Using Liquid Chromatography Tandem Mass Spectrometry Urine Drug Testing to Identify Licit and Illicit Drug-Use in a Community-based Patient Population

Adam S. Ptolemy[1], Colleen Murray[2], Edward Dunn[3], Gayle Waite[1], Dana Bailey[1] and Hui Li[1,3]

[1] Gamma-Dynacare Medical Laboratories, London, ON N6A1P4, Canada
[2] Gamma-Dynacare Medical Laboratories, Edmonton, AB T6B2N7, Canada
[3] Gamma-Dynacare Medical Laboratories, Brampton, ON L6T5M3, Canada

Background: Prescription medications routinely deployed for the treatment of chronic pain have a high potential for abuse or misuse. As such, a physician will often perform urine drug testing (UDT) on a patient to monitor their compliance with prescribed medications and detect the use of non-disclosed or illicit substances. This objective measure may assist in identifying patients with aberrant drug behaviors (e.g., drug addiction, abuse, misuse and/or diversion) and permit the implementation of appropriate clinical actions. Despite the widespread use of UDT in chronic pain therapy, comprehensive information regarding the relative prevalence of prescription and/or illicit substances detected within a given patient cohort is often limited and not widely accessible. Moreover, urine drug detection rates are influenced by the relative composition of the patient population studied and the geographical region for which they reside. This may prevent the direct translation of these results to other patient cohorts or constituencies, as medical practices and illicit drug use frequently vary across clinical and regional settings. Community-based independent physicians in Ontario, Canada are increasingly performing UDT on their patients. However, detailed information regarding the relative composition and frequency for which drugs are detected in this cohort's urine is currently unavailable. Furthermore, many of the clinicians ordering these tests have limited knowledge in UDT methodologies or extensive formal training in how to appropriately interpret the derived test results. These collective deficiencies represent significant barriers to the efficient use of UDT to monitor patient compliance and/or detect potential misuse or abuse of prescription or non-prescription drugs in Ontario patients.

Objective: Characterize the prevalence and urinary excretion patterns of licit and illicit drugs, their metabolites and drug product ingredients within a large cohort of urine specimens submitted for UDT from community-based clinical settings in Ontario, Canada.

Methods: Urine drug testing results from 165209 unique specimens were retrospectively reviewed to determine the number of positive results reported for each drug, metabolite and drug product tested. The requests for UDT came from approximately 5024 independent physicians and treatment facilities located in 401 different cities or towns within 2198 different postal codes across Ontario. 96895 male and 68314 female patients were respectively associated with these specimens. These patients ranged in age from 1 to 100 years old (yo). The mean and median ages of the male and female patients were 41 and 39 yo and 40 and 38 yo, respectively. No clinical history or patient medication lists was available for these patients. All testing was conducted between September 3, 2013 and December 31, 2014.

The urine samples were screened for the presence of commonly prescribed pain medications and illicit substances using an in-house developed and validated liquid chromatography tandem mass spectrometry (LC-MS/MS) method. All urine specimens were pretreated with β-glucuronidase and protein precipitation prior to testing. A Waters Acquity liquid chromatography system, equipped with a 96-well plate auto sampler, was paired with a Waters Xevo TQD triple quadrupole mass spectrometer operated in positive-ion electrospray ionization mode (+ESI). All analytes were detected by their characteristic MS/MS transitions and seven unique deuterated internal standards were included in the method to account for extraction and testing variations. The analytes reviewed in this study are listed in Table 1, along with their respective positive/negative cut-off concentrations. If a listed analyte was detected in the urine and its concentration exceeded its defined positive/negative cut-off concentration, the specimen was considered positive for that specific analyte. Only qualitative UDT results were provided to the ordering physician.

