Community Drug Early Warning System (CDEWS-3): Maryland -- Site 4 of 4

Office of National Drug Control Policy
Executive Office of the President
July 2017

ACKNOWLEDGMENTS

This report was funded by Cooperative Agreement #G14UMARYLAND awarded by the Executive Office of the President, Office of National Drug Control Policy (ONDCP), to the University of Maryland's Center for Substance Abuse Research (CESAR). Eric D. Wish, Ph.D. (Principal Investigator), Amy Billing, MSSA, and Eleanor Erin Artigiani, MA, produced this report. Fe Caces, Ph.D., served as reviewer and Project Manager at ONDCP and Terry Zobeck, Ph.D., also served as a reviewer.

Without the support and assistance of the Maryland Department of Public Safety and Correctional Services and the Maryland Division of Parole and Probation, this project could not have been completed. The laboratory analyses for this report were conducted by the Armed Forces Medical Examiner System (AFMES) Laboratory. We would like to thank the specific staff listed below:

Maryland Department of Public Safety and Correctional Services

Secretary Stephen Moyer

Maryland Division of Parole and Probation

Judith Sachwald, Director (former)
Martha Danner, Deputy Director
Victor Caldarola
Latawnya Stallworth
Bambi Turner

Armed Forces Medical Examiner System Laboratory

Dr. Jeff Walterscheid
Lt. Commander Pedro Ortiz
Major Lynn Wagner
CTR Anastasia Berrier
CTR Kimberley Heine
CTR Theresa Hippolyte
CTR Paul Kaiser

Disclaimer

The information and opinions expressed herein are the views of the authors and do not necessarily represent the views of the Office of National Drug Control Policy (ONDCP) of the Executive Office of the President, or any other agency of the Federal Government.

Notice

> Wish, E.D., Billing, A.S., and Artigiani, E.E. (2017). *Community Drug Early Warning System (CDEWS-3): Maryland – Site 4 of 4*. Office of National Drug Control Policy. Washington, DC: Executive Office of the President.

Electronic Access to Publication

This document can be accessed electronically through the following World Wide Web address:

http://www.whitehouse.gov/ondcp

Originating Office

Executive Office of the President
Office of National Drug Control Policy
Washington, DC 20503

July 2017

Abstract

The Community Drug Early Warning System (CDEWS) provides timely information about emerging drug use in criminal justice populations in local communities by collecting and re-testing urine specimens already obtained 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 over 150 drugs. By using already collected de-identified urine specimens, CDEWS is able to provide a relatively quick and inexpensive snapshot of the types of drugs recently used by participating populations.

The CDEWS methodology has now been piloted in twelve jurisdictions and the results are provided in five reports already released by the Office of National Drug Control Policy (ONDCP). This report presents findings from adult parolees and probationers in a single jurisdiction -- Maryland -- as part 4 of 4 sites for the third CDEWS Study, called CDEWS-3.

This study was conducted somewhat differently from prior CDEWS studies. This is because we wanted to replicate the findings from a study we had conducted in Maryland in 2008. And second, because of the opioid epidemic in Maryland, the State asked us to collect and analyze a separate large sample of specimens statewide that had tested positive for opiates by the laboratory used by the Maryland Division of Parole and Probation (DPP). With the strong support of the DPP, we collected two samples of specimens: the Maryland Regional Sample (N=288) and the Opiate Positive (Opiate+) Sample (N=202 statewide). Specimens were classified as CJS+ (tested positive for any drug) or CJS- (tested negative for all drugs) according to the results from the DPP laboratory's 4-drug screen.

The findings from the Maryland Regional Sample indicated that most of the persons who had tested positive for one of the drugs in the CDEWS larger test panel had also tested positive for one of the four drugs in the DPP drug screen. However, approximately one in ten CJS+ specimens also contained antidepressants, synthetic cannabinoids (SC), methadone and/or other licit pharmaceutical opioids, drugs not tested for by the limited DPP screen. The additional drugs the CDEWS lab detected may not have practical significance for the DPP, given that most of these specimens did test positive for a drug in the DPP's limited screen. It is not possible to tell from the urinalyses if the persons taking the licit drugs were doing so legally under a physician's supervision.

In contrast, 15% of the specimens that the DPP screen indicated did not contain a drug (CJS-) contained an opioid. Methadone and buprenorphine were among the opioids most found in CJS- specimens and it is possible that these persons were receiving treatment with these drugs. Antidepressants were identified in as many CJS- specimens as CJS+ specimens (9%). SC was found in CJS- specimens but these metabolites were less common than in CJS+ specimens. These results suggest that in this population, persons were unlikely to be using SC to avoid detection by the standard DPP tests.

The comparisons of probationers/parolees in this study and our earlier study in 2008 show considerable agreement in the drugs detected. The primary changes were a decline in cocaine (36% to 17%) and buprenorphine (15% to 7%) and an increase in codeine (3% to 13%) among CJS+ specimens. The increase in codeine positives may be the result of the increased sensitivity of the tests used in the current study.

The results from the Opiate+ Sample strongly indicated that probationers/parolees who had tested positive for opiates by the DPP screen were likely to be using a variety of legal and illegal opioids in addition to non-opioid drugs. About one in three also used cocaine, one fifth used marijuana and/or benzodiazepines and about one quarter used a prescription opioid other than morphine or codeine. These results therefore have important implications for the testing used by physicians and diagnosticians who need to know if patients are using other drugs. Use of multiple opioids at the same time may lead to serious health complications and even death.

We also conducted special analyses of the combined specimens found in either sample to be positive for fentanyl, synthetic cannabinoids, or codeine. Perhaps some of the most meaningful results in this study were those showing the large number of opioid and non-opioid drugs found in the fentanyl+ specimens. The 21 specimens positive for fentanyl each contained an average of 5 different drugs, most prominently morphine, codeine, 6-MAM (heroin), cocaine, and/or hydromorphone. The findings for fentanyl+ specimens were similar to those described above for the entire sample of Opiate+ specimens and our recent study of 136 persons who died of a fentanyl related overdose in New Hampshire. It is clear that probationers/parolees in Maryland who screen positive for *any opioids* are likely to be using a variety of other opioid and non-opioid drugs. These findings suggest that treatment will be more effective if one identifies and focuses on the totality of drugs the person may be using.

Our analysis of the combined sample of all specimens positive for SC supported the findings from our previous CDEWS studies that found multiple SC metabolites in specimens. Surprisingly, specimens from the current study often contained both new and older generation SC metabolites. Given the unpredictable composition of synthetic cannabinoids (also known as Spice or K2) being marketed, it is not possible for users to know what chemicals they are consuming and to predict the effects. SC was less likely to be found in the Maryland samples compared to other CDEWS study samples, and few persons who tested CJS- in the Maryland Regional Sample were found to test positive for SC. Probationers in Maryland may therefore be less likely than other populations CDEWS has studied to use SC to avoid screening positive by the CJS test screens, which do not typically test for SC.

We also found that 70% of the Opiate+ specimens contained codeine and that codeine was found across the state. In addition, codeine was detected in 81% of fentanyl+ specimens from the combined Opiate+ and Maryland Regional samples. Acetylcodeine, which metabolizes into codeine, is often produced as an impurity of illicit heroin synthesis, which may explain the large percentage of

specimens positive for codeine given that almost all of the specimens also contained morphine. It is also possible that some of the codeine positives were the result of the direct use of codeine. We suspected that some of the codeine detected might have been caused by the use of “Purple Drank”, a mixture of codeine syrup and promethazine typically sold as a cough suppressant, that has been reported in Maryland. However, only 4% of the codeine positive specimens contained promethazine. Given that the half-life of promethazine is longer than that of codeine, one would expect to have detected promethazine in these specimens had “Purple Drank” been the source of the codeine. It is also possible that the codeine may have resulted from codeine extracted from pills containing the drug. Additional research is needed to learn more about the codeine that was detected in 60% or more of probationers across all regions of Maryland and how the use of codeine may relate to the State’s current opioid epidemic.

Table of Contents

List of Tables

List of Figures

Introduction

The Community Drug Early Warning System (CDEWS) provides timely information about emerging drug use in criminal justice populations in local communities by re-testing urine specimens already obtained 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). The CDEWS methodology is designed to achieve 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 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 150 licit and illicit substances, including opioids, benzodiazepines, antidepressants, and new psychoactive substances (NPS), using more sensitive testing technology - Liquid Chromatography-Tandem Mass Spectrometry (LC/MS/MS).

The CDEWS results are especially important for detecting emerging drugs because prior epidemics in the use of illegal drugs have often shown up in the trends in urinalysis results from criminal justice populations before they have become 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 specific drugs and the CDEWS results for more than 150 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 recently used by their target population.

The CDEWS methodology has now been piloted in twelve jurisdictions and the results are provided in five reports already released by the Office of National Drug Control Policy (ONDCP) (Billing et al., 2017; Wish et al., 2013, 2015, 2016, 2016a). This report contains findings from a single jurisdiction – the Maryland adult parole and probation program (DPP) -- and constitutes part 4 of 4 sites participating in the third iteration of CDEWS (CDEWS-3).

This report differs from prior CDEWS reports because one goal was to replicate the findings from our earlier study of Maryland probationers/parolees that had formed the basis of the CDEWS methodology (Wish et al., 2009). Our study of specimens collected in 2008 examined trends in drug test results for probationers and parolees processed in DPP offices and sent to one of the DPP operated laboratories. The current study therefore selected a sample of specimens from DPP offices that would approximate the 2008 sample so the results would be comparable. In addition, because of the intense interest in the emerging opioid problem in Maryland, the DPP asked us to collect and analyze a set of specimens statewide that had tested positive for opiates according to their limited

drug screen. The DPP had hoped the CDEWS results could shed some light on the specific drugs being used by probationers/parolees testing positive for opiates.

Methodology

Site Selection Procedures

We sought urine specimens from adult participants in the Maryland Division of Parole and Probation (DPP) drug testing program. Logistics for this site were discussed with site staff over the phone to establish the study protocols. Prior to data collection, the Center for Substance Abuse Research (CESAR) submitted an application for the necessary approvals to the Maryland Department of Public Safety and Correctional Services research committee and obtained approval for the CDEWS-3 study from University of Maryland's Institutional Review Board (IRB). The specific steps taken to recruit and work with this site are described in Appendix A, along with more details about the specimen collection in Appendix B. Table 1 provides a description of the study site.

Maryland Adult Parolees and Probationers

DPP collects almost 138,000 urine specimens annually from an average of approximately 14,000 parolees and probationers. These specimens are then tested using an offsite testing laboratory (Phamatech, Inc.). Specimens are analyzed using enzyme immunoassay (EIA) tests for a panel of 4 drugs which can be selected from a list of 7 potential drugs available for testing (benzodiazepines, cocaine, marijuana, opiates, PCP, methamphetamine, and buprenorphine). The drugs tested for are selected by DPP as a unit (rather than by individual agents) and may change over time depending on the testing needs of the unit.

