the CDEWS laboratory. 93 negatives and 83 positives were collected from the General Supervision probation program, and 48 negatives and 38 positives were collected from the SMART probation program. See Table 2 for the number of specimens collected.

Appendix C: Testing of Urine Specimens by the CDEWS Laboratory

Armed Forces Medical Examiner System Laboratory

CESAR contracted with the Armed Forces Medical Examiner System Laboratory for testing, as this laboratory has a shared mission to identify emerging drugs for testing in the United States. The drugs and metabolites included in the CDEWS panel were selected after interviewing 14 chemists at seven labs to identify new psychoactive substances (NPS) to consider adding to our panel and to assess the availability of tests for these drugs (see Table C-1 below). We also reviewed data and information from multiple international, national and local sources before finalizing the testing panel. All specimens were held in cold storage for the duration of the study. Over 160 drugs were tested for using Liquid Chromatography-Tandem Mass Spectrometry (LC/MS/MS). The test results, labeled by study ID, were sent electronically to CESAR.

Selecting Substances for Inclusion in the Testing Panel

Selecting substances to include in the study test panel was critical to the ability of the study to detect emerging drugs, particularly as related to NPS, an area of fast-paced change in terms of availability and use.

To plan our test panel, we reviewed data and information from multiple international, national and local sources. These included a review of the 2015 National data from the Drug Enforcement Administration's (DEA) National Forensic Laboratory Information System (NFLIS), special data runs for 2015 provided by the DEA's Special Testing and Research Laboratory, as well as reports from the United Nations Office on Drugs and Crime (UNODC) Early Warning Advisories, and other sources (Baumann, 2016; Head, 2016; Logan, 2016; NMS Labs, 2015; UNODC, Early Warning Advisory, 2016; U.S. DEA, Office of Diversion Control, 2015; U.S. DEA, Office of Diversion Control, NFLIS, 2016d; U.S. DEA, Special Testing and Research Laboratory, Emerging Trends Program, 2016a, 2016b). We also reviewed data from participating CDEWS jurisdictions and other local data to assess local drug trends (Booze, 2016; Indiana State Epidemiology and Outcomes Workgroup, 2014; Keenan, 2016; Polhemus, 2016; Shewmaker, 2016; U.S. DEA, Office of Diversion Control, NFLIS, 2016a, 2016b, 2016c).

In addition, we also interviewed 14 chemists at seven labs prior to finalizing the test panel. The persons interviewed were selected from existing networks of toxicologists with expertise in the area of NPS and/or urine testing that we have identified from past CDEWS studies, as well as through other professional networks. We also identified contacts through referrals from our existing network of toxicologists, researchers, and law enforcement representatives. A standard set of questions was asked including:

- What specific substances do you think are most important for us to include in our testing panel?
- Are there any new or emerging synthetic drugs that we should include?
- What synthetic drugs do you test for at your agency?

- What synthetic cannabinoid metabolites have you been finding in your most recent specimens? cathinones? other synthetic drugs?
- To your knowledge, are there tests available for each of these drugs? What would be the recommended test (EIA, LC/MS, etc.)?

Table C-1: Toxicologists Interviewed for CDEWS

NAME	TITLE/AFFILIATION
Dr. Gregory Endres; Dr. Donna Iula	Cayman Chemical
Jerome Robinson; Dr. Felix Adatsi	Pretrial Services Agency for the District of Columbia
Jill Head; Emily Dye	Special Testing and Research Laboratory, Drug Enforcement Administration
Lt. Niki Crawford	Indiana State Police
Sgt. Ryan Johnson	Kentucky State Police Crime Laboratory
Dr. Karl Scheidweiler	National Institute on Drug Abuse, National Institutes of Health Biomedical Research Center
Dr. (CDR) Thomas Bosy; Dr. Jeffrey Walterscheid; LCDR Pedro Ortiz; Dr. Paul Kaiser; Theresa Hippolyte	Armed Forces Medical Examiner System (AFMES)