Initially, all positive results associated with the 165209 urine specimens were divided into 4 specific drug Classes such that the within-class prevalence and patterns of detection could be respectively examined. The four unique drug Classes were created as follows: amphetamines

Class; benzodiazepines Class; illicit drug Class; and opioids Class (Table 1). The illicit drug Class was defined as analytes related to cannabinoids, cocaine, ecstasy and heroin use. These drug Classes were then further subdivided into 18 specific drug Groups which contained parent drug(s), known metabolites and associated drug products. These unique Groups were created as follows: methamphetamine Group, methamphetamine and amphetamine; methylphenidate Group, methylphenidate and ritalinic acid; clonazepam Group, clonazepam and 7-aminoclonazepam; diazepam Group, diazepam, nordiazepam, oxazepam and temazepam; alprazolam Group, alprazolam and α-hydroxyalprazolam; nitrazepam Group, nitrazepam and 7-aminonitrazepam; flurazepam Group, flurazepam and desalkylflurazepam; flunitrazepam Group, flunitrazepam and 7-aminoflunitrazepam; cocaine Group, cocaine, benzoylecgonine, norcocaine, cocaethylene and levamisole; heroin Group, 6-acetylmorphine, morphine and codeine; ecstasy Group, methylenedioxyamphetamine (MDA), methylenedioxymethamphetamine (MDMA) and methylenedioxyethylamphetamine (MDEA); cannabinoids Group, 11-nor-9-carboxy-Δ9-tetrahydrocannabinol (THCA); buprenorphine Group, buprenorphine, norbuprenorphine and naloxone; fentanyl Group, fentanyl and norfentanyl; meperidine Group, meperidine and normeperidine; methadone Group, methadone and 2-ethylidene-1,5-dimethyl-2,2-diphenylpyrrolidine (EDDP); opiates Group, codeine, norcodeine, morphine, hydromorphone, hydrocodone, dihydrocodeine and norhydrocodone; and oxycodone Group, oxycodone and noroxycodone. These groups were created such that the potential number of unique drugs used by each patient could be identified and that their respective urine excretion patterns could be deployed as a UDT interpretative aid.

Results: There was strong evidence of drug use within this large patient cohort. Approximately 91.3% of all patient specimens (150771 out of 165209) tested positive for one or more of the analytes listed in Table 1. Of these unique positive specimens, 12.3% (N = 18599) were positive for a single-parent drug, drug metabolite or drug product ingredient. The frequency of urine specimens with multiple positive tests results was respectively determined to be: $N \geq 2$, 80.0%; $N \geq 4$, 14.4%; and $N \geq 8$, 1.1%.

The overall percent positivity rates for each drug Class was: opioid, 84.8%; illicit drug, 39.1%; benzodiazepines, 18.2%; and amphetamines, 7.4%. Opioids are routinely prescribed for the

management of chronic pain and not surprisingly 92.9% of all positive specimens had a positive test result for at least one of the analytes included in the opioid drug Class within this study (e.g., methadone, opiates, oxycodone, buprenorphine, fentanyl and meperidine). Significant benzodiazepine use and abuse has been reported to occur within patients being managed for chronic pain. Approximately 18.7% of specimens with $N \geq 1$ opioid positive test result also had a positive test result for at least one of the analytes included within the benzodiazepine Class. Analyte members of the illicit drug Class were detected ($N \geq 1$ positive test result) in 41.5 and 43.5% of specimens containing positive opioid and benzodiazepine drug Class results, respectively. The observed illicit drug detection frequencies and associations may signal an elevated risk or potential for incidents of aberrant drug behavior within the patient cohort.

An overview of the frequency and detection patterns for all defined drug Groups is provided in Table 2. The highest UDT positivity rate was observed for the methadone Group. Methadone is used to manage chronic pain and/or opioid addiction in Ontario and patients receiving this therapy likely represent a significant portion of the studied cohort.

Analytes within the methamphetamine Group (N = 7324 positive specimens) were respectively detected more frequently than those contained in the methylphenidate Group (N = 5385 positive specimens). Approximately 53.9% of all specimens that tested positive for methamphetamine also had positive amphetamine test results. Amphetamine is included in commercially available products, but it is also an illicit drug and can be a methamphetamine metabolite. Methylphenidate use within the studied cohort could be identified through the detection of ritalinic acid (methylphenidate metabolite) which tested positive in 99.5% of the Group's positive specimens.