The Two Samples of Specimens

This study was conducted somewhat differently from prior CDEWS studies. This is because we wanted to replicate the findings from a study we had conducted in Maryland in 2008. And second, because of the opioid epidemic in Maryland, the State asked us to collect and analyze a separate large sample of specimens that had tested positive for opiates. This report therefore presents results from two samples of urines specimens collected from probationers/parolees.

Maryland Regional Sample

In two prior studies from the Maryland Offender Population Urine Screening Program – OPUS (Wish et al., 2006; 2009), we obtained specimens from Maryland DPP offices that used the Guilford DPP laboratory to process their urine specimens. In order to replicate the findings from the prior studies, we sought 300 specimens from unduplicated adult parolees and probationers from 15 selected DPP offices in Maryland similar to those we had studied previously. Although we are

referring to the sample as a "regional" sample, it is a non-representative collection of Maryland regions. We again wanted to collect both specimens that had tested CJS+ or CJS- for any drug in the standard local CJS drug screen. We therefore worked with DPP's offsite testing laboratory to collect 20 specimens from each of the 15 selected DPP offices, 10 that tested CJS+ and 10 that tested CJS- (see Table 1).

Opiate+ Sample

With the rise of opioid-related overdoses and deaths in Maryland, the DPP was very interested in our studying the opioids being used by their parolee and probationer populations. We therefore sought a sample of 200 Opiate+ specimens from unduplicated adult parolees and probationers statewide. The offsite laboratory sent to CDEWS all unduplicated Opiate+ specimens they had processed until we had received the desired 200.

Table 1: Description of the DPP Testing Program and Specimens Sought

Site	Populations Covered	CJS Testing Protocol	Drugs in Standard CJS Screen	Targeted Number of Specimens to be Collected for CDEWS
Maryland DPP	Adult parolees and probationers (est. 138,000 specimens per year from approximately 14,000 parolees and probationers)	Offsite laboratory testing	4-drug panel screen (selected by DPP from a list of 7 drugs): benzodiazepines, cocaine, marijuana, opiates, PCP, methamphetamine and buprenorphine.	**Opiate+ Sample (Statewide):** 200 Opiate+ specimens **Maryland Regional Sample:** 300 specimens from 15 selected DPP offices (10 CJS+; 10 CJS- from each office)

Collection of Urine Specimens

Prior to collecting the urine specimens, CESAR staff talked with staff from the program and DPP's offsite testing laboratory by phone to determine their policies regarding required specimen holding periods, testing protocols, detection limits and other relevant site details. Specimens were then selected by the offsite laboratory using the specific CDEWS guidelines provided by CESAR. 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-3 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 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 CDEWS-3 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 CDEWS-3 panel. Additional information on the data reviewed and persons interviewed appears in Appendix C (see also Table C-1). Based on the information reviewed, we added six new SC metabolites to the SC test panel we had used in CDEWS-2, along with 14 additional new psychoactive substances (see Table C-2 in Appendix C for the full panel). Other SC metabolites were recently discovered, but urine tests for many of them were not available at the time of CDEWS-3, and could not be included in our test panel.

Testing of Urine Specimens for CDEWS-3

All specimens were sent to the Armed Forces Medical Examiner System (AFMES) Laboratory located in Delaware, for an expanded drug testing panel of 153 drugs, detailed in Table C-2 in Appendix C. All specimens were tested for a panel of 27 SC metabolites and 37 other new psychoactive substances, along with 89 other illicit and prescription drugs.

Results

In this report, *CJS test results* refers to the 4-drug screen routinely used by the local criminal justice agency to screen the adult parolees and probationers. This screen could have been for 4 of 7 potential drugs available for testing, based on DPP's drug selection for specimen testing. The *CDEWS test results* refers to the expanded drug tests for up to 153 substances used by the CDEWS laboratory, which also included all of the drugs on the 4-drug screen used by the CJS testing.

The results for the Maryland Regional and Opiate+ samples are presented separately. We first describe the specimens collected and some basic demographic information about the persons who provided them. Next we describe the CDEWS test results for specimens tested with our expanded drug screen. The results for CJS+ and CJS- specimens are presented separately because we stratified our Regional sample's selection by whether each specimen had tested CJS+ or CJS- for any drug in the local CJS drug screen. Given this sample stratification, it would be inappropriate for our analyses to simply combine and average all of the specimen results. For the Maryland Regional Sample only, we present a comparison of findings from this study with our prior study of adult parolees and probationers from Maryland. Because of the limited numbers of positive specimens available and our interest in these drugs, we conclude with a set of descriptive analyses that utilize all specimens from the combined MD Regional and Opiate+ samples that tested positive for fentanyl, synthetic cannabinoids (SC) and/or codeine.

I. Regional Sample

A. *Specimens Received*

Specimens were collected in August 2015. While we had targeted 300 specimens, we actually received 288, 137 CJS+ and 151 CJS- specimens. Table 2 presents the number of specimens received from each submitting DPP office.

Table 2: Number of CJS+ and CJS- Specimens Received from each Maryland Division of Parole and Probation (DPP) Office
(N=287 specimens from the Maryland Regional Sample)

	Number of Specimens Received	
DPP Submitting Office	CJS+	CJS-
Gay Street	9	10
Northwest Seton	9	12
Southwest Severn	10	9
Northeast Preston	10	11
Guilford Avenue	10	10
Ellicott City	10	10
Essex	9	10
Dundalk	5	10
Catonsville	8	9
Owings Mills	9	10
Hyattsville	9	10
Waldorf	11	10
Upper Marlboro	11	9
Temple Hills	8	10
Hagerstown	9	10
TOTAL	137	150*

*One CJS- specimen was omitted from the table due to missing data for the submitting office.

B. *Gender and Geographic Region of Persons Providing Specimens*

Table 3 shows that the gender and geographic region of the persons who provided CJS+ and CJS- specimens were quite similar. Geographic region was approximated using the location of the DPP office from which each urine specimen was obtained. Most specimens (86-88%) came from men

with more than half submitted to a DPP office in the Baltimore region (58-61%). All specimens came from DPP offices in Maryland.

Table 3: Gender and Geographic Region of Persons Providing Specimens, by CJS Drug Screen Result

(N=287 specimens from the Maryland Regional Sample^)

	CJS+ (N=137)	CJS- (N=150)‡
Gender		
Male	86%	88%
Female	14	12
Total	100%	100%
Geographic Region*		
Baltimore City	35	35
Baltimore County	23	26
	58%	61%
Prince George's County	20	19
Southern Maryland	8	6
Suburban Baltimore	7	7
Washington County	7	7
Total	100%	100%

^One specimen was omitted from the table due to missing data for the submitting office.

‡N's differ for some characteristics due to missing information.

*Geographic Regions are as follows: Southern Maryland (Calvert, Charles, St. Mary's); Suburban Baltimore (Carroll, Harford, Howard). Baltimore City, Baltimore County, Prince George's County, and Washington County reported separately as individual counties.

C. Drugs Detected by the CDEWS Laboratory

All Drugs, except New Psychoactive Substances (NPS) and Synthetic Cannabinoids (SC). Table 4 presents the CDEWS laboratory's test results for these drugs according to whether the specimen had tested CJS+ or CJS-. Significance tests for differences between CJS+ and CJS- specimens were only computed for drugs unlikely to have caused a specimen to be identified as CJS+ by DPP.

CJS+ Specimens: Marijuana (45%) and cocaine (17%) are included in the standard DPP screen and were therefore among the drugs most likely to be detected in CJS+ specimens. Similarly, 37% of the specimens contained any non-fentanyl opioid, most commonly morphine (20%), codeine (13%), methadone (10%) and/or oxycodone (8%). Codeine is metabolized to morphine and may therefore be double counted here. Only a few specimens (3%) contained 6-MAM, a metabolite of heroin, but much of the original heroin may already have been metabolized to morphine. Research on the metabolism of 6-MAM indicates that this compound has a very short detection time of less than 8 hours which may

have made it difficult to detect it in the study specimens (Cone et al., 1991). Fentanyl and its analogues were relatively rare, found in 2% or fewer of specimens. Most other drugs were rarely detected in the CJS+ specimens, with a small percentage containing any benzodiazepines (11%), antidepressants (9%), and/or quinidine/quinine (13%), a substance with which heroin is often cut.

CJS- Specimens: While the CJS- specimens contained few drugs, non-fentanyl opioids were prominent (15%). Non-fentanyl opioids most commonly found in CJS- specimens were buprenorphine (5%), methadone (3%), and/or tramadol (3%). Of these, only buprenorphine could be detected by the DPP test protocol, if it were specifically requested by the submitting agency. The other category of drugs detected in CJS- specimens was antidepressants (9%). It is impossible to discern from urinalysis results if any of these pharmaceutical drugs were being taken legally under a doctor's supervision.

New Psychoactive Substances. Few new psychoactive substances were detected. The most common new psychoactive substance detected in CJS+ or CJS- specimens was mCPP (2%, see Table 4). The presence of mCPP could be caused by the metabolizing of Trazodone (an antidepressant) or by mCPP use alone.

Table 4: CDEWS Test Results, by CJS Drug Screen Result

(N=288 specimens from the Maryland Regional Sample^ collected in August 2015§)

Percent Positive by CDEWS Lab for:	CJS+ (N=137)	CJS- (N=151)
Marijuana^	45%	0%
Cocaine^	17	3
PCP^	9	0
Methamphetamine^	2	0
Any Non-Fentanyl Opioid^	37	15
Morphine	20	1
Methadone Metabolite (EDDP)	10*	3*
Codeine	13	0
Buprenorphine^‡	7	5
Oxymorphone	7*	2*
Oxycodone	8**	1**
Tramadol	2	3
Hydromorphone	4	<1
6-Monoacetylmorphine (6-MAM)	3	<1
Hydrocodone	<1	<1
Any Fentanyl	2	0
Norfentanyl	2	0
Fentanyl	2	0
Acetylfentanyl	<1	0
Any Antidepressant	9	9
Citalopram	3	3
Trazodone†	2	2
Sertraline	3	<1
Amitriptyline	2	1
Nortriptyline	<1	2
Fluoxetine	<1	1
Desvenlafaxine	<1	<1
Bupropion	0	<1
Venlafaxine	<1	0
Any Synthetic Cannabinoid (SC)	10	5
UR-144	9*	3*
5F-PB-22	8*	2*
XLR-11	8*	2*
AB-FUBINACA (Parent)	3	<1
AB-CHMINACA (metab 4)	3	<1

Table 4 (Cont'd): CDEWS Test Results, by CJS Drug Screen Result

AB-PINACA	0	3
ADB-FUBINACA (Parent)	<1	<1
5F-AB-PINACA	0	<1
AB-CHMINACA (Parent)	0	<1
PB-22	<1	0
Any Benzodiazepine^	11	1
Alprazolam	7	0
α-Hydroxyalprazolam	6	<1
Nordiazepam	5**	0**
Oxazepam	4	<1
Temazepam	4	<1
7-Aminoclonazepam	2	0
Demoxepam	<1	0
Any New Psychoactive Substance (NPS)	4	3
mCPP†	2	2
Ethylone	<1	<1
Phenmetrazine	0	<1
Benzylpiperazine	<1	0
Eutylone	<1	0
TFMPP	<1	0
Other Drugs		
Quinidine/Quinine	13%***	<1%***
Naloxone	7	4
Cetirizine	2	3
Haloperidol	<1	2
Amphetamine	2	<1
Ephedrine	2	<1
Promethazine	2	<1
Pseudoephedrine	2	<1
Cyclobenzaprine	2	0
Dextromethorphan	2	0
Hydroxyzine	0	<1

^The Maryland Division of Parole and Probation routinely tests parolees and probationers for a panel of four drugs selected from a list of seven drugs, including: benzodiazepines, cocaine, marijuana, opiates, PCP, methamphetamine and buprenorphine.