Based on the information reviewed, we added 26 new compounds to our previous CDEWS-3 drug screen. Six of these were fentanyl compounds including: 4-ANPP (Despropionyl fentanyl), Betahydroxythiofentanyl, Butyryl Fentanyl, Furanylfentanyl, Parafluorobutyryl fentanyl, and Parafluorofentanyl. In addition, 20 other new psychoactive substances were added: 2C-B-FLY, 2C-T, 4-AAP (Dipyrone metabolite), 4-Fluoroamphetamine (4-FA), 4-Fluoromethamphetamine (4-FMA), 4-MAAP (Dipyrone metabolite), 5-APDB/6-APDB, 5-MEO-MiPT, Bromo-DragonFLY, DHNK (Ketamine metabolite), Dibutylone, Dimethylone, DMT, Ketamine, Loperamide, MT-45, Psilocin, U-47700, W-15, and W-18 (see Table C-2 in Appendix for the full panel). Dipyrone is a prescription drug (sometimes mixed with fentanyl) and Loperamide is an over-the-counter drug subject to abuse (Eggleston et al., 2017; Mian, 2014; Saint Louis, 2016; U.S. FDA, 2016). Several NPS were identified as relevant to the study but were not included due to reference standard availability and cost.

Table C-2: The CDEWS Laboratory Expanded Drug Screening Panel and Limits of Detection (LOD)

SYNTHETIC CANNABINOID PANEL

	COMPOUND	LOD (ng/mL)
1	JWH-018-5-COOH	0.20
2	JWH-019-6-OH	0.20
3	JWH-073-4-COOH	0.20
4	JWH-081-5-OH	0.20
5	JWH-122-5-OH	0.20
6	JWH-210-5-OH	0.20
7	JWH-250-5-OH	0.20
8	AM2201-4-OH	0.20
9	MAM-2201-5-COOH/JWH 122 COOH	0.20
10	RCS-4-5-COOH	0.20
11	UR-144-5-COOH	0.20
12	XLR-11-4-OH	Presence
13	AKB-48 COOH	0.20
14	5F AKB-48 metabolite	0.20
15	BB-22 metabolite	0.20
16	PB-22 Carb Indole	0.20
17	5F PB-22 Carb Indole	0.20
18	AB-PINACA	0.20
19	5F AB PINACA	0.20
20	ADB-PINACA-5-COOH	0.20
21	ADBICA-5-COOH	0.20
22	AB-FUBINACA (Parent)	0.20
23	AB-CHMINACA (Parent)	0.20
24	AB-CHMINACA (metab 4)	0.20
25	AB-CHMINACA (metab 6)	0.20
26	ADB-FUBINACA (Parent)	0.20

Table C-2 (Cont'd): The CDEWS Laboratory Expanded Drug Screening Panel and Limits of Detection

NEW PSYCHOACTIVE SUBSTANCE PANEL (NOT INCLUDING SC)

	COMPOUND	LOD (ng/mL)		COMPOUND	LOD (ng/mL)
1	25B-NBOMe	5	31	α-PVP	5
2	25I-NBOMe	5	32	Mephedrone	5
3	25C-NBOMe	5	33	Methedrone	5
4	2C-B	5	34	Methylone	5
5	2C-B-FLY	5	35	Parafluorobutyryl fentanyl	5
6	4-Fluoroamphetamine (4-FA)	5	36	Parafluorofentanyl	5
7	4-Fluoromethamphetamine (4-FMA)	5	37	Pentedrone	5
8	4-AAP (Dipyrone metabolite)	5	38	Pentylone	5
9	4-ANPP (Despropionyl fentanyl)	5	39	TFMPP	5
10	4-Methylethcathinone (4-MEC)	5	40	Phentermine	5
11	5-MEO-MiPT	5	41	B-Methylphenethylamine	5
12	5-APDB/6-APDB	5	42	Trazodone	5
13	Betahydroxythiofentanyl	5	43	Psilocin	5
14	Bromo-DragonFLY	5	44	Naphyrone	5
15	Buphedrone	5	45	Mitragynine	5
16	Butylone	5	46	Methoxetamine (MXE)	5
17	Butyryl Fentanyl	5	47	PMMA	5
18	Benzylpiperazine	5	48	2C-T	5
19	Cathinone	5	49	Flephedrone	5
20	Dibutylone	5	50	Methiopropamine	5
21	Dimethylone	5	51	U-47700	5
22	DMT	5	52	W-15	5
23	Methcathinone/Ephedrone	5	53	W-18	5
24	Ethylone	5	54	Loperamide	5
25	Eutylone	5	55	4-MAAP (Dipyrone metabolite)	5
26	Furanylfentanyl	5	56	DHMK (Ketamine metabolite)	5
27	mCPP	5	57	Ketamine	5
28	MBDB	5	58	2C-T-7	5
29	MDPV	5	59	Carfentanil	5
30	MT-45	5			