The Group frequencies for positive patient specimens within the benzodiazepine Class (N = 29994 positive specimens) were: clonazepam, 49.4%; diazepam, 40.6%; alprazolam, 3.1%; nitrazepam, 3.0%; and flurazepam, <0.012%. No flunitrazepam use was detected in any of the 165209 urine specimens tested. In patient specimens that had $N \geq 1$ positive benzodiazepine Class test result, the number of unique benzodiazepine Groups that tested positive within these samples was determined to be: N = 1, 84.0%; N = 2, 15.2%; N = 3, 0.7%; and N = 4, 0.02%.

However, correlating the number of positive Group test results to the number of benzodiazepines actually used by the patient is challenging. Diazepam is metabolized to nordiazepam, temazepam and oxazepam, all of which are commercially available products. Temazepam also metabolizes to oxazepam. If chlordiazepoxide is ingested, it can also metabolize to nordiazepam and oxazepam. Within this data set, $N = 14$ different combinations of diazepam related test results were observed. The benzodiazepine excretion patterns observed within $N \geq 20$ patient specimens are listed in Table 2. Oxazepam was the most frequently reported in combinations with other diazepam-related analytes, respectively followed by temazepam and nordiazepam. The relative frequency of clonazepam, alprazolam and nitrazepam use was largely determined through the detection of their respective metabolites. 7-aminoclonazepam, α-hydroxyalprazolam and 7-aminonitrazepam were positive in approximately 99.9, 96.9 and 99.0% of specimens that tested positive for clonazepam, alprazolam and nitrazepam, respectively.

A total of 140132 (84.8%) unique patient specimens had positive opioid (e.g., buprenorphine, fentanyl, meperidine, methadone, opiates or oxycodone) test results. In patient specimens that had $N \geq 1$ positive opioid Class test result, the number of unique opioid Groups that tested positive within these samples was determined to be: $N = 1$, 59.9%; $N = 2$, 16.5%; $N = 3$, 2.2%; $N = 4$, 0.1%; and $N = 5$, <0.01%. Similar to the interpretation of benzodiazepine UDT results, it is difficult to correlate the number of positive opioid test results to the absolute number of opioids used by the patient. Opiate metabolism, for example, is complex and inter-related: codeine can be metabolized to morphine, norcodeine and small amounts hydrocodone; morphine can be metabolized in small amounts to hydromorphone; and hydrocodone can be metabolized to hydromorphone, dihydrocodeine and norcodeine. Codeine, morphine, hydromorphone, hydrocodone and dihydrocodeine are all commercially available products. Within this data set, there were $N = 78$ different combinations of opiate related test results. The opiate excretion patterns observed within $N \geq 20$ patient specimens are listed in Table 2. Hydromorphone and morphine, detected alone and in combination with each other, were the most frequently observed opiate positive test results. Codeine was often detected in combinations with other opiate-related analytes, but the relative prevalence of positive hydrocodone test results was low within the patient cohort. The metabolites of oxycodone, buprenorphine, fentanyl and meperidine tested positive in 86.4, 97.8, 99.3 and 100% of their Group's respective positive specimens. Naloxone

is included in the buprenorphine formulation Suboxone®. A total of 11820 urine specimens had naloxone positive test results, including 11581 specimens that were also positive for buprenorphine and/or norbuprenorphine. Within the methadone Group, methadone tested positive at a slightly higher frequency (98.0%) than EDDP (97.6%). Both methadone and EDDP were positive in 95.6% of these specimens.