§The collection date is unknown for 152 specimens, as it was inadvertently omitted at the time of sampling.

‡All buprenorphine positive specimens were confirmed by LC/MS/MS and contained norbuprenorphine.

†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.

Notes: Bolded synthetic cannabinoid metabolites were newly added to the testing panel for CDEWS-3.

*p<.05 by Pearson Chi-Square or Fisher's exact test.

**p<.01 by Pearson Chi-Square or Fisher's exact test.

***p<.001 by Pearson Chi-Square or Fisher's exact test.

D. SC Metabolites in CJS+ and CJS- Specimens

Synthetic Cannabinoids. SC metabolites were found in both CJS+ (10%) and CJS- (5%) specimens (see Table 4). A few of the SC metabolites were more likely to be detected in CJS+ specimens as compared to those that were CJS-, including UR-144 (9% vs. 3%, p<.05), 5F-PB-22 (8% vs. 2%, p<.05), and XLR-11 (8% vs. 2%, p<.05). Four of the 6 SC metabolites newly added to the CDEWS-3 test panel were detected: AB-FUBINACA (Parent), AB-CHMINACA (metab 4), ADB-FUBINACA (Parent), and AB-CHMINACA (Parent) (indicated in Table 4 by bold type). A combination of older and newer generation SC metabolites were detected in the specimens. Of the 10 total SC metabolites detected, 7 were found in the CJS+ specimens and 9 were detected in the CJS- specimens.

E. Comparison of Test Results for Specimens from Males and Females

Table 5 compares the CDEWS laboratory test results for specimens provided by males and females. The number of specimens available for females was small and can provide only an indication of recent drug use in males and females.

CJS+ Specimens: Antidepressants were more likely to be found in CJS+ specimens from females than males (26% vs. 6%, p<.05). Non-fentanyl opioids were detected in 47% of specimens from females and in 36% of those from males (difference not significant). Also, marijuana was detected in 47% of specimens from males and in 32% of those from females (difference not significant). Benzodiazepines were detected in 21% of specimens from females and 9% of specimens from males (difference not significant).

CJS- Specimens: We reported above that CJS- specimens were found to contain non-fentanyl opioids and antidepressants. The results in Table 5 show that these drugs were found in CJS- specimens from both males and females.

F. Test Results by Geographic Region

Table 6 compares the CDEWS laboratory test results for specimens provided by county of the DPP submitting office from which the specimen was obtained. The number of specimens available for each county was small and can provide only an indication of recent drug use by persons from different geographic areas. No percentages were computed for any area with less than 10 specimens. In such cases we showed only if a drug was present in any specimen provided.

It is clear from Table 6 that opioids, marijuana, cocaine and antidepressants were found largely throughout the state. The exception was Prince George's County, where few specimens tested positive for opioids. PCP was found only in Prince George's, Baltimore and Charles Counties. SC's were detected in all locations studied but Howard County. NPS were very rare and mainly found in specimens from Baltimore and Prince George's County.

Table 5: CDEWS Laboratory Test Results, by Gender and CJS Drug Screen Result

(N=285 specimens from the Maryland Regional Sample^ collected in August 2015§)

	CJS+ (N=137)		CJS- (N=148)	
Percent Positive by CDEWS Lab for:	Males (N=118)	Females (N=19)	Males (N=130)	Females (N=18)
Marijuana	47%	32%	0%	0%
Cocaine	16	21	2	6
Buprenorphine‡	8	0	5	6
PCP	9	11	0	0
Methamphetamine	3	0	0	0
Any Non-Fentanyl Opioid∆	36	47	15	11
Any Fentanyl∆	3	0	0	0
Any Antidepressant∆	6*	26*	10	6
Any Synthetic Cannabinoid (SC)∆	11	5	6	0
Any Benzodiazepine∆	9	21	2	0
Any New Psychoactive Substance (NPS)∆	4	0	4	0

Notes:

^The Maryland Division of Parole and Probation routinely tests parolees and probationers for a panel of four drugs selected from a list of seven drugs, including: benzodiazepines, cocaine, marijuana, opiates, PCP, methamphetamine and buprenorphine.

§The collection date is unknown for 152 specimens, as it was inadvertently omitted at the time of sampling.

‡All buprenorphine positive specimens were confirmed by LC/MS/MS and contained norbuprenorphine.

∆The complete list of drugs detected as part of this category can be referenced in Table 4.

*p<0.05 based on Fisher's Exact Test.

Table 6: CDEWS Test Results, by County and CJS Drug Screen Result

	Maryland Regional Sample (N=287)											
	CJS Screen Positive (for any drug) (N=137)						CJS Screen Negative (for any drug) (N=150)					
Percent Positive by CDEWS Lab for:	Baltimore County (N=31)	Baltimore City (N=48)	Prince George's County (N=28)	Howard County (Ellicott City) (N=10)	Washington County (Hagerstown) (N=9)[Δ]	Charles County (Waldorf) (N=11)	Baltimore County (N=39)	Baltimore City (N=52)	Prince George's County (N=29)	Howard County (Ellicott City) (N=10)	Washington County (Hagerstown) (N=10)	Charles County (Waldorf) (N=10)
Any Opioid*	45%	50%	4%	40%	Present	46%	15%	19%	0%	20%	20%	20%
Marijuana	48	42	46	50	Present	36	0	0	0	0	0	0
Cocaine	23	19	14	20	Present	0	3	6	0	0	0	0
Any Antidepressant	7	8	7	0	Present	27	13	10	3	0	20	10
Any Synthetic Cannabinoid (SC)	0	19	11	0	Present	0	5	6	3	0	10	10
Quinidine/Quinine	19	21	0	20	0	0	0	2	0	0	0	0
Methadone Metabolite (EDDP)	13	10	4	30	Present	0	8	2	0	0	0	10
Any Buprenorphine[§]	13	6	0	0	Present	9	3	10	0	10	0	0
Any Benzodiazepine	16	10	0	40	Present	0	3	2	0	0	0	0
Naloxone	13	6	0	0	Present	9	3	8	0	10	0	0
PCP	10	0	29	0	0	9	0	0	0	0	0	0
Any New Psychoactive Substance (NPS)	7	4	4	0	0	0	3	6	3	0	0	0

Notes:

*Includes both non-fentanyl and fentanyl opioid compounds.

§Buprenorphine positive specimens were defined as those that tested positive for either buprenorphine or norbuprenorphine.

ΔPercentages have not been calculated because of the small number of specimens available.

II. Comparison of the CDEWS-3 Regional Test Results to the 2008 Study

Table 7 shows that the geographic distribution of the DPP offices submitting samples to the Guilford Laboratory in the 2008 study and those selected for the current study were similar, as intended by our sampling scheme. The large majority (82%, 79%) of the specimens from both studies came from DPP offices in the Baltimore Metropolitan area and Prince George's County.

Table 7: Geographic Distribution of Specimens Sampled for the 2008 and 2016 CESAR Studies for the Maryland Division of Parole and Probation (DPP), by Study Sample

County From Which Specimens Were Sampled	OPUS (2008) Guilford Laboratory Study Sample (N=350)		CDEWS-3 (2016) Maryland Regional Study Sample (N=287)^	
Baltimore County	31%		24%	
Baltimore City	28	82%	35	79%
Prince George's County	23		20	
Howard County (Ellicott City)	6		7	
Washington County (Hagerstown)	6		7	
Charles County (Waldorf)	6		7	
TOTAL	100%		100%	

Note: Certain percentages have been rounded in order for the total to equal 100%.

^One specimen from the CDEWS-3 study was omitted from the table due to missing data for submitting office.

Table 8 compares the drug test results from the two studies. It is important to note that this table only includes drugs that were included in both studies. Test results were similar for most drugs, with a few important exceptions. The percentage of CJS+ specimens testing positive for cocaine (36% vs. 17%, $p<.001$) and buprenorphine (15% vs. 7%, $p<.05$) declined. These differences were found even though the AFMES laboratory in the current study used more sensitive tests for cocaine and buprenorphine. In contrast, the percentage of specimens testing positive for codeine increased (3% vs. 13%, $p<.001$), however, it should be noted that the test used to detect codeine in the current study was more sensitive than that used in the 2008 study (25 ng/mL versus 300 ng/mL) and may account for the increase in codeine positives.

Table 8: Drugs Detected in CJS+ and CJS- Specimens for the 2008 and 2016 CESAR Studies^ for the Maryland Division of Parole and Probation (DPP)

	CJS+ (N=412)		CJS- (N=226)	
Drug	2008 (N=275)	2016 (N=137)	2008 (N=75)	2016 (N=151)
Cocaine	36%***	17%***	0%	3%
Marijuana	34	45	0	0
Morphine	24	20	0	1
Buprenorphine	15*	7*	7	5
Any Benzodiazepines	13	11	0	1
Methadone Metabolite (EDDP)	10	10	4	3
Oxycodone/Oxymorphone	7	10	0	2
PCP	6	9	0	0
Codeine‡	3***	13***	0	0
LSD	2	0	1	0
Hydrocodone/Hydromorphone	1	5	0	<1
Any Amphetamine	1	4	0	<1

Notes:

^Some of the levels of detection used to detect the drugs included in this table differ between the 2008 and 2016 studies given that our testing methodology was updated over time.

‡Codeine was detected in the 2008 study using an enzyme immunoassay test for opiates with a level of detection of 300 ng/mL. Codeine was then confirmed by GC/MS to verify its presence. In the current CDEWS study, codeine was detected by LC/MS/MS with a level of detection of 25 ng/mL.

*p<.05 by Fisher's exact test.

***p<.001 by Fisher's exact test.

III. Opiate+ Sample Results

A. *Specimens Received*

Specimens were collected between April 2015 and June 2015. We had targeted 200 specimens and actually received 202.

B. *Gender and Geographic Region of Persons Providing Specimens*

Table 9 shows that the large majority of Opiate+ specimens (78%) came from men. Table 10 shows that this was true across all state regions studied. The largest number of specimens were obtained from DPP offices in Baltimore City (35%), followed by Southern Maryland (12%), Anne Arundel County (11%), and the Upper Eastern Shore (10%). All specimens came from DPP offices located in Maryland. The remaining analyses in this section are presented according to geographic region and combined into one group. It should be noted that the sample sizes in each geographic area were quite small, and for Suburban Washington and Prince George's County, we compute no estimate and show only that a drug was detected.