THC/BUPRENORPHINE/LSD PANEL

	COMPOUND	LOD (ng/mL)
1	THC-COOH	5
2	Buprenorphine	1
3	Norbuprenorphine	1
4	Naloxone	1
5	LSD/Metabolite (2-oxo-3-hydroxy-LSD)	0.05/.25

Table C-2 (Cont'd): The CDEWS Laboratory Expanded Drug Screening Panel and Limits of Detection

GENERAL PANEL

	COMPOUND	LOD (ng/mL)		COMPOUND	LOD (ng/mL)
1	6-Monoacetylmorphine (6-MAM)	5	41	Hydroxyzine	25
2	7-Aminoclonazepam	25	42	Ketamine	25
3	Acetylfentanyl	1	43	Lorazepam	25
4	Alprazolam	25	44	MDA	25
5	Amitriptyline	25	45	MDEA	25
6	Amphetamine	25	46	MDMA	25
7	Atomoxetine	25	47	Meperidine	25
8	Benzoyllecgonine (Cocaine)	25	48	Methadone	25
9	Bupropion	25	49	Methamphetamine	25
10	Carisoprodol	50	50	Methylphenidate	25
11	Cetirizine	25	51	Morphine	25
12	Chlorpromazine	25	52	Naloxone	25
13	Citalopram	25	53	Nordiazepam	25
14	Clonazepam	25	54	Norfentanyl	4
15	Codeine	25	55	Normeperidine	25
16	Cyclobenzaprine	25	56	Nortriptyline	25
17	Demoxepam	25	57	Oxazepam	25
18	Desalkflurazepam	25	58	Oxycodone	25
19	Desomorphine	25	59	Oxymorphone	25
20	Desvenlafaxine	25	60	Paroxetine	25
21	Dextromethorphan	25	61	PCP	10
22	Diazepam	25	62	Phenmetrazine	25
23	Diclazepam	25	63	Phenazepam	25
24	Doxepin	25	64	Prazepam	25
25	Duloxetine	25	65	Promethazine	25
26	EDDP	25	66	Pseudoephedrine	25
27	Ephedrine	25	67	Pyrazolam	25
28	Estazolam	25	68	Propoxyphene	25
29	Etizolam	25	69	Quinidine	25
30	Fentanyl	1	70	Quinine	25
31	Flubromazepam	25	71	Sertraline	25
32	Flunitrazepam	25	72	Tapentadol	25
33	Fluoxetine	25	73	Temazepam	25
34	Flurazepam	25	74	Thioridazine	25
35	Haloperidol	25	75	Tramadol	25
36	Hydrocodone	25	76	Venlafaxine	25
37	Hydromorphone	25	77	Zaleplon	5
38	α -Hydroxyalprazolam	25	78	Zolpidem	5
39	α -Hydroxymidazolam	5	79	Zopiclone	5
40	α -Hydroxytriazolam	25			

Appendix D: Glossary of Abbreviated Terms

6-MAM: 6-Monoacetylmorphine, a unique metabolite of heroin used to definitively determine heroin use

CDEWS: Community Drug Early Warning System

CESAR: Center for Substance Abuse Research

CJS: Criminal Justice System

DEA: Drug Enforcement Administration

EIA: Enzyme Immunoassay, a method of urine drug testing

IRB: Institutional Review Board at the University of Maryland, a committee that must approve all human subjects research at the University of Maryland

LC/MS: Liquid Chromatography/Mass Spectrometry, a method for confirming drug positives in urine

LC/MS/MS: Liquid Chromatography-Tandem Mass Spectrometry, a method for confirming drug positives in urine

LOD: Limit(s) of detection

LSD: Lysergic Acid Diethylamide, a hallucinogen

MDMA: 3,4-methylenedioxy-N-methylamphetamine, also known as ecstasy or Molly

NFLIS: National Forensic Laboratory Information System

NIDA: National Institute on Drug Abuse

NPS: New psychoactive substances, defined by UNODC as “substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat”

ONDCP: Office of National Drug Control Policy

PCP: Phencyclidine, a dissociative anesthetic and hallucinogen

SC: Synthetic Cannabinoid, also known as synthetic marijuana, K2, or spice

THC: Tetrahydrocannabinol, the primary active ingredient in marijuana

UM: University of Maryland

UNODC: United Nations Office on Drugs and Crime