A total of 72564 (43.9%) unique patient specimens had $N \geq 1$ positive illicit drug (e.g., cannabinoid, cocaine, ecstasy or heroin) test result. The observed illicit drug Class prevalence within the studied population was: cannabinoids > cocaine > heroin >> ecstasy. In patient specimens that had $N \geq 1$ positive illicit drug Class test result, the number of unique illicit drug Groups that tested positive within these samples was determined to be: $N = 1$, 78.2%; $N = 2$, 10.5%; $N = 3$, 0.3%; and $N = 4$, <0.01%. Table 3 summarizes the prevalence and percent positivity for specimens containing positive licit and illicit drug test results for each of the drug Classes and Groups included in the study. For drug Groups with $N \geq 10$ positive tests results, the percent positivity from specimens containing both a positive licit and illicit result respectively ranged from: 22.1% (meperidine) to 39.0% (methadone) for cannabinoids; 9.9% (meperidine) to 19.3% (fentanyl) for cocaine; 0.6% (methylphenidate) to 2.8% (opiates) for heroin; and 0.1% (methylphenidate, clonazepam, alprazolam, nitrazepam, methadone, opiates and oxycodone) to 0.6% (meperidine) for ecstasy. Notably, 9.6% of specimens with positive alprazolam (Xanax®) test results were also positive for heroin (6-acetylmorphine). It has been previously reported that opiate addicts self-administer benzodiazepines either before or during opiate use and that alprazolam use can potentiate the rewarding effects of low dose heroin. Less than 1.1% of specimens with positive test results for the other benzodiazepine Groups were also positive for heroin. The observed prevalence of illicit drugs and their positive result associations support the idea that patients using prescription drugs for the treatment of chronic pain and/or opioid addiction may also be engaged in illicit drug use during therapy.

Conclusions: Specific information regarding the frequency of licit and illicit drug use and the parent drug/metabolite/drug product ingredient excretion patterns was obtained from this comprehensive review of urine toxicology results. The observed drug Group prevalence within the studied population was: methadone > cannabinoids > opiates > oxycodone > cocaine >

clonazepam > buprenorphine > diazepam > fentanyl > amphetamine > methylphenidate > heroin > alprazolam > nitrazepam > ecstasy > meperidine > flurazepam > flunitrazepam. The tested urine specimen cohort is likely linked to a significant number of patients receiving opioid antagonist therapy with methadone or buprenorphine. Relatively elevated UDT positivity rates were also observed for the opioids: oxycodone; hydromorphone; and morphine. These findings collectively suggest that prescription medications routinely deployed for the treatment of chronic pain and addiction therapy are being used and potentially abused by patients in Ontario, Canada. Cannabinoids use was also prevalent in this community-based population. Translating the observed urine drug prevalence from this study to other jurisdictions should be done with caution. Each of the observed drug detection rates are influenced by the regional and demographic composition of the studied patient cohort.

Identifying and communicating UDT positivity rates and drug associations to independent physicians and treatment facilities should broaden and enhance their understanding of drug use within their community-based clinical settings. Physicians can potentially integrate knowledge of licit and illicit drug associations into their clinical practice and use it to help identify patients at risk for illegal drug use. They may also be able to use this study's collective findings to create a more efficient and informed process for monitoring patient compliance and interpreting their UDT results. More specifically, the presented information can be referenced by the ordering physician to determine if a patient's UDT results are consistent with disclosed and/or known drug use. For example, if a patient uses methylphenidate and produces a specimen within the drugs post-dose urine detection window, the physician may expect positive test results for ritalinic acid only or methylphenidate and ritalinic acid. If a positive test result for methylphenidate only is obtained the physician would know that this scenario is possible, but that its singular detection is relatively rare compared to ritalinic acid in combination. This interpretive process can be applied to each of the drugs included in the deployed LC-MS/MS UDT method within this study. All UDT results must however be interpreted within the clinical context of the associated patient.

This study's respective drug prevalence may also be considered by clinical scientists charged with the development of LC-MS/MS-based urine toxicology testing. Such UDT procedures

must be appropriate for the specific patient population they serve and ensure that the clinical needs of the ordering physician are meet. As such, the identified percent positivity rates may be used to guide the design of targeted LC-MS/MS UDT testing panels for licit and/or illicit drugs. When choosing what analytes to include in these panels, scientists must ensure that potential drug use is determined in the most clinically efficient and comprehensive manner possible. The LC-MS/MS UDT panel used in our laboratory included relevant drug metabolites and drug product ingredients, which assisted in the detection of prescription and non-prescription drugs within the tested urine specimens. This was evident by the significant number of drugs identified through their respective metabolites and the frequency of positive test results for naloxone (Suboxone®) and levamisole (cocaine). Including drug metabolites and drug product ingredients in a LC-MS/MS-based UDT panel can: facilitate the informed interpretation of both positive and negative test results; permit the identification of patients engaged in non-compliant or aberrant activities; and identify patients with atypical drug metabolism.