Table 9: Gender and Geographic Region of Persons Providing Specimens

(N=200 specimens from the Maryland Opiate+ Sample)^

	f	%
Gender		
Male	156	78%
Female	44	22
Geographic Region*		
Baltimore City	70	35%
Southern Maryland	24	12
Anne Arundel County	21	11
Upper Eastern Shore	19	10
Baltimore County	15	8
Washington County	15	7
Lower Eastern Shore	13	6
Suburban Baltimore	10	5
Suburban Washington	7	3
Prince George's County	6	3
Total	200	100%

^Two specimens were omitted from this table due to missing data for the submitting office and/or gender.

*Geographic Regions are as follows: Lower Eastern Shore (Dorchester, Somerset, Wicomico, Worcester); Southern Maryland (Calvert, Charles, St. Mary's); Suburban Baltimore (Carroll, Harford, Howard); Suburban Washington (Frederick, Montgomery); Upper Eastern Shore (Caroline, Cecil, Kent, Queen Anne's, Talbot). Anne Arundel County, Baltimore City, Baltimore County, Prince George's County, and Washington County reported separately as individual counties.

Table 10: Gender, By Geographic Region‡
(N=199 specimens from the Maryland Opiate+ Sample)^

Geographic Region	% Males
Baltimore City (N=69)	88%
Washington County (N=15)	87
Anne Arundel County (N=21)	81
Baltimore County (N=15)	80
Upper Eastern Shore (N=19)	79
Southern Maryland (N=24)	67
Lower Eastern Shore (N=13)	62
Suburban Baltimore (N=10)	50
Suburban Washington (N=7)	*
Prince George's County (N=6)	*
Total (N=199)	78%

‡Geographic Regions are as follows: Lower Eastern Shore (Dorchester, Somerset, Wicomico, Worcester); Southern Maryland (Calvert, Charles, St. Mary's); Suburban Baltimore (Carroll, Harford, Howard); Suburban Washington (Frederick, Montgomery); Upper Eastern Shore (Caroline, Cecil, Kent, Queen Anne's, Talbot). Anne Arundel County, Baltimore City, Baltimore County, Prince George's County, and Washington County reported separately as individual counties.

^Three specimens were omitted from this table due to missing data for the submitting office and/or gender.

*Percentages have not been calculated because there were less than 10 specimens available.

C. Drugs Detected in Opiate+ Specimens by the CDEWS Laboratory

Table 11 shows clearly that the Opiate+ specimens tended to contain many other drugs. A third of them contained cocaine, which was detected in every region studied. About one fifth contained marijuana, which also was detected in every region. The next most common drugs detected were benzodiazepines (19%) and antidepressants (17%). New psychoactive substances (NPS) were relatively rare and not detected in Southern Maryland, Lower Eastern Shore and Prince George's County. SC metabolites and PCP were each found in only 2% of the specimens. PCP was detected only in Southern Maryland and SC was detected in Southern Maryland and Baltimore County.

Table 12 shows opioids detected in 9% or more of the Opiate+ specimens. Almost all of the Opiate+ specimens tested positive for morphine (97%) and approximately 70% tested positive for codeine. The morphine positives could have resulted from persons taking heroin (6-MAM, 32%) which metabolizes quickly to morphine. Acetylcodeine, which metabolizes into codeine, is often produced as an impurity of illicit heroin synthesis, which may explain the large percentage of specimens positive for codeine given that almost all of the specimens also contained morphine (O'Neal & Poklis, 1997; Staub et al., 2001). However, it is not possible to determine with certainty whether this large percentage of codeine positives resulted from heroin impurities or direct codeine

use. Significant percentages of the Opiate+ specimens also contained methadone (21%) or buprenorphine (18%), which are legal opioids that could have been taken under a doctor's supervision. These Opiate+ specimens also contained other pharmaceutical opioids which were detected such as oxymorphone, hydromorphone and oxycodone. Fentanyl was found in 9% of these specimens, and was detected in all but 3 regions (Washington County, the Lower Eastern Shore, and Prince George's County). It is clear from the results in Tables 11 and 12 that probationers/parolees throughout Maryland who tested CJS+ for opiates had been using a variety of opioid and non-opioid drugs. Additional drug test results for the Opiate+ group can be found in Table D-1 of Appendix D.

Table 11: Percentage of Specimens Testing Positive for Other Drugs, by Geographic Region*

(N=200 specimens from the Maryland Opiate+ Sample)^

Percent Positive by CDEWS Lab for:	Baltimore City (N=70)	Southern Maryland (N=24)	Anne Arundel County (N=21)	Upper Eastern Shore (N=19)	Baltimore County (N=15)	Washington County (N=15)	Lower Eastern Shore (N=13)	Suburban Baltimore (N=10)	Suburban Washington (N=7)Δ	Prince George's County (N=6)Δ	Total (N=200)
Cocaine	40%	13%	14%	37%	60%	13%	39%	40%	Present	Present	33%^
Marijuana	19	17	19	32	7	13	23	40	Present	Present	21^
Any Benzodiazepine	11	25	24	5	27	20	15	30	Present	Present	19^
Any Antidepressant	9	33	10	21	33	20	8	20	Present	Present	17
Any New Psychoactive Substance (NPS)	4	0	5	11	7	7	0	10	Present	0	6^
Any Synthetic Cannabinoid (SC)	0	8	0	0	7	0	0	0	0	0	2
PCP	0	4	0	0	0	0	0	0	0	Present	2

*Geographic Regions are as follows: Lower Eastern Shore (Dorchester, Somerset, Wicomico, Worcester); Southern Maryland (Calvert, Charles, St. Mary's); Suburban Baltimore (Carroll, Harford, Howard); Suburban Washington (Frederick, Montgomery); Upper Eastern Shore (Caroline, Cecil, Kent, Queen Anne's, Talbot). Anne Arundel County, Baltimore City, Baltimore County, Prince George's County, and Washington County reported separately as individual counties.

^Two specimens were omitted from this table due to missing data for the submitting office. Some percentages may therefore vary slightly from the full sample findings shown in Table D-1.

ΔPercentages have not been calculated because of the small number of specimens available.

Table 12: Percentage of Specimens Testing Positive for Specific Opioids, by Geographic Region*

(N=200 specimens from the Maryland Opiate+ Sample)^

Percent Positive by CDEWS Lab for:	Baltimore City (N=70)	Southern Maryland (N=24)	Anne Arundel County (N=21)	Upper Eastern Shore (N=19)	Baltimore County (N=15)	Washington County (N=15)	Lower Eastern Shore (N=13)	Suburban Baltimore (N=10)	Suburban Washington (N=7)Δ	Prince George's County (N=6)Δ	Total (N=200)
Morphine	99%	100%	100%	95%	100%	93%	92%	100%	Present	Present	97%
Codeine	79	63	76	63	67	60	62	60	Present	Present	70
6-Monoacetylmorphine (6-MAM)	39	13	33	21	33	20	39	40	Present	Present	32^
Oxymorphone	19	46	29	16	20	40	15	30	0	0	24
Hydromorphone	16	25	29	32	33	27	31	30	Present	Present	24
Methadone Metabolite (EDDP)	29	8	29	11	20	13	23	30	0	0	21^
Any Buprenorphine§	23	8	5	26	13	20	23	20	Present	0	18
Oxycodone	6	29	14	0	13	13	8	20	0	0	11^
Any Fentanyl±	13	8	10	11	7	0	0	10	Present	0	9

*Geographic Regions are as follows: Lower Eastern Shore (Dorchester, Somerset, Wicomico, Worcester); Southern Maryland (Calvert, Charles, St. Mary's); Suburban Baltimore (Carroll, Harford, Howard); Suburban Washington (Frederick, Montgomery); Upper Eastern Shore (Caroline, Cecil, Kent, Queen Anne's, Talbot). Anne Arundel County, Baltimore City, Baltimore County, Prince George's County, and Washington County reported separately as individual counties.

^Two specimens were omitted from this table due to missing data for the submitting office. Some percentages may therefore vary slightly from the full sample findings shown in Table D-1.

ΔPercentages have not been calculated because of the small number of specimens available.

§Any Buprenorphine positive specimens were defined as those that tested positive for either buprenorphine or norbuprenorphine.

±Any fentanyl includes specimens that tested positive for fentanyl, norfentanyl, or acetylfentanyl.

IV. Combined Sample Results for Fentanyl, SC, and Codeine Positive Specimens

Given the interest in the use of fentanyl and synthetic cannabinoids and the paucity of specimens that contain them, this section analyzes all specimens positive for these drugs that we obtained from the Maryland Regional and Opiate+ samples. In addition, we also analyzed all specimens positive for codeine from both samples given our unexpected finding of so many specimens that tested positive for codeine.

A. Fentanyl Compounds Detected in the Combined Sample

Of the 21 specimens positive for any fentanyl in the two samples, 48% were positive for both fentanyl and its metabolite norfentanyl and 38% were positive for norfentanyl only (see Table 13). A small number of these specimens (14%) also contained acetylfentanyl, which is a metabolite produced from an illicitly manufactured form of fentanyl. All but 3 of the fentanyl positive specimens came from the Opiate+ sample.

Table 13: Combinations of Fentanyl, Norfentanyl, or Acetylfentanyl Detected
(N=21 specimens from the Maryland Opiate+ and Regional Samples)

Percentage Positive for Each Combination of Fentanyl, Norfentanyl, or Acetylfentanyl Detected	
Fentanyl and Norfentanyl	48%
Norfentanyl only	38%
Fentanyl, Norfentanyl, and Acetylfentanyl	9%
Fentanyl and Acetylfentanyl	5%
Total	100%

B. Other Drugs Detected in Fentanyl Positive Specimens

Table 14 shows all of the drugs detected in the 21 specimens from both samples that contained fentanyl. Because 18 of these specimens came from the Opiate+ sample, they would have had to contain an opiate (which was why they were selected for the Opiate+ sample) in addition to fentanyl, which is not detected by DPP's opiate screen. It is noteworthy that 11 of these specimens contained 6-MAM which indicates recent heroin use. However, other specimens containing morphine could have been caused by heroin in which the 6-MAM was already metabolized and not present in the urine. Nevertheless, a number of these specimens contained hydromorphone (8), methadone (7) and/or oxymorphone (5). Only one specimen (from the MD Regional Sample) contained fentanyl but no other opioid.

In addition to opioids and fentanyl, 8 of the 21 specimens also contained cocaine and 5 contained marijuana. Pharmaceutical non-opioids also detected include Cetirizine (4), Naloxone (4)

which may have been taken as part of Suboxone (a prescription drug which contains both buprenorphine and naloxone), and Oxazepam (4). Counting all drugs, many of which could have been double counting the same source drug, we found 102, or an average of 5 per specimen.

It is clear from the results in Table 14 that while 18 of these specimens were selected because they contained an opiate, these persons had used a variety of other licit and illicit drugs.

C. Synthetic Cannabinoid Metabolites Detected in the Combined Sample

Figure 1 shows the combination of SC metabolites detected in the 25 specimens that contained any SC. We found that 28% of these SC+ specimens contained only 1 metabolite and 20% contained only 2. However, 52% of specimens contained 3 or more metabolites. In total, 10 different SC metabolites were detected in the SC+ specimens, of which 4 were SC metabolites newly added to the testing panel (indicated in bold type). The older generation SC metabolites, including 5F-PB-22 (64%), UR-144 (64%), and XLR-11 (60%) were most frequently detected in the specimens. But 24% contained AB-FUBINACA (Parent) and 20% contained AB-CHIMINACA (metab 4), two of the newer forms of SC. The synthetic cannabinoid metabolites contained in each of the 25 SC positive specimens are shown in Table 15.