Key Words: Urine Drug Testing, Drug Positivity Rates, Drug Excretion Patterns, LC-MS/MS, Pain Management, Interpreting Urine Drug Screen Results

Table 1: Parent drug/metabolite/drug product ingredient positive/negative cut-off concentrations, prevalence and percent positivity for 165,209 patient specimens.

Drug Class	Cut-off (ng/mL)	# Positive	% Positive[†]
Amphetamines			
Amphetamine	250	6296	3.8
Ritalinic Acid	500	5359	3.2
Methamphetamine	250	4976	3.0
Methylphenidate	100	3000	1.8
Total Positives[ǂ]		19631	
Total Specimens*		12206	
Benzodiazepines			
7-Aminoclonazepam	100	14796	9.0
Oxazpeam	100	11594	7.0
Temazepam	100	8896	5.4
Lorazepam	100	8170	4.9
Nordiazepam	100	4522	2.7
α-Hydroxyalprazolam	100	891	0.5
7-Aminonitrazepam	100	876	0.5
Alprazolam	100	605	0.4
Nitrazepam	100	214	0.1
Clonazepam	100	178	0.1
Diazepam	100	26	0.02
Desalkylflurazepam	100	2	<0.01
7-Aminoflunitrazepam	100	0	0
Flunitrazepam	100	0	0
Flurazepam	100	0	0
Phenazepam	100	0	0
Triazolam	100	0	0

Analytes	Cut-off (ng/mL)	# Positive	% Positive[†]
Illicit Drugs			
THCA[‡]	40	52219	31.6
Benzoylecgonine	100	17331	10.5
Levamisole	10	14323	8.7
Cocaine	100	4888	3.0
Norcocaine	100	1373	0.8
6-Acetlymorphine	10	1062	0.6
Cocaethylene	100	780	0.5
MDA	250	152	0.09
MDMA	250	109	0.07
MDEA	250	0	0
Total Positives		92237	
Total Specimens		64535	
Opioids			
Methadone	100	83121	50.3
EDDP	100	82812	50.1
Noroxycodone	100	27725	16.8
Oxycodone	100	26706	16.2
Hydromorphone	100	19595	11.9
Morphine	100	19439	11.8
Norbuprenorphine	15	14402	8.7
Buprenorphine	15	12007	7.3
Naloxone	15	11820	7.2
Codeine	100	11371	6.9
Norfentanyl	25	10536	6.4

Total Positives	50770	Norcodeine	100	9767	5.9
Total Specimens	29994	Fentanyl	25	5751	3.5
		Norhydrocodone	100	3455	2.1
		Hydrocodone	100	1951	1.2
		Dihydrocodeine	100	499	0.3
		Normeperidine	200	181	0.1
		Meperidine	200	89	0.05
		Total Positives		341228	
		Total Specimens		140132	

† Percent positive for each analyte was calculated as 100 x # positive specimens/total # specimens tested.

‡ Abbreviations: MDA, methylenedioxyamphetamine; MDMA, methylenedioxymethamphetamine; MDEA, methylenedioxyethylamphetamine; THCA, 11-nor-9-carboxy-Δ9-tetrahydrocannabinol; and EDDP, 2-ethylidene-1,5-dimethyl-2,2-diphenylpyrrolidine.

ǂ Total number of positive test results for all of the drugs listed within the Class.

* Total number of specimens with $N \geq 1$ positive result for the drugs listed within the Class.

Table 2: Within-class parent drug/metabolite/drug product ingredient positivity patterns: prevalence and percent positivity for 165,209 patient specimens.

Drug Groups	**# Positive**	**% Positive†**
Amphetamines		
Methamphetamine		
Methamphetamine + Amphetamine	3948	53.9
Amphetamine	2348	32.1
Methamphetamine	1028	14.0
Total	7324	100.0
Methylphenidate		
Methylphenidate + Ritalinic Acid	2974	55.2
Ritalinic Acid	2385	44.3
Methylphenidate	26	0.5
Total	5385	100.0
Benzodiazepines		
Clonazepam		
7-Aminoclonazepam	14636	98.8
Clonazepam + 7-Aminoclonazepam	160	1.1
Clonazepam	18	0.1
Total	14814	100.0
Diazepam		
Nordiazepam + Temazepam + Oxazepam	4373	35.9
Temazepam + Oxazepam	3939	32.3
Oxazepam	3200	26.3
Temazepam	513	4.2
Nordiazepam + Oxazepam	70	0.6
Nordiazepam + Temazepam	58	0.5
Other combinations, < 20 prevalence	30	0.2
Total	12183	100.0
Alprazolam		
Alprazolam + α-Hydroxyalprazolam	576	62.6
α-Hydroxyalprazolam	315	34.2
Alprazolam	29	3.2
Total	920	100.0
Nitrazepam		
7-Aminonitrazepam	671	75.8
Nitrazepam + 7-Aminonitrazepam	205	23.2
Nitrazepam	9	1.0
Total	885	100.0

Flurazepam		
Desalkylflurazepam	2	100.0
Total	2	100.0
Illicit Substances		
Cannabinoids		
THCA‡	52219	100.0
Total	52222	100.0
Cocaine		
Benzoylecgonine + Levamisole	7968	41.8
Benzoylecgonine	4563	23.9
Cocaine + Benzoylecgonine + Levamisole	2814	14.8
Levamisole	1582	8.3
Cocaine + Benzoylecgonine + Norcocaine + Levamisole	1068	5.6
Cocaine + Benzoylecgonine + Cocaethylene + Levamisole	410	2.1
Cocaine + Benzoylecgonine + Norcocaine + Cocaethylene + Levamisole	277	1.5
Cocaine + Levamisole	132	0.7
Cocaine + Benzoylecgonine	117	0.6
Benzoylecgonine + Cocaethylene + Levamisole	67	0.4
Cocaine	32	0.2
Other combinations, < 20 prevalence	47	0.2
Total	19077	100.0
Heroin		
6-Acetylmorphine + Codeine + Morphine	886	83.4
6-Acetylmorphine + Morphine	113	10.6
6-Acetylmorphine	62	5.8
6-Acetylmorphine + Codeine	1	0.1
Total	1062	100.0
Ecstasy		
MDA	88	44.7
MDMA + MDA	64	32.5
MDMA	45	22.8
Total	197	100.0
Opioids		
Methadone		
Methadone + EDDP	81095	95.6
Methadone	2026	2.4
EDDP	1717	2.0
Total	84838	100.0

Opiates		
Hydromorphone	13564	38.1
Morphine	6329	17.8
Morphine + Hydromorphone	3902	11.0
Codeine + Norcodeine + Morphine	3824	10.7
Codeine + Norcodeine	1240	3.5
Codeine + Norcodeine + Morphine + Norhydrocodone	1098	3.1
Codeine + Norcodeine + Morphine + Hydrocodone + Norhydrocodone	997	2.8
Codeine + Morphine	988	2.8
Codeine + Norcodeine + Morphine + Hydromorphone	956	2.7
Codeine	442	1.2
Codeine + Morphine + Hydromorphone	270	0.8
Codeine + Norcodeine + Morphine + Hydrocodone + Dihydrocodeine + Norhydrocodone	268	0.8
Codeine + Norcodeine + Norhydrocodone	219	0.6
Codeine + Norcodeine + Morphine + Hydrocodone + Norhydrocodone + Hydromorphone	207	0.6
Codeine + Norcodeine + Morphine + Norhydrocodone + Hydromorphone	197	0.6
Codeine + Norcodeine + Hydromorphone	138	0.4
Codeine + Norcodeine + Morphine + Hydrocodone + Dihydrocodeine + Norhydrocodone + Hydromorphone	132	0.4
Norcodeine	134	0.4
Codeine + Norcodeine + Morphine + Hydrocodone	112	0.3
Codeine + Hydromorphone	83	0.2
Codeine + Norcodeine + Hydrocodone + Norhydrocodone	66	0.2
Norcodeine + Norhydrocodone	44	0.1
Norhydrocodone	32	0.1
Dihydrocodeine	22	0.1
Codeine + Norcodeine + Morphine + Hydrocodone + Hydromorphone	22	0.1
Hydrocodone	20	0.1
Other combinations, < 20 prevalence	277	0.8
Total	35583	100.0
Oxycodone		
Oxycodone + Noroxycodone	22355	69.7
Noroxycodone	5370	16.7
Oxycodone	4351	13.6
Total	32076	100.0