D. Other Drugs Present in Specimens Testing Positive for Fentanyl, Synthetic Cannabinoids, or Codeine in the Combined Sample

Table 16 shows that specimens containing fentanyl were most likely to also contain morphine (95%), codeine (81%), 6-MAM/heroin (52%), cocaine (38%), hydromorphone (38%) and/or methadone (33%). A wide variety of both legal and illegal drugs were also found in the fentanyl+ specimens. The SC+ specimens were most likely to contain marijuana (32%), codeine (12%), morphine (12%) and/or cocaine (12%). Codeine+ specimens were most likely to also contain morphine (97%), a metabolite of codeine or heroin, 6-MAM/heroin (42%), cocaine (35%), oxymorphone (27%), hydromorphone (23%), marijuana (23%), and/or methadone (22%). Acetylcodeine, which metabolizes into codeine, is often produced as an impurity of illicit heroin synthesis, which may explain the large percentage of specimens positive for 6-MAM and morphine in the codeine positive specimens (O'Neal & Poklis, 1997; Staub et al., 2001). The results in Table 16 suggest that probationers/parolees who test positive for fentanyl or codeine had recently used a larger variety of other drugs than users of SC.

Table 14: Drugs Detected in Fentanyl Positive* Specimens

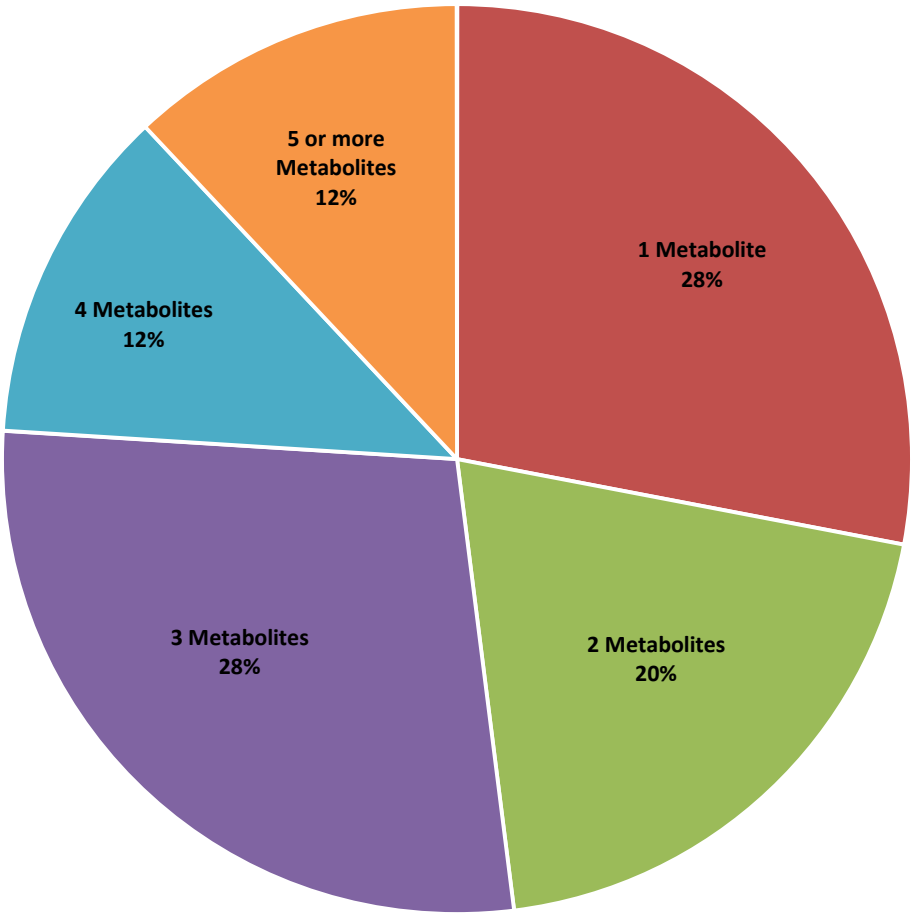
(N=21 Fentanyl Positive specimens from the Maryland Opiate+ and Regional Samples)^

	Opioids								Illicit Non-Opioid Drugs		Pharmaceutical Non-Opioid Drugs					
Specimen	Morphine	Codeine	6-Monoacetylmorphine (6-MAM)	Hydromorphone	Methadone Metabolite (EDDP)	Oxymorphone	Norbuprenorphine	Buprenorphine	Cocaine	Marijuana	Cetirizine	Naloxone	Oxazepam	7-Aminoclonazepam	Nordiazepam	Total # of Drugs Detected‡
1	✓	✓	✓	✓	✓				✓	✓	✓					8
2	✓	✓			✓				✓	✓	✓		✓			7
3	✓	✓	✓			✓			✓	✓	✓					7
4	✓	✓	✓						✓	✓	✓					6
5	✓	✓	✓		✓				✓	✓						6
6	✓	✓	✓				✓	✓					✓			6
7	✓	✓		✓									✓	✓	✓	6
8	✓	✓	✓	✓	✓				✓							6
9	✓	✓				✓			✓					✓		5
10	✓	✓			✓	✓						✓				5
11	✓	✓	✓	✓		✓										5
12	✓		✓				✓	✓				✓				5
13	✓	✓		✓								✓				4
14	✓			✓	✓							✓				4
15	✓	✓				✓	✓									4
16	✓	✓		✓					✓							4
17	✓	✓	✓													3
18	✓			✓	✓											3
19	✓	✓	✓													3
20	✓	✓	✓													3
21													✓		✓	2
Total	20	17	11	8	7	5	3	2	8	5	4	4	4	2	2	102

*Includes specimens positive for any fentanyl compound on the testing panel. Fentanyl compounds detected: fentanyl, norfentanyl, and acetylfentanyl.
^Includes drugs detected in at least 10% of specimens. Drugs detected in under 10% included: a-Hydroxyalprazolam, Alprazolam, Amphetamine, Citalopram, Cyclobenzaprine, Dextromethorphan, Hydroxyzine, mCPP, Methamphetamine, Oxycodone, Promethazine, Temazepam, and Trazodone.
‡Two or more of the drugs may have been detected as a result of taking one substance.

Figure 1: Metabolites Detected in All Synthetic Cannabinoid (SC) Positive Specimens from Adult Parolees and Probationers in Maryland

(N=25 specimens from the Maryland Opiate+ and Regional Samples collected between April 2015-August 2015)



Percentage Positive for Each Metabolite (N=25)	
5F-PB-22	64%
UR-144	64%
XLR-11	60%
AB-FUBINACA (Parent)	24%
AB-CHMINACA (metab 4)	20%
AB-PINACA	20%
ADB-FUBINACA (Parent)	8%
AB-CHMINACA (Parent)	4%
5F-AB-PINACA	4%
PB-22	4%

Table 15: Metabolites Detected in All Synthetic Cannabinoid (SC) Positive Specimens from Adult Parolees and Probationers in Maryland

(N=25 Specimens from the Maryland Opiate+ and Regional Samples collected between April 2015-August 2015)

SC Positive Specimen #	5F-PB-22	UR-144	XLR-11	AB-FUBINACA (Parent)	AB-CHMINACA (metab 4)	AB-PINACA	ADB-FUBINACA (Parent)	AB-CHMINACA (Parent)	5F-AB-PINACA	PB-22	Total # of Metabolites Detected
1	✓	✓	✓	✓	✓		✓			✓	7
2	✓	✓	✓	✓		✓			✓		6
3	✓	✓	✓	✓	✓						5
4	✓	✓	✓	✓							4
5	✓	✓	✓		✓						4
6	✓	✓	✓		✓						4
7	✓	✓	✓								3
8	✓	✓	✓								3
9	✓	✓	✓								3
10	✓	✓	✓								3
11	✓		✓	✓							3
12	✓					✓		✓			3
13		✓	✓				✓				3
14	✓	✓									2
15		✓	✓								2
16		✓	✓								2
17		✓				✓					2
18			✓	✓							2
19	✓										1
20	✓										1
21	✓										1
22		✓									1
23					✓						1
24						✓					1
25						✓					1
TOTAL	16	16	15	**6**	**5**	5	**2**	**1**	1	1	-

Note: **Bolded** metabolites were newly added to the testing panel for CDEWS-3.

Table 16: Other Drugs Present in Specimens Testing Positive for Fentanyl, Codeine, and/or Synthetic Cannabinoid for the Combined Maryland Opiate+ and Regional Samples

	Positive for Any Fentanyl* (N=21)	Positive for Codeine (N=159)†	Positive for Any SC (N=25)	Total (of all Opiate + and Regional specimens) (N=490)†
Other Drugs Present^				
Morphine	95%	97%	12%	46%
Codeine	81	–	12	32
Quinidine/Quinine	76	69	8	28
6-Monoacetylmorphine (6-MAM)	52	42	8	14
Cocaine	38	35	12	19
Hydromorphone	38	23	8	11
Methadone Metabolite (EDDP)	33	22	4	12
Oxymorphone	24	27	4	12
Marijuana	24	23	32	21
Cetirizine	19	11	0	6
Naloxone	19	11	4	9
Oxazepam	19	4	0	3
Any Buprenorphine§	14	15	4	11
7-Aminoclonazepam	10	3	0	2
Nordiazepam	10	3	0	2
Alprazolam	5	11	4	6
α-Hydroxyalprazolam	5	15	4	8
Promethazine	5	4	0	2
Any Fentanyl	–	11	0	4
Any Synthetic Cannabinoid	0	2	–	5

*Includes specimens positive for any fentanyl compound on the testing panel. Fentanyl compounds detected: fentanyl, norfentanyl, and acetylfentanyl.
†N's differ for some characteristics because of missing information.
^Includes drugs detected in at least 10% of any group. Drugs detected in under 10% in the Fentanyl group included: Amphetamine, Cyclobenzaprine, Dextromethorphan, Hydroxyzine, mCPP, Methamphetamine, Temazepam, and Trazodone. Drugs detected in under 10% in the SC group included: Doxepin, Ethylone, Haloperidol, PCP, Sertraline, and Tramadol. Drugs detected in under 10% in the Codeine group included: AB-FUBINACA (Parent), AB-PINACA, Acetylfentanyl, Amitriptyline, Amphetamine, β-Methylphenethylamine, Carisoprodol, Cyclobenzaprine, Dextromethorphan, Doxepin, Ephedrine, Fentanyl, Fluoxetine, Hydrocodone, Hydroxyzine, Lorazepam, mCPP, Methamphetamine, Nortriptyline, Paroxetine, 5F-PB-22, PCP, Pseudoephedrine, Sertaline, Temazepam, Tramadol, Trazodone, XLR-11, and Zolpidem. Drugs detected in under 10% all groups included: Citalopram and Oxycodone.
§Buprenorphine positive specimens were defined as those that tested positive for either buprenorphine or norbuprenorphine.

Study Limitations

This study has a number of important limitations that must be kept in mind when interpreting the results.

The CDEWS model depends on collecting a small number of specimens that have already tested positive or negative by the CJS agency's routine drug screen. Every attempt was made to have the DPP off site laboratory staff systematically select the specimens that met our selection criteria. The Maryland Regional Sample was designed to replicate that used in our 2008 study and was not representative of the State probationer/parolee population. Moreover, the Opiate+ Sample was a convenience sample of all available specimens that had tested positive for opiates and may not represent all persons who tested positive for opiates. Nevertheless, prior CDEWS results have been found to be internally consistent and often agree with other indicators of drug use in the studied jurisdictions. CDEWS is designed to produce an indication of emerging drugs in a community rather than precise prevalence estimates.

CDEWS obtains samples of urine specimens that have already been collected and tested by the criminal justice system (CJS) as part of a drug testing program. The persons selected for testing are typically at high risk for drug use because of 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 uncovering emerging drugs, it also means that the CDEWS findings do not necessarily represent all persons in the CJS populations we studied. Nevertheless, drug trends in high risk criminal justice populations often foreshadow trends that appear later in the general population (DuPont & Wish, 1992).

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

Decisions regarding modifying CJS drug testing protocols should not be based solely on CDEWS results alone. Rather, local policymakers should review the CDEWS results as they weigh the complex law enforcement, public health, and budgetary considerations in their jurisdiction to determine what drugs to test for. CDEWS provides critical information with which to paint a picture of the age and gender characteristics of likely CJS 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+ and CJS- Specimens from the Maryland Regional Sample

As one would expect, the CJS+ specimens contained primarily the drugs that might have been detected by the smaller DPP test panel and resulted in their being placed in our CJS+ sample. There were some exceptions. Fentanyl was rare, but almost one in ten CJS+ specimens contained antidepressants. Synthetic cannabinoids (SC), methadone and other licit pharmaceutical opioids would have gone undetected. This may not have practical significance for the DPP, given these specimens did test CJS+ for the drugs in their panel. It is impossible to tell from the urinalyses if the persons taking the licit drugs were doing so under a physician's supervision.

In contrast, it is noteworthy that the DPP tests were missing as many of 15% of CJS- specimens that contained a non-fentanyl opioid. Methadone and buprenorphine were among the opioids most found in CJS- specimens and it is possible that these persons were receiving treatment with these drugs. Antidepressants were identified in as many CJS- specimens as CJS+ specimens (9%). SC was found in CJS- specimens but the metabolites were less common than in CJS+ specimens. These results suggest that in this population, persons were unlikely to be using SC to avoid detection by the standard DPP tests.

Antidepressant use was found in our prior study of male inmates in two prisons in Ohio (Wish et al., 2016a). In the current study, antidepressants were found both in the Opiate+ sample and especially among CJS+ females in the Maryland Regional Sample. More research needs to be done to study whether persons are using these drugs under a doctor's supervision, for self-treatment, or for abuse purposes. It is also important to understand how the antidepressants might interact in harmful ways with the other drugs being taken.

Our findings regarding the drugs detected according to geographic region were limited by the small number of specimens available. However, it is clear that opioids, marijuana, cocaine and antidepressants were found largely throughout the state. The exception was Prince George's County, where few specimens tested positive for opioids. PCP was found only in Prince George's, Baltimore and Charles Counties. The presence of PCP in Prince George's County is not surprising given that we had detected a high percentage of PCP use in that county in our earlier OPUS study (Wish et al., 2009) and also given the proximity of Prince George's County to Washington, DC where the availability and use of PCP is also well documented (Pretrial Services Agency for the District of Columbia, 1984-2017). SC was detected in all locations studied but Howard County. Other NPS were very rare and mainly found in specimens from Baltimore and Prince George's County.

Comparisons of the 2008 and the Current CDEWS Study Results

The Maryland Regional Sample was selected to approximate the sample from our 2008 study of Maryland probationers/parolees. Test results for 9 of 12 drugs from the two studies were similar

and suggests that the samples were comparable. However, there were significant changes in 3 drugs. The findings indicated significant declines in cocaine positives. This decline is consistent with the declines in cocaine reported during this period by the DC Pretrial Services Agency testing program of arrestees (Pretrial Services Agency for the District of Columbia, 1984-2017). The significant decline in buprenorphine positives may reflect less prescribed use or misuse on the street. However, The State of Maryland has been increasing physician access to buprenorphine and it might be expected that we would have seen an increase in those testing positive for the drug. The increase in codeine positives may be the result of the increased sensitivity of the test for codeine used in the current CDEWS study as compared to the 2008 study.

Opiate+ Sample Results

The Opiate+ specimens provide a picture of the drugs that probationers statewide are using. The results show that these persons were also using a variety of other drugs. Cocaine, marijuana, benzodiazepines and antidepressants were found in 17% or more of these specimens. These drugs were detected in persons from DPP offices throughout the state. The results show that these persons were also using legal and pharmaceutical opioids not capable of being detected by the CJS tests that had classified them as opiate positive. Oxymorphone, hydromorphone, methadone, buprenorphine, oxycodone and fentanyl were all detected in these specimens.

These results strongly suggest that probationers/parolees in Maryland who were using the opiates detected by the limited screen used by DPP were likely also to be using a variety of legal and illegal opioids as well as non-opioid drugs. The inability of the DPP tests to identify all of these opioids may not have practical negative limitations because all of these specimens did test positive by their opiate screen. However, these results have important implications for physicians and diagnosticians who need to know if a person is using other opioids. Use of multiple opioids at the same time may lead to serious health complications and even death. These findings suggest that treatment will be more effective if one identifies and focuses on the totality of drugs the person may be using.

Special Analyses of Fentanyl, SC, and Codeine using the Combined Samples

Because SC and fentanyl were rarely detected in the Maryland Regional and Opiate+ samples but remain of considerable interest, we conducted special analyses of all SC+ and Fentanyl+ specimens that were found in either sample. We also conducted additional analyses of all codeine positive specimens from the two samples.

While most of the 21 Fentanyl+ specimens contained fentanyl or its metabolite, norfentanyl, about 14% also contained acetylfentanyl. Acetylfentanyl is a metabolite of illegally manufactured fentanyl. It is not possible to tell if the other positive specimens resulted from legal fentanyl or diverted drugs.

Perhaps some of the most meaningful results in our study were those showing the large number of opioid and non-opioid drugs found in these fentanyl+ specimens. The findings for fentanyl+ specimens were similar to those described above for the entire sample of Opiate+ specimens and our recent study of 136 persons who died of a fentanyl related overdose in New Hampshire (CESAR, 2017). It is clear that probationers/parolees in Maryland who test positive for *any opioids* are likely to be using a variety of other opioid and non-opioid drugs. These findings suggest that for treatment to be effective, providers will have to identify and focus on the totality of drugs being used.

Our findings regarding the 25 SC+ specimens from the two samples are consistent with those found in previous CDEWS studies we have completed (Billing et al., 2017; Wish et al., 2013; 2015). SC+ specimens contained multiple combinations of new and older generation metabolites. The users of SC are taking drugs with rapidly changing and unknown composition with unknown effects on the human body.

We also found that 70% of the Opiate+ specimens contained codeine and that codeine was found across the state. In the Opiate+ sample, codeine was detected in all 10 regions of Maryland studied, with 60% or more of specimens testing positive for codeine in the 8 regions with sufficient numbers to estimate use. In addition, 81% of fentanyl positive specimens in the combined sample (Opiate+ and Maryland Regional) contained codeine. Acetylcodeine, which metabolizes into codeine, is often produced as an impurity of illicit heroin synthesis, which may explain the large percentage of specimens positive for codeine given that almost all of the specimens also contained morphine (O'Neal & Poklis, 1997; Staub et al., 2001). It is also possible that some of the codeine positives were the result of the direct use of codeine. It is not possible to determine with certainty whether the presence of codeine was from heroin impurities or codeine use. The lack of promethazine in the specimens that contained codeine (found in only 4% of the codeine positive specimens in the combined sample) suggested to us that the codeine use detected did not stem from the use of "Purple Drank", a mixture of codeine syrup and promethazine typically sold as a cough suppressant, that has been reported in Maryland (Richardson, 2016). Further, given that the half-life of promethazine is longer than that of codeine, one would anticipate detecting promethazine in the specimens, were "Purple Drank" to be the source of the codeine (Cone et al., 1991; Paton & Webster, 1985; Ponder & Stewart, 1995). Purple Drank is known by several street names, including "lean", "drank", "barre", "purple stuff", "syrup", and "sizzurp" (Burns & Boyer, 2013). "Purple Drank" has been abused by young adults, especially in Texas (Agnich et al., 2013; Burns & Boyer, 2013). It is possible that the presence of codeine in these specimens originates from users extracting codeine from pills. A review of the online reddit forum (Reddit, 2017) indicates that individuals are extracting acetaminophen from combined codeine/acetaminophen pills (e.g., Tylenol #3) in order to create codeine only pills. Additional research is needed to better understand how the use of codeine may relate to the current opioid epidemic in Maryland.

As a whole, this special study of Opiate+ probationers/parolees has revealed considerable polydrug use in this population. It is inaccurate to characterize persons as heroin or fentanyl users as if these are the only drugs that the person is using. The findings for the more diverse Regional sample appear to show less use of SC than we have found in other CDEWS sites, but also document the considerable variety of old and new SC metabolites seen in specimens in Maryland that do test positive for SC.

References

Agnich, L.E., Stogner, J.M., Miller, B.L., and Marcum, C.D. (2013). Purple drank prevalence and characteristics of misusers of codeine cough syrup mixtures. *Addictive Behaviors,* 38, no. 9: 2445-2449.

Baumann, Michael. (2015). Pharmacology of "bath salts" and their newly-emerging analogs [PowerPoint slides]. Baltimore, MD: National Institutes of Health, National Institute on Drug Abuse, Designer Drug Research Unit.

Billing, A.S., Artigiani, E.E., Robinson, J., Adatsi, F. and Wish, E.D. (2017). Community drug early warning system (CDEWS-3): Washington, DC – Site 3 of 4. Office of National Drug Control Policy. Washington, DC: Executive Office of the President.

Burns, J.M. & Boyer, E.W. (2013). Antitussives and substance abuse. *Substance Abuse and Rehabilitation,* 4: 75-82.

Center for Substance Abuse Research (2017). National drug early warning system (NDEWS) New Hampshire hotspot studies: Overview and initial results. College Park, MD: Center for Substance Abuse Research.

Cone, E.J., Welch, P., Mitchell, J.M., & Paul, B.D. (1991). Forensic drug testing for opiates: I. Detection of 6-acetylmorphine in urine as an indicator of recent heroin exposure; drug and assay considerations and detection times. Journal of Analytical Toxicology, 15(1): 1-7.

Cone, E.J., Welch P., Paul, B.D. & Mitchell, J.M. (1991). Forensic drug testing for opiates, III. Urinary excretion rates of morphine and codeine following codeine administration. Journal of Analytical Toxicology, 15(4): 161-166.