Buprenorphine		
Buprenorphine + Norbuprenorphine + Naloxone	10752	73.0
Norbuprenorphine	1725	11.7
Buprenorphine + Norbuprenorphine	1166	7.9
Norbuprenorphine + Naloxone	759	5.2
Naloxone	239	1.6
Buprenorphine + Naloxone	70	0.5
Buprenorphine	19	0.1
Total	14730	100.0
Fentanyl		
Fentanyl + Norfentanyl	5680	53.5
Norfentanyl	4856	45.8
Fentanyl	71	0.7
Total	10607	100.0
Meperidine		
Meperidine + Normeperidine	92	50.8
Normeperidine	89	49.2
Total	181	100.0

† Percent positive for each analyte was calculated as 100 x # positive specimens/total # positive specimens in the Group.

‡ Abbreviations: MDA, methylenedioxyamphetamine; MDMA, methylenedioxymethamphetamine; MDEA, methylenedioxyethylamphetamine; THCA, 11-nor-9-carboxy-Δ9-tetrahydrocannabinol; and EDDP, 2-ethylidene-1,5-dimethyl-2,2-diphenylpyrrolidine.

Table 3: Prevalence and percent positivity for 165,209 patient specimens with positive licit and illicit drug test results.

Drug Classes and Groups	Total # Positive	Total % Positive‡	Cannabinoids # Positive	Cannabinoids % Positive†	Cocaine # Positive	Cocaine % Positive†	Heroin # Positive	Heroin % Positive†	Ecstasy # Positive	Ecstasy % Positive†
Amphetamines										
Methamphetamine	7324	4.4	2742	37.4	1134	15.5	84	1.1	45	0.6
Methylphenidate	5385	3.3	1621	30.1	791	14.7	11	0.2	7	0.1
Benzodiazepines										
Clonazepam	14814	9.0	5535	37.4	2320	15.7	74	0.5	21	0.1
Diazepam	12183	7.4	3828	31.4	2051	16.8	132	1.1	29	0.2
Alprazolam	920	0.6	251	27.3	171	18.6	88	9.6	1	0.1
Nitrazepam	885	0.5	312	35.3	156	17.6	1	0.1	1	0.1
Flurazepam	2	<0.01	0	0	0	0	0	0	0	0
Opioids										
Methadone	84838	51.4	33079	39.0	12570	14.8	696	0.8	114	0.1
Opiates	35583	21.5	10669	30.0	5515	15.5	1003	2.8	48	0.1
Oxycodone	32076	19.4	8045	25.1	3678	11.5	159	0.5	32	0.1
Buprenorphine	14730	8.9	4557	30.9	1947	13.2	57	0.4	24	0.2
Fentanyl	10607	6.4	3902	36.8	2042	19.3	144	1.4	19	0.2
Meperidine	181	0.1	40	22.1	18	9.9	1	0.6	1	0.6

‡ Total percent positive for each Group was calculated as 100 x # positive specimens/total # tested.

† Percent positive for each drug Group and cannabinoids, cocaine, heroin and ecstasy was calculated as 100 x # positive specimens/total # positive.