DuPont, R.L. & Wish, E.D. (1992). Operation Tripwire revisited. *The Annals of the American Academy of Political and Social Science*, 521: 91-111.

Dye, Emily K. (2014). The expansion of emerging drug markets in the United States - An update [PowerPoint slides]. Dulles, VA: U.S. Drug Enforcement Administration, Special Testing and Research Laboratory, Emerging Trends Program.

European Monitoring Centre for Drugs and Drug Addiction (2015). New psychoactive substances in Europe. An update from the EU Early Warning System March 2015. Luxembourg: Publications Office of the European Union.

Head, Jill M. (2014). A forensic perspective on synthetic drug trends [PowerPoint slides]. Dulles, VA: U.S. Drug Enforcement Administration, Special Testing and Research Laboratory, Emerging Trends Program/Reference Material Program.

Maryland Poison Center, University of Maryland School of Pharmacy (2015). Synthetic cannabinoids urgent notice. [Brochure].

NMS Labs (2015). Designer Drug Testing at NMS Labs. Willow Grove, PA: NMS Labs.

O'Neal, C.L., & Poklis, A. (1997). Simultaneous determination of Acetylcodeine, Monoacetylmorphine, and other opiates in urine by GC-MS. Journal of Analytical Toxicology, 21: 427-432.

Paton, D.M. & Webster D.R. (1985). Clinical pharmacokinetics of H1-receptor antagonists (the antihistamines). Clinical Pharmacokinetics, 10(6): 477-97.

Ponder, G.W. & Stewart J. T. (1995). A liquid chromatographic method for the determination of promethazine enantiomers in human urine and serum using solid-phase extraction and fluorescence detection. Journal of Pharmaceutical and Biomedical Analysis, 13: 1161-1166.

Pretrial Services Agency for the District of Columbia. (1984, March – 2017, February). Drug Testing Statistics (Adult Arrestees) Memorandum.

Reddit User. (2017, April 29). Codeine CWE? [Online Forum]. Retrieved May 23, 2017.

Richardson, J. (August 8, 2016). Personal communication.

Staub, C., Marset, M., Mino, A., & Mangin, P. (2001). Detection of Acetylcodeine in urine as an indicator of illicit heroin use: Method validation and results of a pilot study. Clinical Chemistry, 47(2): 301-307.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2013a). United States: DEA announces largest-ever synthetic drug takedown. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2013b). United States: temporary ban on three NBOMe substances (synthetic phenethylamines). Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2013c). USA: drug in 'bath salts' caused teen's overdose death. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2014a). United States: DEA places 10 synthetic cathinones under temporary control. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2014b). United States: DEA places four synthetic cannabinoids under temporary control. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2014c). United States of America: Louisiana, State Officials ban new synthetic cannabinoid. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2014d). United States of America: NIH system to monitor emerging drug trends. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2014e). United States of America: State of New Hampshire declares state of emergency as a result of overdoses from synthetic cannabinoid. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2015a). Survey on NPS reveals 69 newly emerged substances in 2014. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2015b). United States of America: DEA issues nationwide alert on fentanyl as threat to health and public safety. Vienna, AT: UNODC.

United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory (2015c). United States of America: Three synthetic cannabinoids placed under temporary control under Schedule I of the Controlled Substances Act. Vienna, AT: UNODC.

U.S. Drug Enforcement Administration (DEA), Office of Diversion Control (2014). National Forensic Laboratory Information System Special Report: Synthetic cannabinoids and synthetic cathinones reported in NFLIS, 2010-2013. Springfield, VA: U.S. Drug Enforcement Administration.

U.S. Drug Enforcement Administration (DEA), Office of Diversion Control (2015). National Forensic Laboratory Information System: Midyear report 2014. Springfield, VA: U.S. Drug Enforcement Administration.

U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, National Forensic Laboratory Information System (2015a). [NFLIS 2014 – County of Honolulu, Hawaii]. Unpublished raw data.

U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, National Forensic Laboratory Information System. (2015b). [NFLIS 2014 – Maryland]. Unpublished raw data.

U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, National Forensic Laboratory Information System. (2015c). [NFLIS 2014 – National]. Unpublished raw data.

U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, National Forensic Laboratory Information System. (2015d). [NFLIS 2014 – State of Hawaii]. Unpublished raw data.

U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, National Forensic Laboratory Information System. (2015e). [NFLIS 2014 – Washington, D.C]. Unpublished raw data.

U.S. Drug Enforcement Administration (DEA), Special Testing and Research Laboratory, Emerging Trends Program/Reference Material Program. (2015). [National trend data]. Unpublished raw data.

U.S. Drug Enforcement Administration (DEA), Special Testing and Research Laboratory, Emerging Trends Program/Reference Material Program. (2016). [2009-2015 Cannabinoids]. Presentation Slide.

Washington Baltimore HIDTA, Investigative Support Center. (2015). [Results of ROI 1087: RFI on Synthetic Compound Testing]. Unpublished raw data.

Winter, W., Flaherty, W.S., & Carr, T.H. (2014). Washington/Baltimore HIDTA threat assessment and strategy for program year 2015. Elkridge, MD: Washington/Baltimore HIDTA.

Wish, E.D. (1997). The crack epidemic of the 1980's and the birth of a new drug monitoring system in the United States. Paper Presented at The Crack Decade: Research Perspectives and Lessons Learned Conference November 4-5, 1997.

Wish, E.D., Artigiani, E.E. & Billing, A.S. (2013). Community drug early warning system: The CDEWS pilot project. Office of National Drug Control Policy. Washington, DC: Executive Office of the President.

Wish, E.D., Billing, A.S., & Artigiani, E.E. (2015). Community drug early warning system: The CDEWS-2 replication study. Office of National Drug Control Policy. Washington, DC: Executive Office of the President.

Wish, E.D., Billing, A.S., and Artigiani, E.E. (2016). Community drug early warning system (CDEWS-3): Honolulu, Hawaii – Site 1 of 4. Office of National Drug Control Policy. Washington, DC: Executive Office of the President.

Wish, E.D., Billing, A.S., and Artigiani, E.E. (2016a). Community drug early warning system (CDEWS-3): Ohio – Site 2 of 4. Office of National Drug Control Policy. Washington, DC: Executive Office of the President.

Wish, E.D., Billing, A.S., Rinehart, C., & Artigiani, E.E. (2009). The Maryland adult offender population urine screening (OPUS) program. Center for Substance Abuse Research. College Park, MD: Center for Substance Abuse Research.

Wish, E.D., Rinehart, C., Hsu, M., & Artigiani, E.E. (2006). DEWS Investigates: Using urine specimens from parolees/probationers to create a statewide drug monitoring system. College Park, MD: Center for Substance Abuse Research.

Appendices

Appendix A: Site Selection Procedures

This site was of interest to the study as Maryland had participated in an earlier pilot study run by CESAR, known as the Offender Population Urine Screening (OPUS) project. This study was conducted with funding from the Governor's Office of Crime Control and Prevention prior to the first CDEWS study and served as a pilot for the method now utilized by CDEWS. The CDEWS-3 study replicated as closely as possible the urine specimen collection from the Guilford Laboratory as part of the OPUS study in 2008 in Maryland (Maryland Regional Sample). The Maryland DPP was also interested in learning more about their opiate using population (given increasing levels of heroin and other opiate use in Maryland) and elected to conduct an additional statewide sub-study of their opiate positive specimens as part of CDEWS-3 to better understand the drugs being used by this population (Opiate+ Sample). Maryland DPP tests its specimens using an offsite testing laboratory (Phamatech). We collaborated with both the Maryland DPP and the offsite testing laboratory, Phamatech, in order to collect the specimens. In order to obtain approval to collect specimens from Maryland DPP, we began by meeting in person and by phone with both the DPP administrators and Phamatech laboratory staff to share information on the study and learn about the procedures being used by their site. A research application was submitted to the Maryland DPP research committee for review and approval. Following approval of the research application, an MOU was established and processed for approval. Following approval of the MOU, the proposed methods were sent to Phamatech laboratory staff for review. Negotiations and approval took approximately 2.5 months (see Table A-1). The University of Maryland (UM) Institutional Review Board (IRB) application was then submitted and approved. Using a specified protocol, specimens were prepared by Phamatech laboratory staff and sent to the CDEWS laboratory. Specimen collection took approximately 6 months.

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

Site	Time to Obtain Approval	Researcher Time On-Site Collecting Specimens
Maryland: Adult Parole and Probation – Maryland Division of Parole and Probation	2.5 months	No time spent on site

Appendix B: Collection of Urine Specimens

Over the period of approximately 6 months (September 2015 to March 2016), staff at Phamatech laboratory, the contracted testing laboratory for the Maryland DPP program, identified specimens for possible inclusion in the study. Specimens are routinely tested for a panel of four drugs which can be selected from a list of seven potential drugs for testing (benzodiazepines, cocaine, marijuana, opiates, PCP, methamphetamine, and buprenorphine). The drugs tested for are selected by DPP as a unit (rather than by individual agents) and may change over time depending on the testing needs of the unit. Positive specimens are held for a period of 3 months and negative specimens held for a period of 2 weeks, therefore only specimens that had expired this holding period were included in the study. If a person had contributed more than one specimen, only one specimen per donor (if feasible, the most recent) was selected for the CDEWS study. All specimens were refrigerated during the holding period. Two groups of specimens were sampled by Phamatech: 1) Maryland Regional Sample, and 2) Opiate+ Sample (Statewide).

The **Maryland Regional Sample** targeted 300 specimens – 20 specimens (10 positive/10 negative) from each of 15 selected DPP offices. These 15 DPP offices were selected due to their inclusion in the earlier pilot study (OPUS) completed by CESAR (see Table B-1 below). We sought to replicate these findings to the extent possible by collecting specimens from the same DPP offices that participated in this earlier study.

Table B-1: Maryland DPP Offices that Submitted Specimens as part of the Regional Sample

15 DPP Offices for Urine Specimen Sampling
Gay Street Field
Northwest Seton Field
Southwest Severn Field
Northeast Preston Field
Guilford Avenue Field
Ellicott City Field
Essex Office Field
Dundalk Office Field
Catonsville Office Field
Owings Mills Field
Hyattsville Office Field
Waldorf Office Field
Upper Marlboro Office Field
Temple Hills Office Field
Hagerstown Office Field

The **Opiate+ Sample (Statewide)** targeted a sample of 200 opiate positive specimens from unduplicated persons from any DPP office statewide.

Specimens meeting the study criteria were identified by Phamatech using their laboratory database. A list of available specimens was generated and these specimens were identified from their

inventory. Each selected specimen was de-identified by Phamatech staff and labeled with demographic details, including specimen collection date, submitting DPP office number, gender and test result (positive/negative). Only specimens with a minimum urine volume of 15mL were included in the study. The specimens were sent by mail in large batches. They were packaged and shipped to the CDEWS laboratory.

201 CJS+ and 1 specimen with an unknown test result (assigned to the CJS+ group based on the CDEWS laboratory results) were collected for the Opiate+ Sample (Statewide). 137 CJS+ and 151 CJS- specimens were collected as part of the Maryland Regional Sample.

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-3 panel were selected after conducting interviews with toxicology experts and a review of relevant international, national, and local data sources to identify new psychoactive substances (NPS) to consider adding to our panel and to assess the availability of tests for these drugs. All specimens were held in cold storage for the duration of the study. 153 drugs were tested for using Gas Chromatography/Mass Spectrometry (GC/MS) and 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 synthetic cannabinoids since those in use are constantly altered, presumably to avoid detection and legal sanction. NPS are also 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. This included a review of the 2014 National data from the Drug Enforcement Administration's (DEA) National Forensic Laboratory Information System (NFLIS), special data runs for 2014-2015 provided by the DEA's Special Testing and Research Laboratory, as well as reports from the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), United Nations Office on Drugs and Crime (UNODC) Early Warning Advisories, and other sources (Baumann, 2015; Dye, 2014; EMCDDA, 2015; Head, 2014; NMS Labs, 2015; UNODC, Early Warning Advisory, 2013a, 2013b, 2013c, 2014a, 2014b, 2014c, 2014d, 2014e, 2015a, 2015b, 2015c; U.S. DEA, Office of Diversion Control, 2014, 2015; U.S. DEA, Office of Diversion Control, NFLIS, 2015c; U.S. DEA, Special Testing and Research Laboratory, Emerging Trends Program/Reference Material Program, 2015, 2016). We also reviewed local NFLIS data, as well as any other local data available, to assess local drug trends in our participating CDEWS sites (Maryland Poison Center, University of Maryland School of Pharmacy, 2015; U.S. DEA, Office of Diversion Control, NFLIS, 2015a, 2015b, 2015d, 2015e; Washington Baltimore HIDTA, Investigative Support Center, 2015; Winter et al., 2014).

In addition, we also interviewed 13 chemists at 9 labs, as well as 3 other experts from programs including the High Intensity Drug Trafficking Area Program (HIDTA) and other law enforcement drug testing divisions prior to finalizing the test panel for CDEWS-3. 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. All persons interviewed are listed in Table C-1 below. 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-3

NAME	TITLE/AFFILIATION
Dr. (CDR) Thomas Bosy; Major William McCalmont	Armed Forces Medical Examiner System (AFMES)
Dr. Gregory Endres; Donna Iula	Cayman Chemical
Dr. Barry Logan	NMS Labs
Dr. Jeffery Moran	Arkansas Public Health Laboratory, Arkansas Department of Health
Dr. Marilyn Huestis	National Institute on Drug Abuse, National Institutes of Health Biomedical Research Center
Staff (2 unnamed per request)	State of HI Narcotics Enforcement Division
Wayne Kimoto; Michele Shishato	Honolulu Police Department Crime Laboratory
Kathy Pung	Hawaii Police Department Crime Laboratory
Jerome Robinson	Pretrial Services Agency for the District of Columbia
Gary Yabuta	Hawaii HIDTA
Jill Head; Emily Dye	Special Testing and Research Laboratory, Drug Enforcement Administration

Based on the information reviewed, we added six new SC metabolites to our previous CDEWS-2 metabolite screen: 5F-AMB, AB-CHMINACA (parent), AB-CHMINACA (metab 4), AB-CHMINACA (metab 6), AB-FUBINACA (parent), and ADB-FUBINACA (parent) (see Table C-2 in Appendix C for the full panel). We also tested specimens for the following SC metabolites that were part of our earlier CDEWS studies: JWH-018, JWH-019, JWH-073, JWH-081, JWH-122, JWH-210, JWH-250, AM-2201, MAM-2201, RCS-4, UR-144, XLR-11, AKB-48, 5F-AKB-48, BB-22, PB-22, 5F-PB-22, AB-PINACA, 5F-AB-PINACA, ADB-PINACA, and ADBICA. Many additional SC metabolites were identified as relevant to the study, however, urine tests were not available for these metabolites at the time the study began. The synthetic cannabinoid tests were performed using LC/MS/MS.

Further, for CDEWS-3, we expanded the new psychoactive substances (designer stimulant) panel to add 14 new compounds. The new additions are: 25C-NBoMe, 2C-T-7, AH-7921, alpha-PVP, B-Methylphenethylamine, Flephedrone, Methiopropamine, Methoxetamine, Mitragynine, Naphyrone, Phenmetrazine, Phentermine, PMMA, and Trazodone. Several additional NPS were identified as relevant to the study but were not included due to test availability and cost.

Table C-2: The CDEWS-3 Laboratory Expanded Drug Screening Panel and Levels of Detection

SYNTHETIC CANNABINOID PANEL

	COMPOUND	LOD (ng/mL)
1	JWH-018-5-COOH	0.25
2	JWH-019-6-OH	0.25
3	JWH-073-4-COOH	0.25
4	JWH-081-5-OH	0.25
5	JWH-122-5-OH	0.25
6	JWH-210-5-OH	0.25
7	JWH-250-5-OH	0.25
8	AM2201-4-OH	0.50
9	MAM-2201-5-COOH/JWH 122 COOH	0.50
10	RCS-4-5-COOH	0.50
11	UR-144-5-COOH	0.50
12	XLR-11-4-OH	Presence
13	AKB-48 COOH	0.50
14	5F AKB-48 metabolite	0.50
15	BB-22 metabolite	0.50
16	PB-22 Carb Indole	0.50
17	5F PB-22 Carb Indole	0.50
18	AB-PINACA	0.50
19	5F AB PINACA	0.50
20	ADB-PINACA-5-COOH	0.50
21	ADBICA-5-COOH	0.50
22	AB-FUBINACA (Parent)	0.50
23	AB-CHMINACA (Parent)	0.50
24	AB-CHMINACA (metab 4)	0.50
25	AB-CHMINACA (metab 6)	0.50
26	ADB-FUBINACA (Parent)	0.50
27	5F-AMB	0.50

Table C-2 (Cont'd): The CDEWS-3 Laboratory Expanded Drug Screening Panel and Levels of Detection

NEW PSYCHOACTIVE SUBSTANCES PANEL

	COMPOUND	LOD (ng/mL)
1	25B-NBoMe	2.5
2	25I-NBoMe	2.5
3	25C-NBoMe	2.5
4	2C-B	10
5	2-Fluoroamphetamine	10
6	2-Fluoromethamphetamine	10
7	3-Fluoromethcathinone	10
8	4-Methylethcathinone (4-MEC)	10
9	Buphedrone	10
10	Butylone	10
11	Benzylpiperazine	10
12	Cathinone	10
13	Methcathinone/Ephedrone	10
14	Ethylone	10
15	Eutylone	10
16	mCPP	10
17	MBDB	10
18	MDPV	10
19	α-PVP	10
20	Mephedrone	10
21	Methedrone	10
22	Methylone	10
23	Pentedrone	10
24	Pentylone	10
25	TFMPP	10
26	Phentermine	10
27	B-Methylphenethylamine	10
28	Trazodone	10
29	Phenmetrazine	10
30	Naphyrone	10
31	Mitragynine	10
32	Methoxetamine	10
33	PMMA	10
34	2C-T-7	10
35	Flephedrone	10
36	AH-7921	10
37	Methiopropamine	10

Table C-2 (Cont'd): The CDEWS-3 Laboratory Expanded Drug Screening Panel and Levels of Detection

THC/BARBS/BUPRENORPHINE/LSD PANEL

	COMPOUND	SCREEN	LOD (ng/mL)	CONFIRM	LOD (ng/mL)
1	THC-COOH	PMOD	15	LC/MS/MS	5
2	Amobarbital	PMOD	200	LC/MS/MS	25
3	Butalbital	PMOD	200	LC/MS/MS	25
4	Pentobarbital	PMOD	200	LC/MS/MS	25
5	Phenobarbital	PMOD	200	LC/MS/MS	25
6	Secobarbital	PMOD	200	LC/MS/MS	25
7	Buprenorphine	PMOD	10	LC/MS/MS	1
8	Norbuprenorphine	na	na	LC/MS/MS	1
9	Naloxone	na	na	LC/MS/MS	1
10	LSD	PMOD	0.5	LC/MS/MS	0.05

Table C-2 (Cont'd): The CDEWS-3 Laboratory Expanded Drug Screening Panel and Levels 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	Benzoylecgonine	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	Desmorphine	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: Specific Drug Test Results for the Opiate+ Sample

Table D-1: CDEWS Laboratory Test Results for the Maryland* Opiate+ Sample

(N=202 specimens collected between April 2015-June 2015‡)

Percent Positive by CDEWS Lab for:	CJS+ (for any opiate)
Cocaine*	32%
Marijuana*	20
PCP*	2
Any Non-Fentanyl Opioid*	99
Morphine	97
Codeine	70
6-Monoacetylmorphine (6-MAM)	31
Oxymorphone	24
Hydromorphone	24
Methadone Metabolite (EDDP)	20
Any Buprenorphine*	18§
Oxycodone	10
Tramadol	3
Hydrocodone	3
Normeperidine	<1
Any Fentanyl	9
Norfentanyl	8
Fentanyl	5
Acetylfentanyl	1
Any Benzodiazepine*	18
α-Hydroxyalprazolam	14
Alprazolam	10
7-Aminoclonazepam	4
Oxazepam	3
Nordiazepam	2
Temazepam	2
Lorazepam	2
Any Antidepressant	17
Citalopram	6
Trazodone†	5
Sertraline	4
Fluoxetine	2
Doxepin	1

Paroxetine	1
Nortriptyline	<1
Desvenlafaxine	<1
Bupropion	<1
Venlafaxine	<1
Any New Psychoactive Substance (NPS)	5
mCPP†	5
β-Methylphenethylamine	<1
Any Synthetic Cannabinoid (SC)	2
5F-PB-22	1
XLR-11	<1
AB-FUBINACA (Parent)	<1
AB-PINACA	<1
Other Drugs	
Quinidine/Quinine	58%
Naloxone	14
Cetirizine	12
Cyclobenzaprine	7
Hydroxyzine	5
Promethazine	4
Dextromethorphan	3
Amphetamine	2
Ephedrine	1
Pseudoephedrine	1
Carisoprodol	1
Zolpidem	1
Methylphenidate	<1

*The Maryland Division of Parole and Probation routinely tests parolees and probationers for a panel of four drugs selected from a list of seven drugs, including: benzodiazepines, cocaine, marijuana, opiates, PCP, methamphetamine and buprenorphine.

‡The collection date is unknown for 1 specimen, as it was inadvertently omitted at the time of sampling.

§Any buprenorphine positive specimens were defined as those that tested positive for either buprenorphine or norbuprenorphine. 34 specimens tested positive for norbuprenorphine, while only 31 specimens tested positive for buprenorphine. This may be due to a combination of factors, including: time and route of administration, speed of metabolism, and/or the drug's half-life.

†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.

Notes: **Bolded** synthetic cannabinoid metabolites were newly added to the testing panel for CDEWS-3.

Appendix E: Glossary of Abbreviated Terms

6-MAM: 6-Monoacetylmorphine, a unique metabolite of heroin used to definitively determine heroin use
AFMES: Armed Forces Medical Examiner System, the laboratory which conducted the expanded drug testing for the Community Drug Early Warning System study
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
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
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